Advances in Psychiatry

Afzal Javed
Kostas N. Fountoulakis
Editors

WORLD PSYCHIATRIC ASSOCIATION

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Using *AniCare* Child

AniCare Child offers an approach for assessing and treating childhood cruelty to nonhuman animals (hereafter animals) and is designed for two audiences. The primary audience consists of mental health professionals working with children in agencies, domestic violence organizations, hospitals, schools, and private practice. Secondarily, *AniCare Child* will be useful to other professionals who work with children and their families—day-care providers, social service workers, probation department and other law enforcement officials, teachers, clergy, animal control and humane society personnel, and veterinarians.

For ease of use and to suit the different needs of potential users, *AniCare Child* is divided into three sections: Theory, Assessment, and Treatment. Some users, such as day-care providers or teachers, might find the assessment section most useful but will refer children to a mental health professional for treatment. All three sections of *AniCare Child* will be useful to mental health professionals. *AniCare Child* can be used in a number of ways. It can be the major focus of treatment with children who are referred—either by the courts, schools, or their parents—specifically for animal abuse. In other cases, the clinician may determine that a child, referred to treatment for some other reason, mistreats animals. In these instances, *AniCare Child* may supplement the ongoing treatment. In all cases, *AniCare Child* should be used within the framework of a comprehensive assessment and treatment plan.

Although we developed *AniCare Child* for use in an individual counseling setting, most of the assessment and interventions are readily adaptable for working with groups. With the further recognition of the need for the treatment of juveniles who abuse animals, in future it could become more practical to provide intervention in a group setting. Particularly when dealing, as in this clinical population, with socially unacceptable behavior, the dynamics of a group of peers can be an important vehicle for change.

This third edition of *AniCare Child* (2013) reflects the collective experience garnered from the presentation of 65 AniCare Child and AniCare Adult workshops in 23 states. Since 2008, we have also offered an online course on the AniCare approach through the School of Social Work at Arizona State University. (The course is one of a series of two leading to a certificate in the treatment of animal abuse.) In addition to the direct contributions of the individuals listed in the Acknowledgments, we have gained from the suggestions of the 18 certified AniCare trainers who colead workshops.

As a result of these experiences and input from these individuals, the third edition contains much new material. Note the following major changes:

- Theory section with emphasis on attachment theory
- Integration of the "Working with Parents" section into the Treatment section
- Material on trauma-informed narrative
- Updated research findings on witnessing abuse

In addition, the following supplemental materials and services are available from the Animals and Society Institute (ASI):

- The AniCare Demonstration DVD illustrates some of the assessment instruments and interventions in the handbook through role-played interviews. References to relevant segments are provided throughout the text.
- The AniCare Workshop DVD is a tape of major segments of a recent workshop (September 2011), emphasizing the conceptual material.
- *The AniCare Child Companion Workbook* provides homework and exercises for clients.
- *The AniCare Model for Treatment of Animal Abuse*, a handbook and accompanying demonstration DVD for adults who abuse animals, may be useful, particularly when assessing and treating juveniles 16 years and older.
- AniCareAction is a listserv that allows therapists and other interested parties to share their experiences with the AniCare Approach: http://groups.yahoo.com/group/anicareaction

To obtain these helpful supplemental materials, information about consultation on cases involving AniCare, training to become a trainer in the AniCare approach, and an opportunity to participate in an evaluation study, contact us at:

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Foreword by Helen Herrman

The publication of *Advances in Psychiatry* volume 4 is most welcome for the WPA. Dr. Afzal Javed has worked with dedicated colleagues to prepare the volume with skill and care.

The volume's 39 chapters cover a wide spectrum of topics related to psychiatry. The authors are colleagues from many countries, including leaders in the scientific sections pivotal to the functions of the WPA. The chapters provide comment on a range of practical and scientific topics that are of current interest and debate and illustrate the strength of WPA's scientific contribution.

The book will interest psychiatrists, mental health professionals from other disciplines, family doctors, and students of medicine and related disciplines. Many of the chapters will appeal to wider groups in communities around the world. On behalf of the WPA I thank all those who have contributed to producing this important publication.

Geneva, Switzerland — Helen Herrman

Foreword by Ahmed Okasha

The Sections of the World Psychiatric Association (currently 73) are the "scientific backbone" of our Association. It is so is documented by the richness, quality, and diversity of activities of the Sections, from research, genetics and psychopharmacology, psychology, psychotherapy, ecology and humanities, scientific meetings and congresses to educational programs, consensus statements, and publications. It is further documented by the production of this fourth volume of state-of-the-art papers by Section Leaders which follows the first volume produced in 2002.

Each of the papers included in this volume is an update on the progress achieved in the area covered by each participating section during the last triennium. It is difficult to find such condensed information elsewhere, especially if one considers that these articles have been prepared by worldwide authorities in their field.

It is my conviction that the volume will be invaluable as a reference book not only to the Sections and the WPA components but also to the psychiatric community at large.

I want to congratulate the editors of this volume and "Advances" have developed into a tradition in the WPA. I would also like to thank our Sections for their contributions, which represent the state of the art of psychiatric development.

I am confident that the volume will contribute immensely to much needed dissemination of scientific information in our field and that it will be received enthusiastically.

Geneva, Switzerland — Ahmed Okasha

Foreword by George N. Christodoulou

When, back in 2000, I suggested to my WPA executive committee colleagues the creation of the series *Advances in Psychiatry*, there were many who doubted whether this plan would be successful and lasting. They were wrong. The series proved both successful and lasting. It could not have been otherwise as the WPA sections have always had expertise, thrust, and diversity. They are often referred to as the "scientific backbone" of the WPA and by their contributions they proved that this was (and still is) the case.

"Advances" *volume 1*, edited by George Christodoulou appeared in 2002 and comprised of 232 pages, prepared by 32 sections (Beta Publishers in Athens)

"Advances" *volume 2*, was published in France, was edited again by George Christodoulou, appeared in 2005, comprised of 282 pages, and 32 sections participated

"Advances" *volume 3*, was edited by George Christodoulou, Miguel Jorge, and Juan Mezzich, comprised of 289 pages, included the contributions of 29 sections, and was published in Athens by Beta Publishers in 2009.

All three volumes were received with enthusiasm not only by the WPA family but also by the psychiatric community as a whole.

I am glad that Afzal Javed took my advice to continue the tradition of "Advances" and as a result of his efforts and those of the co-editor Kostas Fountoulakis but especially the thrust and efforts of the sections we are presented with this small treasure, the fourth volume of *Advances in Psychiatry*, an update of the most important latest developments in psychiatry.

As expected, on account of its nature, the volume contains a great diversity of topics. In its 39 chapters, one can find topics ranging from general ones like "Public Health" and "Schizophrenia: Trends in Diagnosis and Treatment" to more specific ones like "How the Brain Creates Art and Dreams" and "Biobanking for 'Omics' in Psychiatry."

I want to very warmly congratulate all contributors to this important volume and to express the hope that the tradition of *Advances in Psychiatry* will continue in the years to come.

Athens, Greece — George N. Christodoulou

Foreword by Miguel R. Jorge

The new volume of *Advances in Psychiatry*, the book that reflects the current work being done by the World Psychiatric Association (WPA) Scientific Sections, is now available to all psychiatrists, other mental health professionals, and the medical community worldwide.

The strength and quality of hundreds of people, internationally representing the rich membership of the WPA Scientific Sections, are well known and those authoring the different chapters of this book constitute a wonderful sample of them.

As the Scientific Sections themselves, there is a wide range of themes approached throughout the book, some of them being updates in specific areas and others as an in-depth view of important matters concerning issues of interest to patients, their families, and the society as a whole.

We, psychiatrists from all over the world, expect that the clinical and research activities done by the WPA Scientific Sessions' members continue to be disseminated by books like *Advances in Psychiatry* as well as by any other printed or digital media, in order to reach everyone in need of mental health care of quality.

São Paulo, Brazil — Miguel R. Jorge

Preface

We are pleased to present the fourth volume of *Advances in Psychiatry* that includes update papers by the chairs or the representatives of scientific sections of the World Psychiatric Association.

WPA Sections cover practically all aspects of psychiatry and mental health, and the richness, diversity, and independent function of the Sections have promoted and strengthened many themes that are of significant importance to theory, research, and clinical perspectives in the entire field of psychiatry.

This volume of *Advances in Psychiatry* is composed of update papers by the chairs or the representatives of a number of scientific sections of the World Psychiatric Association. The network of Sections of the World Psychiatric Association is perhaps the most extensive network not only in psychiatry but also in medicine as a whole. The expansion of the Sections and their more extensive work in the last triennium has underlined the need for their better coordination, including their clustering in groups. Similarly, the benefits of collaboration between them have become more evident and advocate for a continuation of intersectional collaboration especially for educational and research perspectives.

We are proud of the accomplishments of our Sections. Their spirit of collaboration has played a pivotal role in their achievements. Their role in dissemination of scientific knowledge is well acknowledged and is apparent in the publication of the current volume of this publication. The update papers will certainly occupy a special position in the psychiatric literature and would prove a real service to psychiatrists and especially to younger colleagues and will meet with the appreciation from the WPA components.

We wish to thank all the contributors to this volume. Springer has been very supportive of this scientific work and we hope for our continued relationship with them for our future scientific work.

We do hope that that "Advances" will continue being published as a contribution to the advancement of psychiatric knowledge and as an offer to the international psychiatric community.

Nuneaton, UK — Afzal Javed
Thessaloniki, Greece — Kostas N. Fountoulakis

Acknowledgments

Thanks to major funding from the Kenneth A. Scott Charitable Trust and additional grants from the Claire Giannini Fund, the Max Factor Family Fund, and the Frederick H. Leonhardt Foundation, we are pleased to present the third edition of *AniCare Child*.

We also would like to thank the following therapists and researchers who have contributed generously to sections of the revision: Aubrey Fine, Maya Gupta, Antonia Henderson, Risa Mandell, Kate Nicoll, Nancy Parrish, and Sharon Scott. Special thanks to Jill Howard Church for copyediting, Kate Brindle for formatting, and Jojo Shapiro for artwork.

Contents

Using School-Based Interventions for Depression Education and Prevention

1

Danielle S. Taubman, Sagar V. Parikh, Helen Christensen, and Jan Scott

Abstract

Depression is the most burdensome noncommunicable condition among young persons aged 10–24 years, with rates of depression rising steeply during the post-pubertal period corresponding to the intermediate and secondary school years. Although a high number of children and adolescents experience depressive symptoms or clinical depression, many will not or cannot access health services, and the number of potential cases cannot be dealt with entirely by the health-care system. As such, a public health perspective, which encourages the application of mental health promotion and primary and early secondary prevention, has gained increasing acceptance, as represented by the expansion of school-based depression and mental health interventions. The objective of this chapter is threefold. First, it provides an overview of the accomplishments in school-based depression intervention and mental health promotion and prevention research by presenting both universal and selective prevention approaches, which are delivered prior to the onset of symptoms or a diagnosis. Second, the chapter showcases two successful school-based intervention programs and presents guidance on how to implement each of these models. Third, the chapter discusses limitations in the field, highlights recommendations for implementation, and offers a roadmap for potential future avenues for research, including lessons for adaptation of programs to allow translation to other settings and nations.

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1.1 Introduction

Depression is the most burdensome noncommunicable condition among young people aged 10–24 years [1], with rates of depression rising steeply during the intermediate and secondary school years [2, 3]. Depression adversely affects developmental trajectories in adolescents and is strongly associated with functional impairment [4], comorbid mental disorders, recurrent depression in adulthood, and risk for suicide [5]. Adolescent depression is also linked with substance use [6–8], negative self-perception, social problems, and impaired academic performance [9]. While current depression research primarily focuses on treatments for acute symptom relief and relapse prevention, primary and early secondary prevention efforts may be more cost-effective [10, 11] and have been shown to minimize the individual and public health burden of depression by preventing between 22% and 50% of cases of depression (as cited in [12]). Successful early secondary prevention can help in the prompt identification and treatment of depression in youth and can lead to a number of positive health and behavioral outcomes, including increased social engagement and educational attainment and decreased suicidal and self-injurious behavior [5]. Indeed, recognizing depressive illnesses as early as possible is a crucial step in managing depression more effectively and preventing negative outcomes and tragedies in our schools and communities.

1.2 A Global Perspective

To appreciate a global perspective on the burden of depression among adolescents and young adults, research efforts should include youth from low- and middle-income countries (LMIC) in addition to their high-income counterparts. The youth from LMICs face the largest share of worldwide adversity and risk exposure and, among other pressing health problems, experience high rates of depression [1]. In addition, adolescents and young adults have the lowest rate of health-care coverage worldwide [13]. This difficulty in obtaining treatment via traditional health-care services for the youth has led to consideration of a number of novel approaches, including school-based health promotion and prevention programs. However, given that many low-resource settings cannot afford to implement such programs, limited research in LMICs in effective depression prevention and treatment strategies for young people are available to date [14]. As such, we are primarily reliant on studies undertaken in high-income countries. A recent review by Fazel and colleagues [15] offers some evidence for the translation of programs from high-income to LMIC and comments on mental health interventions designed specifically in LMIC schools; it also discusses service development priorities in this region of the world.

1.3 Barriers to Early Detection and Intervention

The most notable barriers to the early identification and treatment of depressive and related disorders among individual adolescents include stigma (a circumstance or quality that elicits negative attitudes and beliefs), problems recognizing symptoms as being related to an underlying psychological problem (poor mental health literacy), a preference for self-reliance, and failure to perceive a need for help [16, 17]. Mental illness stigma has emerged as a significant barrier to help-seeking and treatment [16, 18]. Depression stigma includes both self-stigma, which occurs when one internalizes the public's stigmatizing attitudes about depression, and perceived stigma, which is the belief that the public holds stigmatizing thoughts or stereotypes about depression [19]. These negative self-views compound the already distressing symptoms that are characteristic of most mental disorders [17]. Another potential barrier is engaging the youth in intervention programs, particularly when there are sensitivities around mental health issues. These barriers, along with issues of accessibility, including treatment cost, location, and time, make it extremely challenging to effectively reach young people who are in need of help [20, 21].

1.4 Official Recommendations

Although mental disorders have largely been overlooked within the global health agenda [22], several well-known organizations have recently highlighted the importance of promotion of mental health and prevention of mental disorders. One of the primary goals of the Grand Challenges in Global Mental Health Initiative, funded in part by the National Institute of Mental Health, includes advancing prevention and the implementation of early interventions to improve the lives of people living with mental illnesses, including depressions [23]. The World Health Organization's Comprehensive Mental Health Action Plan (CMHAP) recommends that children and adolescents with mental disorders be provided with early evidence-based interventions based in the community [24]. The National Strategy for Suicide Prevention also calls for public health approaches that increase knowledge and awareness in support of early identification of risk [25]. Moreover, a report published by the Institute of Medicine (IOM) of the United States [26] recommends implementing preventative interventions among young people in order to avoid substantial costs to individuals and society. Finally, the most recent Lancet Commission on adolescent health and well-being notes that there is a clear need for innovation and more sustained effects of mental health interventions [27].

1.5 Core Concepts and Definitional Issues

Recent decades have witnessed a shift toward early intervention paradigms for improving mental health and reducing mental disorders in young people. Depression prevention may occur on three distinct levels (primary, secondary, tertiary) that aim to reduce risk factors for depression (or recurring depression), as well as enhance the protective factors that promote mental health. *Primary prevention* of depression aims to prevent depression by intervening prior to its onset. Three distinct IOM prevention models (universal, selective, and indicated) to reduce rates of depression and other mental illnesses have been proposed in the literature [28] and are classified as primary prevention. Universal interventions are delivered to all children and adolescents irrespective of symptoms or risk. Selective interventions target groups of children and adolescents with specific risk factors that increase their likelihood of developing a depressive disorder, such as having a depressed parent. Finally, indicated interventions target children and adolescents with early signs or symptoms of depression. *Secondary prevention* of depression aims to prevent depression from progressing to symptomatic disease through early detection and treatment, while *tertiary prevention* aims to reduce disability and prevent depression relapses and recurrences [29].

Whereas depression prevention is focused on avoiding disease, depression promotion is focused on maximizing health, mood states, and well-being. Though promotion and early prevention have different goals, both interventions aim to alter developmental processes and trajectories [26]. Moreover, effective promotion of health and well-being in childhood may enhance prospects for prevention. For example, promotion interventions may increase resilience to adversity in children, which can then act as a protective factor, reducing the likelihood of onset of mental disorders in the future [30]. The most common health promotion interventions in this field are based on mentoring and youth development models or some combination of these approaches. Most interventions target adolescents, with few reports about approaches to or benefits for younger school-age children (5–11 years) [31]. Mental health promotion particularly aims to establish competencies, increase the completion of developmentally appropriate tasks, enhance the chances of positive development, and strengthen an individual's adaptability and tolerance of adversity [26, 32, 33]. As such, the goals can be seen to overlap with those for primary prevention of mental disorders. The specific examples we provide in this chapter, namely, The University of Michigan Peer-to-Peer Depression Awareness Campaign (P2P) and SPARX-R, are principally prevention strategies rather than health promotion strategies.

1.6 Key Strategies: Reaching Adolescents and Young Adults

The need to reduce depression at a population level in adolescents and young adults has led to greater interest in prevention programs. A majority of this research has been in high-income countries (HICs); the research we discuss below primarily

focuses on children and adolescents from these nations. To date, depression research does not definitively favor one type of intervention over another [34–36], but some sources suggest that universal depression prevention interventions have mixed results and demonstrate lower levels of statistical significance than targeted programs [37–40]. A possible explanation for this is that there is greater potential for change among youth who have subclinical symptoms or are at increased risk for the disorder, since initial symptom levels are likely to be higher [40, 41]. Indeed, youth with depressive symptoms may benefit most from universal depression programs [42]. Advocates of universal and selective interventions argue that such programs provide both the potential for immediate symptom reduction and the tools to sustain psychological well-being in the general population by building young people's resilience and capacity to deal with depression or other problems in the future. As universal interventions are delivered in community settings such as everyday school environments, they are less stigmatizing of already vulnerable students and may be more cost-effective by reaching many youth at once [43]. Whereas universal interventions capture everyone who might develop depression in the future, targeted interventions may fail to capture individuals who are symptomatic but do not meet the criteria to be considered at risk or clinically depressed. Universal mental health programs may also encourage schools to address the emotional problems of previously unidentified and untreated youth [21]. In order to highlight the benefits of primary prevention interventions, this chapter covers both universal and selective prevention approaches, which are delivered prior to the onset of symptoms or a diagnosis.

The early age of onset of depression and the high number of children and adolescents who suffer from depressive symptoms or clinical depression have prompted the expansion of school-based depression and mental health interventions. Schools play a key role in students' social, academic, cognitive, emotional, and behavioral development and, in turn, mental health [27]. As a place of learning, schools enable youth to acquire and practice skills in a real-world context. Given that youth spend more time in school than any other formal institutional structure [21], the school setting is a relatively unthreatening environment in which a majority of youth can be reached.

1.7 Overview of School-Based Interventions for Depression Education and Prevention

In the past decade, researchers have conducted a number of randomized controlled trials to evaluate prevention-focused interventions in schools. These studies, in addition to several recent meta-analytic reviews, have demonstrated the promise of delivering depression prevention programs in the school system [15, 37–39, 44–47]. Table 1.1 presents an overview of 35 school-based therapeutic depression prevention programs [41, 43, 48–80]. Table 1.2 presents an overview of four school-based depression education programs [42, 81–83]. The inclusion criteria were: (a) study participants were children or adolescents; (b)

Table 1.1 School-based therapeutic depression prevention programs

Study	Country	Program	Preventive approach	Program content	Number of sessions	Sample	Intervention providers	Depression outcome measure
Arnarson and Craighead 2011	Iceland	NR	Selective and indicated	CBT	14	14–15 years (n = 171)	School psychologists	CDI
Barrett et al. 2006	Australia	FRIENDS	Universal	CBT	10	6th and 9th grade (n = 669)	Teachers	CDI
Calear et al. 2009	Australia	MoodGYM: YouthMood project	Universal	iCBT	5	12–17 years (n = 1477)	Computer (teacher assisted)	CES-D
Cardemil et al. 2007	The United States	PRP	Universal (selective stratification)	CBT	12	Middle school children (n = 168)	Graduate students, undergraduate student assistants	CDI
Chaplin et al. 2006	The United States	PRP	Universal	CBT	12	11–14 years (n = 208)	School personnel	CDI
Cutuli et al. 2006	The United States	PRP	Selective	CBT	12	NR (n = 294)	NR	CDI
Garber et al. 2009	The United States	CB prevention program	Selective	CBT	8	13–17 years (n = 316)	MHP	CES-D
Gillham et al. 2007	The United States	PRP	Universal	CBT	12	11–14 years (n = 697)	School personnel, graduate students	CDI + CDRS-R
Gillham et al. 2012	The United States	PRP-A	Selective	CBT + IPT	10	10–15 years (n = 408)	School personnel	CDI
Horowitz et al. 2007	The United States	CWSC; IPT-AST	Universal	CBT + IPT	8	14–15 years (n = 380)	MHP, psychology students	CDI

Johnstone et al. 2014	Australia	AOP-PTS	Universal	CBT	10	9–10 years (n = 370)	Teachers	CDI
Kindt et al. 2014	The Netherlands	OVK	Selective	CBT	16	11–16 years (n = 1343)	Teachers	CDI
Lowry-Webster et al. 2003	Australia	FRIENDS	Universal	CBT	10	10–13 years (n = 594)	Graduate students	CDI
Manz 2001	Germany	GO!	Universal (indicated and selective stratification)	CBT	8	15–17 years (n = 929)	Supervised trainers	BDI
Merry et al. 2004	New Zealand	RAP-Kiwi	Universal	CBT + IPT	11	13–15 years (n = 392)	Teachers	BDI-II + RADS
Pattison and Lynd-Stevenson 2001	Australia	PRP	Universal	CBT	11	9–12 years (n = 63)	MHP	CDI
Perry et al. 2015	Australia	SPARX-R	Universal	iCBT	7	16–18 years N = 1600 (target)	Computer (teacher assisted)	MDI
Pössel et al. 2004	Germany	LISA-T	Universal	CBT	10	13–14 years (n = 347)	MHP, graduate students	CES-D
Pössel et al. 2011	Germany	LARS and LISA	Universal	CBT	10	13–14 years (n = 301)	MHP, graduate students	SBB-DES
Pössel et al. 2013	The United States	LARS and LISA	Universal	CBT	10	14–16 years (n = 518)	MHP, graduate students	CDI

(continued)

Table 1.1 (continued)

Study	Country	Program	Preventive approach	Program content	Number of sessions	Sample	Intervention providers	Depression outcome measure
Quayle et al. 2001	Australia	PRP	Universal	CBT	8	11–12 years (n = 42)	MHP	CDI
Raes et al. 2014	Belgium	Mindfulness program	Universal	MBCT	8	13–20 years (n = 408)	MHP	DASS
Rivet-Duval et al. 2011	Mauritius	RAP	Universal	CBT + IPT	11	12–16 years (n = 160)	Teachers	RADS-2
Roberts et al. 2003	Australia	PRP	Universal	CBT	12	11–13 years (n = 189)	MHP	CDI
Roberts et al. 2010	Australia	AOP	Universal	CBT	20	11–13 years (n = 496)	Teachers	CDI
Rooney et al. 2006	Australia	PTP	Universal (indicated stratification)	CBT	8	8–9 years (n = 136)	MHP	CDI
Rose et al. 2014	Australia	RAP + PIR	Universal	CBT + IPT	20	9–14 years (n = 210)	Graduate students	RADS-2
Sawyer 2010	Australia	Beyond blue	Universal	CBT	10	8th grade (n = 5633)	NR	CES-D
Sheffield et al. 2006	Australia	PSFL	Universal, indicated, combined	CBT	8	14–15 years (n = 1045)	Teachers	CDI + CES-D
Shochet et al. 2001	Australia	RAP-A + RAP-F	Universal	CBT	10	9th grade (n = 260)	MHP, graduate students	CDI + RADS + BHS
Stallard et al. 2012	The United Kingdom	RAP	Universal (indicated stratification)	CBT + AC	9 + 2 booster	12–16 years (n = 1064)	Trained professionals	SMFQ
Spence et al. 2005	Australia	PSFL	Universal	CBT	8	12–14 years (n = 1500)	Teachers	BDI

Tak et al. 2015	The Netherlands	OVK	Universal	CBT	12	8th grade (n = 1341)	MHP	CDI
Wahl et al. 2014	Germany	LARS and LISA	Universal	CBT	10	13–14 years (n = 648)	MHP, teachers	CES-D
Wong et al. 2014	Australia	TWU	Universal	CBT	10	15–16 years (n = 976)	Computer (teacher assisted)	PHQ-9

Table 1.2 School-based depression education programs

Study	Country	Program	Preventive approach	Program content	Number of sessions	Sample	Intervention providers	Depression outcome measure
Schilling et al. 2016	The United States	SOS	Universal	EDU	Semester of classes	9th grade (n = 1052)	School personnel	Knowledge and attitudes about depression
Swartz et al. 2010	The United States	ADAP	Universal	EDU	3	14–15 years (n = 3538)	Mental health professionals	ADKQ
Tomyn et al. 2016	Australia	THW	Universal	EDU	6	13–17 years (n = 252)	Mental health professionals	SMFQ
Parikh et al. in press	The United States	Michigan P2P	Universal	EDU	Year-long	14–17	Peers	P2P depression awareness questionnaire

Note: *ADAP* Adolescent Depression Awareness Program, *ADKQ* Adolescent Depression Knowledge Questionnaire, *AOP* Aussie Optimism Program, *AOP-PTS* Aussie Optimism Program: Positive Thinking Skills, *BDI* Beck's Depression Inventory, *BHS* Beck Hopelessness Scale, *CES-D* Center for Epidemiologic Depression Scale, *CDI* Children's Depression Inventory, *CBT* Cognitive Behavioral Therapy, *CWSC* Coping With Stress Course, *DASS* Depression Anxiety Stress Scale, *EDU* Education, *iCBT* Internet Cognitive Behavioral Therapy, *IPT* Interpersonal Therapy, *IPT-AST* Interpersonal Psychotherapy-Adolescent Skills Training, *MHP* Mental Health Professional, *NR* Value not Reported, *OVK* Op Volle Kracht, *PHQ-9* Patient Health Questionnaire-9, *PIR* Peer Interpersonal Relatedness Program, *PRP* Penn Resiliency Program, *PTP* Positive Thinking Program, *PSFL* Problem Solving for Life, *RAP* Resourceful Adolescent Program, *RAP-A* Resourceful Adolescent Program-Adolescent, *RAP-F* Resourceful Adolescent Program-Family, *RAP-Kiwi* Resourceful Adolescent Program-New Zealand version, *RADS* Reynolds Adolescent Depression Scale, *RADS-2* Reynolds Adolescent Depression Scale – 2nd. Ed., *SBB-DES* Measure of Child and Adolescent Major Depression and Dysthymia Symptoms, *SMFQ* Short Mood and Feelings Questionnaire, *SOS* Signs of Suicide Program, *THW* Think Health and Wellbeing, *TWU* The Thiswayup Schools Depression Intervention

a primary prevention approach was employed (i.e., universal or selective); (c) the primary aim was depression prevention or mental health promotion; (d) the intervention was school-based (delivered as part of the school curriculum or as an after school activity); (e) the study was published in a peer-reviewed, English language journal in the past 15 years; and (f) when two or more studies by the same author(s) have overlapping data and results, the older of two studies was excluded.

Broadly speaking, two types of school-based interventions have been explored: [1] formal therapeutic depression prevention programs and [2] broader mental health education and anti-stigma campaigns. However, as evidenced from our overview of existing school-based depression prevention programs, most can be categorized as therapeutic prevention programs. Each approach has its merits and limitations. Depression prevention programs feature a highly structured approach requiring strict adherence to detailed manuals and procedures to ensure standardization, which is admirable, but also creates an approach that can be inflexible and difficult to adapt to the needs of each school. Additionally, this often relies on external health professionals rather than empowering school staff to sustain the program or to manage self-referrals.

Broader mental health and anti-stigma campaigns offer another approach: delivering a purely educational intervention to address depression literacy in high schools, which is not designed to change mood or emotions. One example is the Adolescent Depression Awareness Program (ADAP) from Johns Hopkins, an empirically supported school-based curriculum designed to teach depression literacy to high school students to improve knowledge and lessen attitudinal barriers surrounding depression [84]. ADAP features a three-hour curriculum taught by health professionals during health class and has been demonstrated to improve knowledge in two studies [82] and to improve self-identification of depression in one of these studies [85]. These findings have not been replicated, nor have impacts on depression stigma been reported. Such health education campaigns may benefit from several principal characteristics of effective prevention programming, including (a) providing contact with adults and peers in a way that promotes strong relationships and supports positive outcomes; (b) tailoring the program to the community and cultural norms of the participants; and (c) including the target group in program planning and implementation [86].

This chapter will specifically showcase two unique models of successful school-based intervention programs and present guidance on how to implement each of these types of programs, as well as lessons for adaptation of different programs to other settings and nations.

1. The University of Michigan Peer-to-Peer Depression Awareness Campaign (P2P): The P2P project is a well-established universal peer-to-peer program with eight years of outcome data from high school students. The P2P program uses a novel peer-to-peer approach of program delivery. The target outcome is a melange of mental health literacy, depression symptom reduction, suicide reduction, and stigma reduction.

2. SPARX-R: SPARX-R is a universal intervention that uses a novel online, CBT-based, gamified technology designed to prevent the development of depression in high school students. Derived from its parent treatment program, SPARX [87], it has been tested to see whether it can prevent depression in young people approaching their final year exams. The primary target outcome for this trial was a reduction of depression symptoms prior to the final school exams.

Given the theoretical value, and the solid evaluation results from these two approaches (shown later), they may serve as useful models for other settings. To facilitate uptake, this chapter will add comments as "Implementation Tips for Other Settings" or "Lessons Learned" after key sections.

1.8 The P2P Project: A Prototype for Schools Worldwide?

One common philosophy is "think global, act local." We begin by describing a local project that we believe has global applicability. In response to the growing awareness of the importance of adolescent depression and the hands-on role children and adolescents can play in educating their peers, the University of Michigan Depression Center (UMDC) and the Ann Arbor Public Schools (AAPS) developed and implemented the Peer-to-Peer Depression Awareness Campaign (P2P) in Washtenaw County schools. The P2P project aims to empower high school students as both learners and educators. The goals of the project are to (1) educate high school students about clinical depressions, stress, sleep disturbances, known precipitants, and (2) support them in finding creative ways to convey this knowledge to their peers to reduce stigma, raise awareness, encourage help-seeking when needed, and help to promote earlier detection of depressions, bipolar disorders, and related illnesses. Unlike the large majority of extant school-based prevention programs in the available literature, the P2P program employs a peer-to-peer framework that is largely "bottom-up" rather than "top-down." As explained below, there are a number of significant benefits to this type of model.

1.8.1 P2P Development

Over a period of 5 years, the number of young adults in Washtenaw County, a small region near Detroit, Michigan, with a population of approximately 350,000, reporting ten or more poor mental health days in the past month more than doubled [88]. Moreover, schools in the AAPS district began requesting educational presentations about depression, stress, and other mental health concerns from the UMDC for their students. In response, the UMDC and AAPS began a collaboration to provide depression awareness and suicide prevention education, training, and support to AAPS personnel.

The AAPS Initiative was designed to (1) address the need for early recognition of depression, bipolar disorder, and risk for suicide among youth; (2) educate

teachers, counselors, and other "frontline" personnel working with young people to raise their awareness and knowledge of depressive and bipolar illnesses and suicide risk factors; (3) and provide professional development to school personnel using a "train-the-trainer" model, so that staff members in each school would be qualified to train their colleagues in suicide awareness and prevention techniques. A planning committee comprised of several AAPS teaching staff and administrators and two UMDC staff members guided this initiative. The planning committee was created to inform the project and ensure that the school system was a full partner in developing a training and education model that would best serve the needs of the district. In addition, the goals of the partnership were aligned with the Washtenaw County Health Improvement Plan, which identified depression as one of the four primary focus areas for the 2020 objectives [88].

A peer-based student education component called the P2P project became the centerpiece of the UMDC and AAPS Initiative in 2009. The project was initially conceptualized and designed as a community education and outreach initiative in high schools without emphasis on a rigorous scientific research or evaluation methodology. However, encouraging preliminary results and anecdotal evidence indicated that the P2P program warranted formal evaluation. In 2010, the project coordinators added a new research and evaluation component to obtain data about the effects of the program on knowledge of depressive illnesses, stigma associated with depressive illnesses, and awareness of help-seeking behaviors linked with depressive illnesses among high school students. Recent evaluation results are discussed later in this chapter and suggest the high acceptability and effectiveness of this program.

Since the P2P project's inception, the UMDC has provided education and resources to support participating high school students in developing innovative ideas to effectively reach their peers with depression awareness and stigma reduction messages. While some have suggested caution around peer-to-peer programs [89], this concern was primarily driven by cases in which adolescents indiscriminately share their stories about personal experiences of mental illness and recovery with peers, which is distinct from the P2P program approach.

A number of peer-delivered interventions involve individuals with a mental illness providing a support intervention to their peers [89–91]. In this case, P2P students are *not* screened for depression and are *instead* selected for their leadership skills. The P2P students do not provide any kind of "peer counseling"—rather, they are "peer advocates" who help to create a supportive environment in their schools and connect their peers with appropriate resources, information, and appropriate venues for clinical interventions.

1.8.1.1 Implementation Tips for Other Settings

1. Establishing a partnership between a medical center/university and a school district is extremely valuable and necessary to ensure proper buy-in by the schools. Furthermore, such a partnership ensures appropriate educational content is delivered along with accurate information about appropriate use of health-care facilities for any particularly ill students.

2. While teachers and school personnel must be trained in depression prevention and support the school intervention program, they are not the main deliverers of the intervention; the students are. The local culture must be able to identify and respect the capacity of students to be the "intervention" and must be able politically to grant students the authority to act.
3. Since the students are the main instigators of the intervention, they will need ongoing training and support as they implement the peer-to-peer intervention. The school authorities—and to a small extent, the medical center/university authorities—must have the time and resources to provide ongoing supervision for the overall program.

1.8.2 How Did We Choose Participants?

The P2P program has been carried out in Washtenaw County since 2009. More schools in Washtenaw County were recruited in 2011–2012 under a pilot expansion. Interest in the program continues to grow, with the number of participating schools increasing from five Ann Arbor high schools in 2009 to ten high schools throughout Washtenaw County during the 2015–2016 academic year. Since the program began in 2009, over 550 students have participated directly on P2P teams in 11 different schools across Washtenaw County, over 150 P2P student-run events have taken place, and thousands of students have been reached through the awareness campaigns.

Two samples of students were selected from each high school.

1. Students who participated in the P2P projects (referred to as "P2P team members").
2. Students who did not participate in the P2P projects (referred to as "non-P2P students").

Recruitment of P2P students involved teachers and counselors selecting student "champions" from all grade levels for participation. In addition, any student who expressed an interest in becoming involved was considered for participation. Schools with many students expressing an interest have developed official applications for participation. Recruitment of the non-P2P student sample was conducted by collaborators at each high school. Due to the community-based participatory nature of the proposed project, the sample sizes were determined by interest and engagement of students at each school. The institutional review board (IRB) waived the need for informed consent from participants; the study received exemption under the category of normal educational practices.

1.8.2.1 Implementation Tips for Other Settings

1. An identified group of student champions to be the heart of the peer-to-peer intervention is needed. These students will need political support to be allowed to implement these activities.
2. Collaborators at each school should help researchers recruit a student comparison sample.

1.8.3 What Program Did We Institute in the Schools?

The intervention, based in part on the ADAP framework [84], features (a) an educational component to train P2P team members on broad mental health issues and teach them to develop and implement a variety of strategies to spread important depression awareness and mental health information in their schools and (b) a peer-to-peer component in which these individuals provided peer-to-peer advocacy. P2P team members first attended a six-hour, one-day Kickoff Conference at the UMDC that covered the latest evidence-based information as well as social marketing strategies, active listening skills, and other peer support resources. Students were encouraged to brainstorm ideas for developing tailored public awareness campaigns at their schools. Finally, attendees were provided a menu of options for potential campaign formats, including recommendations to incorporate each of three domains (support, anti-stigma, education), as well as four specified overarching messages capturing key themes, namely, (a) depression is real; (b) professional help is available and effective; (c) depression can take many forms (i.e., has multiple symptoms); and (d) do not keep knowledge about a suicidal peer a secret. After the initial educational training, each P2P student team spent October through December developing a depression awareness campaign tailored to fit their particular school. Schools that had participated in the P2P program previously were encouraged to plan a more focused campaign (according to each school's self-identified needs) that addressed special topics such as depression and sleep, depression and substance abuse, and depression and LGBTQ students. The P2P student proposals were reviewed by the P2P faculty mentors in each school, as well as UMDC staff, and proposals were modified based on the feedback received. Projects were implemented in January of the following year, and P2P teams submitted a final implementation report to the UMDC in May of each school year. In May, P2P teams from each school returned to the UMDC for the Closing Conference during which each P2P student team gave an oral presentation on their campaign. P2P teams also submitted a final implementation report to the UMDC in May.

1.8.3.1 Implementation Tips for Other Settings

1. Training needs to be provided to the student team members to prepare them and develop practical health promotion and depression prevention skills.
2. These students must then create the campaign and be prepared for possible challenges in running the program or any unforeseen modifications that need to be made during implementation.
3. A "train-the-trainer" approach is helpful to use during the initial educational conference in order to prepare students to present information effectively and lead activities that reinforce learning.

1.8.4 What Questionnaires Did We Use for Evaluation?

Under the guidance of the University of Michigan Institute for Social Research (ISR), the existing P2P Depression Awareness Questionnaire was adapted from a

previous version. It includes 14 questions with 44 items. Survey items cover six domains: (a) demographics; (b) helping others with a mental illness (three items); (c) helping yourself (two items); (d) depression knowledge, using a modified Adolescent Depression Knowledge Questionnaire (ADKQ; [80]) comprised of 13 yes/no items; (e) depression help-seeking, involving reporting their formal and informal intentions to seek help from 12 targeted help sources; and (f) school environment and depression stigma, modified from the Revised Attribution Questionnaire (r-AQ; [92]), with 10 items asking about participant response in reference to a new student whom they heard had depression, as well as an item addressing their own comfort in discussing mental health issues with other students. At post-intervention only, there were five additional questions to assess the visibility of each school's P2P campaign (e.g., "During the last school year, did you notice a student group in your school promoting mental health awareness?").

1.8.4.1 Implementation Tips for Other Settings

We chose to conduct a more comprehensive evaluation. For other sites, a brief questionnaire modeled after our questionnaire should be sufficient.

1.8.5 What Were the Outcomes of Our School Intervention?

Prior to the P2P student participant Kickoff Conference in October, all P2P students were asked to complete a baseline questionnaire. The survey consisted of a series of items designed to assess students' knowledge of depression, perceived stigma associated with depression, and awareness of help-seeking behaviors associated with depressive illnesses. Participants were assigned a confidential ID number, and the questionnaire instructions clearly explained the confidential and anonymous nature of the study, as well as the voluntary nature of participation.

Prior to the campaign implementation, convenience samples of non-P2P students from each school were asked to complete the baseline questionnaire at their schools. This questionnaire was identical to the surveys completed by the P2P students prior to the Kickoff Conference. Surveys were provided in hard copy, and the project coordinator entered all data into the project database.

After the Closing Conference in May, all P2P team members were asked to complete the post-intervention questionnaire. This allowed assessment of whether being on a P2P team had any influence on P2P students' depression-related knowledge and attitudes. Similarly, within one week of the Closing Conference, all non-P2P students were asked to complete the post-intervention questionnaire to determine whether the intervention had any influence on non-P2P students' depression-related knowledge and attitudes, stigma reduction, and help-seeking.

1.8.5.1 Implementation Tips for Other Settings

It is important to conduct at least a brief evaluation questionnaire with a pre- and post-intervention comparison in order to understand the areas in which the intervention was effective or ineffective in changing your target outcome(s).

1.8.6 Quantitative Outcomes of Our School Intervention

1.8.6.1 P2P Campaign Components

In the domain of public education, each school created a depression awareness campaign consisting of three to ten components. The average number of activities implemented among eight schools was 5.8 in 2014. The most frequently used activities included school assemblies, displays around school (e.g., bulletin boards, posters, flyers, banners), and giveaways (e.g., pens, wristbands, fortune cookies).

1.8.6.2 Detailed Questionnaire Results

All analyses were conducted with the SPSS software package (SPSS/22.0; [93]) which was used to produce the calculations. Descriptive analyses focus on estimating the overall effects of the P2P program on knowledge, stigma, and awareness of help-seeking behaviors by assessing changes from baseline to post-intervention among P2P team members and non-P2P students. Results are based on baseline and post-intervention pairwise comparisons. Baseline and post-intervention means, standard deviations, and percentages are reported. The alpha level was set at 0.05.

Table 1.3 displays the overall pre- and post-intervention results for P2P team members and non-P2P students. Under the domain of helping others, all three questions demonstrated statistically significant improvements. Under the domain of helping yourself, one item was statistically significant. Under the knowledge domain, statistically significant improvements were made in two of the five subquestions, and students were more likely to correctly identify depression symptoms from a provided list. In the domain of help-seeking, students showed a statistically significant increase in their likelihood of seeking help for a personal or emotional problem. At post-intervention, students were more likely to consider seeking help from seven out of 12 sources. In the domain of school environment and stigma, three out of ten subquestions were statistically significant. At post-intervention, students were also statistically significantly more comfortable discussing mental health issues with their peers.

1.8.6.3 Did Noticing the P2P Work or Attending P2P Events Influence Results?

Results were also separated out according to whether or not respondents noticed the P2P group promoting mental health awareness in their school and whether or not respondents attended any P2P programs. All non-P2P students were potentially exposed to the general publicity campaign, with 60.4% of respondents stating that they noticed the P2P group and activities and 30.1% of respondents proceeding to attend additional specialized programs.

Respondents who had either noticed the P2P student group or who had attended any P2P programs were more likely to feel confident helping others and talking about mental health issues. These students were statistically significantly more likely to have reported lower levels of mental illness stigma in their schools and lower mental illness stigma themselves. Moreover, at post-intervention, students

Table 1.3 P2P Depression awareness questionnaire baseline and post-intervention results[a]

	Baseline		Post-intervention			
	M	SD	M	SD	*t*	df
Helping others						
How confident are you in your ability to identify someone who is showing the common signs of depression?[b]	4.45	1.45	4.93	1.37	−7.48*	519
How confident are you in your ability to help a friend access mental health support services in your school or in the community?[b]	4.40	1.56	5.06	1.45	−9.66*	518
	Baseline (%) "tell someone"		*N*	Post-intervention (%) "tell someone"		*N*
If your friend tells you that he/she is thinking about suicide and asks you to keep it a secret because no one else knows, what do you do?	88.0*		448	94.2*		478
	Baseline (%) "yes"		*N*	Post-intervention (%) "yes"		*N*
Helping yourself						
If you had symptoms of depression that lasted for more than 2 weeks, would you ask for help?	66.5*		339	74.0*		379
	Baseline		Post-intervention		*t*	df
	M	SD	M	SD		
If you were seen going into the office of your school social worker or school psychologist, how would you feel?[c]	3.06	1.67	2.92	1.64	1.94	515
Indicate, to the best of your knowledge, whether each statement is true or false		Baseline (%) correct		*N*	Post-intervention (%) correct	*N*
Knowledge about depression						
Depression runs in some families		80.8		408	84.6	427
Depression can be controlled through willpower		62.8*		316	72.0*	362
Depression is a treatable health condition		90.9		459	94.0*	477
The abuse of alcohol and drugs can be a sign of depression		95.0		480	96.6	488
Depression is a sign of personal weakness		83.9		422	86.1	433
Which of the items below could be symptoms of depression if they continue for more than 2 weeks? Check all that apply		Baseline (%) correct			Post-intervention (%) correct	
Difficulty concentrating or making decisions		76.0*		385	87.4*	443
Feeling angry		74.0*		375	81.3*	412

(continued)

Table 1.3 (continued)

	Baseline		Post-intervention			
	M	SD	M	SD	*t*	df
Changes in sleep patterns	87.5*		442		95.4*	482
Frequent, unexplained aches and pains	43.2*		219		62.3*	316
Feeling tired or less energetic	92.1*		467		96.3*	488
Eating more than usual	64.7*		328		83.6*	424
Feeling irritable or restless	86.8*		439		90.5*	458
	Average correct baseline				Average correct post-intervention	
Number of depression symptoms circled correctly from a list (max 7)	5.23*				5.96*	
Imagine that you recently heard about a new student at your school who has depression. To what extent do you agree or disagree with the following statements?[d]	Baseline		Post-intervention		*t*	df
	M	SD	M	SD		
School environment and stigma						
The new student is more dangerous than other students	2.04	0.96	1.88	0.96	3.65*	508
The student is to blame for his or her condition	1.60	0.84	1.55	0.80	1.29	508
I would have sympathy for the new student	3.98	0.85	3.84	0.86	3.28*	508
The new student makes me feel scared	1.66	0.83	1.67	0.84	−0.31	508
The new student makes me uncomfortable	1.84	0.97	1.86	0.92	−0.49	508
I would help the new student even if I did not know him or her well	3.72	0.94	3.64	0.96	1.87	509
I would try to stay away from the new student	1.80	0.83	1.80	0.92	0.00	508
The new student would be made fun of at my school	2.33	1.01	2.31	1.01	0.55	508
The new student would be ignored at my school	2.64	1.03	2.58	1.03	1.22	509
I think other students in my school would try to help the new student	3.29	0.98	3.44	0.95	−3.41*	507
	Baseline		Post-intervention		*t*	df
	M	SD	M	SD		
How comfortable are you discussing mental health issues (e.g., depression and anxiety) with your peers?[e]	4.57	1.69	4.87	1.60	−4.49*	505
Help-seeking						
If you were having a personal or emotional problem, how likely is it that you would seek help from the following people?[f]	Baseline		Post-intervention		*t*	df
	M	SD	M	SD		
Friend	3.12	0.89	3.19	0.82	−1.94	507
Parent/guardian	2.86	1.05	2.93	1.04	−1.95	505

(continued)

Table 1.3 (continued)

	Baseline		Post-intervention				
	M	SD	M	SD	*t*		df
School counselor		2.17	0.97	2.37	0.10	−5.08*	506
Teacher		1.99	0.91	2.18	0.93	−5.21*	506
Mental health professional		2.79	0.10	2.95	0.95	−3.80*	504
Doctor		2.74	1.00	2.89	0.95	−3.28*	504
Internet website		2.33	1.08	2.38	1.11	−1.15	505
Clergy		1.68	0.93	1.77	0.97	−2.46*	504
Phone help line		1.51	0.75	1.73	0.88	−5.87*	506
Other relative		2.55	1.10	2.59	1.02	−0.83	502
Boyfriend or girlfriend		2.71	1.05	2.77	1.03	−1.30	502
Coach		1.86	1.01	1.99	1.01	−3.21*	503

*Significant at 5% probability level
[a]Results based on baseline/post-intervention pairwise comparisons ($p \leq 0.05$)
[b]Scores range from 1 to 7 with higher scores indicating greater confidence
[c]Scores range from 1 to 7 with higher scores indicating greater embarrassment
[d]Scores range from 1 to 5 with higher scores indicating greater agreement
[e]Scores range from 1 to 7 with higher scores indicating greater comfort
[f]Scores range from 1 to 4 with higher scores indicating greater likelihood

who reportedly noticed or attended a P2P program were more likely to seek help from five out of ten sources than at baseline.

1.8.6.4 Implementation Tips for Other Settings

For research purposes, it was useful to analyze separately whether being a student team member influenced students' outcomes as well as to compare whether noticing the intervention or attending a program-sponsored event influenced the overall outcome results. However, for most sites looking at pre-/post-changes, it is sufficient to simply evaluate changes in the entire group.

1.8.7 What Kind of Feedback Did We Receive on the School Intervention?

While the major thrust of evaluation was on questionnaires, qualitative remarks were also collected. Qualitative feedback from P2P members included 11 comments, seven of which reiterated that the P2P program increased their knowledge about depression. Specifically, one P2P student said, "Throughout all of this I learned so much more about depression and it helped me get help for my own depression." One parent commented that after a P2P depression awareness month at school, her child was able to identify depression symptoms in his brother and encourage him to seek help. Seven teachers/mentors also commented on the P2P program, with the majority discussing the openness and engagement of the students

in relation to the P2P program. For instance, one P2P mentor noted that students were engaged and "enjoyed that peers did the performance because it made it more relatable." A teacher said, "I'm so glad to see such a concerted effort to raise awareness about mental health issues."

The P2P intervention results in greater awareness and earlier detection of depressive disorders among adolescents. This in turn may translate to lower levels of depression-related academic problems, social difficulties, substance use, other psychiatric disorders, and suicide.

1.8.7.1 Implementation Tips for Other Settings

It is important to collect feedback through questionnaires and perhaps conduct a focus group to acquire a different perspective on the effects of this intervention and capture subtleties that can be missed through quantitative methods alone. In addition, the qualitative remarks serve as key summaries of the benefit of the intervention, and for the public and policy-makers, the ability to quote a statement is often more effective than quoting statistics in conveying the benefit of the intervention. The participants' comments are a form of "story-telling," and even in scientific conferences, "telling a story" about a study or intervention is considered the most effective way to convey results.

1.8.8 Expansion of the P2P Program

We are currently in the process of developing systematic methodology to replicate the P2P program in other regions and to expand the program to middle schools. Specifically, we will be expanding the P2P program to three other counties next year covering urban, rural, and remote locations and then across multiple states in the United States (we have satellite programs in two other states currently), with an explicit dissemination strategy and budget. We are also promoting access to program consultation and ongoing support through the development of a P2P Guidelines Manual and web-based didactic P2P resources.

1.8.8.1 Implementation Tips for Other Settings

If possible, expanding the reach of the program to additional geographic locations and educational stages will enable more students and communities to benefit from the program's curriculum. This can be done after successful implementation in one school district and then careful, step-by-step cultivation of partners in other districts.

1.9 SPARX-R and the Use of Digital Technologies

The key challenges to successful prevention activities are population reach and engagement. One strategy to overcome access to potentially useful prevention programs and to reach more young people is via digital technologies. Smartphone

technology, the Internet of Things, and social media have been likened to a revolution similar to the printing press [94]. In comparison with the 15 years it took for the PC, and seven years for the web, it took only two years for a quarter of people to use a smartphone: 77% of Australians currently own an application (app)-capable smartphone, and nearly all (95%) of those aged 18–34 own one [95]. Young people are much more likely to use the Internet for banking, communication, social networking, and shopping, and almost a third now exclusively use mobile devices for these reasons [96]. This revolution is occurring across the world, even in the most remote areas. Technologies such as the smartphone and the Internet offer huge opportunities to deliver at scale and directly into the hands of these young people. In Australia for example, we have just demonstrated the use of an app for suicide prevention that reduces depression [97]. Technologies also offer the opportunity for engagement, and games or interactive games can provide opportunities for young people to learn about techniques such as cognitive behavior therapy (CBT).

In the last few years, the Black Dog Institute has partnered with Sally Merry and her team in Auckland to adapt her treatment program SPARX [87] to develop a prevention program. We have previously demonstrated the effectiveness of digital technologies for prevention using MoodGYM [49]. However, we were interested in whether the timing of these interventions could achieve better results if prevention occurred prior to a major stressor and if more contemporary interactions using serious games would improve engagement.

The SPARX-R trial commenced in 2014. SPARX-R is an online, gamified universal depression prevention intervention based on cognitive behavioral principles delivered to school students in advance of a specific, significant stressor. The SPARX-R introduction informs participants that "This version of SPARX was made to help young people who are having hassles and feeling down, stressed or angry a lot of the time. Even if you are doing fine, SPARX-R can help strengthen your skills for dealing with problems when they do come along." Participants personalize an avatar and navigate through a series of challenges and obstacles within a fantasy world that has been overrun by gloomy, negative, automatic thoughts. The student's mission is to restore balance in the game world. The program has seven modules (levels), each of which takes approximately 20–30 minutes to complete. For further details on the project, please see the published research protocol [61]. The rationale was that rates of depression begin to increase at 12–13 years of age, but the growth in incidence is continuous, with new cases of depression emerging at a similar rate throughout adolescence. In determining the point at which a preventive intervention might be optimally delivered, it is notable that stressful life events act as predictors and candidate causal factors in the development of depression. Final examinations represent a significant stressor for most adolescents. More specifically, in cultures where significant emphasis is placed on university entrance examinations in the final year of school, students tend to spend much more time doing schoolwork and less time in discretionary activities and to have more negative affective states across daily activities and higher rates of depression, relative to cultures without this focus on examinations.

This study was a cluster-randomized controlled superiority trial with two parallel arms, consisting of an experimental condition and an attention-matched control condition in ten schools. We adopted an adaptive design, such that accumulating data will be used to decide if or how to modify the study as it continues. To facilitate this design and to stagger recruitment, the trial took place in two stages across consecutive years, with each stage designed to begin at the start of the academic calendar (February 2015 and February 2016). The intervention phase lasted five weeks with a follow-up period of 18 months. Results from the 2015 cohort were subject to an interim analysis to determine preliminary effects and to determine whether any modifications would be required in the conduct of the trial in 2016. The findings were significant, so the second recruitment period was not commenced. The findings of the study clearly demonstrated that we were able to reduce depression, a result that continued for six months but was not present at 18 months (results in submission).

However, effectiveness is not sufficient to ensure implementation, and the lessons learned from this trial suggest that more work is required, much of which we have now instigated.

- Technical problems associated with SPARX both internally and in its use in sometimes poorly Internet-based environments need to be resolved before any licensing agreements or rollout to control schools occurs.
- Very few parents were interested in completing questionnaires about the mental health of their children.
- Qualitative and focus group data from staff ($n = 14$) from government, selective, secondary schools in inner Sydney showed that the majority of school staff (57.1%) reported that they were comfortable using computer/online programs; however others also felt uncomfortable (42.9%). When asked about a specific stand-alone online mental health program (SPARX), the majority of respondents liked the look and style of it (92.8%), while no one reported they did not like it. Importantly, all participants reported they liked the messages and information in the program, and all were willing to use SPARX in their school.
- Qualitative and focus group data from students were provided by 15 students from two government, selective, secondary schools in inner Sydney, aged between 15–17 years, with a roughly equal spread across gender (53.3% male). Of these, 33% reported they have felt low for a two-week period at some point in their life. In regard to the online program (SPARX) showed to the students, 73.4% reported that they liked the look and feel, and 86.7% reported they liked the messages/information of SPARX, while no one reported that they did not like these aspects. 53.4% said they would be willing to use SPARX if they were feeling depressed, and 40% were willing to use it to prevent them from becoming depressed.

A more formal implementation plan will commence in 2017 conducted by Dr. Aliza Werner-Seidler at the Black Dog Institute. The goal of this project is to investigate optimal implementation strategies to support the rollout of SPARX-R in the school context. Despite major advances in the availability of effective mental health

programs such as SPARX-R, there is a serious shortfall in the translation and delivery of such programs in practice. This project is comprised of two phases. Phase 1 involves a qualitative investigation into the barriers and facilitators to implementing SPARX-R in schools. Based on anecdotal evidence from our RCT, it is likely that aligning SPARX-R with educational curriculum outcomes will address at least one of the key barriers faced by schools. However, this has not yet been systematically addressed, as research on this topic is scarce [98]. Phase 2 involves the development of an implementation plan as determined by key themes emerging from Phase 1. The implementation strategies identified will then be tested in a randomized implementation trial comparing two key strategies (these might include delivery of educational resources to schools, teacher training with accreditation for continued professional development, and aligning content to the standard curriculum). Primary outcomes will be program uptake and completion rates. The endpoint will be an evidence-based implementation strategy that is acceptable to schools, which will inform the large-scale rollout of this program across Australia.

1.10 Translation of Models to Low- and Middle-Income Countries

We have identified two strategies that both rely on school-based interventions as the most appropriate and likely cost-effective method for easy access to adolescents. These two programs offer different approaches, one very "participatory," involving cultivating students themselves as the backbone of the intervention, and the other involving use of Internet-based and app-based interventions. These approaches therefore offer choices for application to other regions of the world; for some developing countries, Internet access and smartphone uptake may be excellent and growing. For other countries, the cultural tradition of engaging students may be strong and so lend support to the implementation of student-led approaches. Both approaches might be needed to promote and engage young people and offer a range of interventions, not just for depression but also for other risk areas such as drug and alcohol, suicide, and eating disorders. For example, the most recent review reports rapid uptake of technology and smartphone use in developing economies. Smartphone ownership is rapidly climbing from a median of 21% in 2013 to 37% in 2015 [99]. Unsurprisingly, the rates are much higher in the younger age groups.

1.11 Limitations in the Field

Despite advancements in the field of depression prevention and the growing number of studies focused on depression prevention programs delivered in schools, most of these interventions are built around delivery by health professionals, a major limitation in the field. Programs led and implemented by health professionals give students and school personnel little buy-in or feelings of ownership over the program. When an intervention program is constructively co-created and implemented by

students, school personnel, and health professionals, it is more likely to be adopted, institutionalized within the school, and sustained as a program. More broad limitations to the idea of school-based interventions must be acknowledged, such as the reality that some youth do not attend school or would benefit more from external mental health services. Furthermore, in considering the results from research studies, overall effect sizes in extant school-based depression intervention research have been small [38, 46, 47], as would be expected for prevention rather than treatment interventions.

1.12 Recommendations for Immediate Implementation

In order to ensure the most cost- and time-efficient service delivery, prevention programs should capitalize on the resources already available in each school. For instance, programs can be integrated into the school curriculum with teachers or other school personnel trained in prevention and supported by ongoing consultation to deliver these programs (e.g., [40, 89]). In addition, based on our results from implementing the University of Michigan P2P program, depression intervention programs can successfully enlist youth as valuable mental health advocates and peer educators. These methods may in turn strengthen relationships between teachers, students, and parents and create a healthier school environment overall. Importantly, however, the youth need resources, mentorship, and concrete platforms for engagement and participation, which may be less available in certain settings [27]. Furthermore, whenever possible, prevention programs should be designed to be flexible and should be tailored to individual communities and student populations. For instance, low-income youth, minority youth, or youth from rural communities may have specialized mental health needs that should be incorporated into program content. However, few studies have specifically focused on these populations of youth (e.g., [13, 41]), even though they may be particularly vulnerable to depression [50]. Lastly, when developing and implementing programs, researchers and clinicians should make use of existing data to better understand what makes interventions most and least effective.

1.13 Future Directions for Research and Implementation

Moving forward, large-scale effectiveness trials are needed to identify best practices for implementing school-based depression prevention and education programs. Successful randomized controlled trials (RCTs) must be replicated, and, whenever possible, researchers should follow participants over longer periods of time so longer-term effects can be detected.

A simple approach to conducting such trials involves randomizing some schools to receive the intervention, and others to serve as a control, and then the following year having the control schools receive the intervention. This wait-list control design allows randomization but also enables schools to know that they will

eventually receive the intervention. A more sophisticated approach might include cluster randomization, participant preference arms, and action research.

Cost-effective measures, encompassing both direct and indirect costs, need to be prioritized in future trials in order to demonstrate that the program provides good value and implementation is a good investment. Moreover, greater attention to mediator and moderator variables within the field will guide theory-driven program evaluation and lend insight into the validity of intervention programs. To date, most depression intervention RCTs have primarily focused on clinical treatments such as CBT that is delivered in person. However, it is worth looking into additional educational interventions as well as online and mobile interventions.

Additionally, the vast majority of depression prevention trials are from HICs that are English-speaking (although this observation may partly be due to our specified inclusion and exclusion criteria). At present, the availability of prevention programs is unevenly distributed around the world. Expanding the reach and availability of prevention programs will provide more countries and communities with a gamut of preventive tools and resources to reduce the impact of mental disorders. Additional depression prevention programs need to be systematically adapted to economically and socially marginalized adolescent and young adult populations, such as refugees, LGBTQ youth, and minorities, as well as among different regional, cultural, and ethnic groups. Some existing examples in the e-health world include Little Prince is Depressed, an interactive tour of depression information from Hong Kong [100], and the Chinese MoodGYM Project [101], an interactive program based on cognitive behavior therapy, though these programs are not school-based. Successful programs should also be conducted in more languages to reach youth worldwide (e.g., [102]). One way to make evidence-based prevention programs widely available is to create a database with detailed program and program implementation information. In addition, access to program consultation and ongoing support through the development of official guidelines and online resources should be made available to mental health researchers worldwide. Moreover, given the early onset of depression [3], it is important to implement more interventions that begin in primary school. Lastly, in order for interventions to achieve the greatest impact globally, depression prevention and mental health promotion need to be included in national and international legislation and policy measures.

Conclusions

School-based depression education and prevention interventions may reduce the risk of poor mental health outcomes in children and adolescents in LMICs and HICs as well as the incidence, duration, and costs of depression [15, 44, 103]. Though effect sizes are small, findings from universal and selective school-based interventions for depression education and prevention suggest the feasibility and scalability of these interventions [37, 38, 46, 47]. In order to improve the success of future research initiatives and ensure positive mental health outcomes, the field now needs to refine program implementation and identify best practices for implementation based on lessons learned from exist-

ing programs. This will hopefully result in more effective, practical, and flexible programs that lead to lower levels of depression-related academic problems, difficulties with friends and family members, substance use, other psychiatric disorders, and suicide.

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Anxiety Disorders: From Bench to Bedside and Beyond

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Abstract

The anxiety disorders are prevalent, associated with high comorbidity and cause considerable disability. Despite efficacious treatment options, they are frequently misdiagnosed, and management is often suboptimal. With the recent publication of the DSM-5 and the imminent release of the ICD-11, there have been important debates about how best to categorize and conceptualize these disorders. In addition, their underlying neurobiology is being explored at multiple levels from systems neuroscience to molecular biology and genetics—an endeavour that is delivering insights with relevance to clinical practice. Furthermore, several international anxiety disorder treatment guidelines have recently been published, and large systematic reviews and meta-analyses have addressed important questions around clinical management. All of this indicates the need for an update on advances in this rapidly developing field, and this chapter therefore provides an overview of the epidemiology and classification, cognitive-affective neuroscience and clinical management of the anxiety disorders.

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2.1 Introduction

Anxiety disorders are the most prevalent group of mental illnesses globally and are associated with a significant disease burden, which is compounded by underdiagnosis and incorrect or inadequate treatment [1, 2]. Though anxiety disorders can have a chronic or relapsing and remitting course, many treatment options are now available, and there can often be considerable improvement in response to appropriate interventions.

The best outcomes for patients are achieved through a sound understanding of three interlinking issues: the clinical features and epidemiology of anxiety disorders, so that the right diagnosis is considered and made; the neurobiological factors underlying the clinical presentation, which inform both research and treatment strategies; and the efficacy and effectiveness of the psychotherapeutic and psychopharmacological options, which allows for evidence-based and individualized care. The preceding volumes of the Advances in Psychiatry series have not focused on anxiety disorders directly, meaning this chapter is an opportunity to update readers on a range of advances in the field. The literature is vast, however, so instead of trying to be exhaustive, this review focuses on key developments that have particular relevance for conceptualization, improving diagnosis and achieving the best possible treatment outcomes.

We begin by discussing the epidemiology and recent developments in the diagnosis and classification of the conditions, including reference to the *Diagnostic and Statistical Manual of Mental Disorders* 5 (DSM-5) and upcoming *International Classification of Diseases* version 11 (ICD-11), and consideration of how the Research Domain Criteria (RDoC) framework may inform our conceptualization and management of these disorders. Subsequently, we give an overview of the neurobiological characteristics of the anxiety disorders extending from functional neuroimaging to genetics. Finally, we discuss treatment options and guidelines based on recent psychotherapeutic and pharmacological research, with a specific focus on generalized anxiety disorder, panic disorder and agoraphobia, specific phobia and social anxiety disorder.

2.2 Understanding a Worried World….

2.2.1 Epidemiology and Disease Burden of Anxiety Disorders

Though it has long been recognized that anxiety disorders are common, robust evidence clarifying the full extent of the problem globally has been lacking, due to both inadequate measurement tools, as well as mental health being given a lower priority than other health issues in epidemiological research [3]. This lack of evidence is an important problem that has contributed to under-detection and poorly informed mental health policy [3]. In recent years, large-scale epidemiological studies are beginning to address this gap and are providing important insights.

The World Mental Health Survey (WMHS) is a groundbreaking set of community surveys using structured interviews aimed at providing information about the

prevalence, distribution, burden and unmet need for treatment of common mental disorders, including the anxiety disorders [1]. Anxiety disorders are consistently the most prevalent group of mental disorders in the general population globally, with conservative lifetime prevalence estimates for any anxiety disorder averaging 16% and as high as 31% [1, 4]. This is in comparison with the next most prevalent disorders, namely, mood disorders, with an average lifetime prevalence of 12% [1].

In terms of individual anxiety disorders, specific phobia is the most prevalent (7–9% 12-month prevalence), followed by social anxiety disorder (2–7% 12-month prevalence) and then general anxiety disorder (approx. 3% 12-month prevalence) [1, 5]. A more recent WMHS has also highlighted the high lifetime prevalence of panic attacks (13.2%), though the lifetime prevalence for panic disorder was only 1.7%, which is equivalent to the prevalence of agoraphobia [1, 6, 7]. As a group, the anxiety disorders are more common in women [4] and on average have their onset in the late teens or early 20s [8]. It is also recognized that while appropriate treatment can modify the long-term trajectory of these disorders, they naturally have a chronic or relapsing and remitting course [7, 9] and are also commonly underdiagnosed and undertreated [2, 10].

A further important clinical and epidemiological factor is the high comorbidity associated with anxiety disorders. This includes having more than one anxiety disorder, as well as comorbid mood, substance use and physical disorders [8, 11]. In those with at least one anxiety disorder diagnosis (i.e. a clinical sample), an estimated 10% will have a second anxiety disorder, 29% will have an anxiety disorder and a depressive disorder and 31% will have two anxiety disorders and at least one depressive disorder [11]. This is in comparison with general population estimates which suggest a lifetime prevalence of 5% of an anxiety disorder and comorbid mood disorder (including bipolar disorder and major depression) and approximately 3% for an anxiety disorder and a comorbid substance use disorder [8]. In the majority of cases, the anxiety disorder presents first, which is important from a diagnostic and management perspective [8].

The presence of comorbid disorders adds considerably to the disease burden associated with anxiety disorders, specifically in terms of chronicity, more severe symptoms, more social disability and greater utilization of health services [11]. Apart from the impact of comorbid conditions, the disease burden associated with anxiety disorders directly is an important focus of current research, most notably through the WMHS and Global Burden of Disease Studies [1, 12, 13]. In part due to their early onset and chronicity, anxiety disorders are particularly associated with problematic long-term consequences, including increased risk for physical illness, reduced educational attainment, marital instability, lower occupational and financial achievement and substantially increased utilization of healthcare resources [1]. In a global analysis of mental disorders, anxiety disorders were second only to major depressive disorder in terms of disease burden [12].

Central to understanding the consequences of anxiety disorders, and mental illness in general, is realizing that their impact is under-represented if only mortality rates are considered. So, even though anxiety disorders may predict increased mortality [14, 15], and even when they have contributed directly to death, for example,

in the case of suicide, the cause of death will usually be recorded as the proximate cause (such as hanging, poisoning, etc.), and the associated mental illness may not be highlighted [13]. To counter this potential misrepresentation of the importance of mental illness, epidemiologists now calculate additional measures of impact, specifically disability-adjusted life years (DALYs), years of life lost (YLL) and years lived with disability (YLDs) [13]. When seen from this perspective, the high burden of anxiety disorders becomes clear, as they account for 3.5% of the global disease burden due to disability (measured in YLDs), second only to major depressive disorders amongst mental disorders and the sixth leading global cause of disability overall in both high, middle and low income countries [12, 13].

The factors described so far emphasize the need for a coordinated effort to better manage anxiety disorders. This can best be achieved by screening in at-risk groups, making the diagnosis based on standardized criteria and initiating evidence-based treatment, for both the anxiety disorder and any comorbid conditions. In line with this, clear agreement on the clinical features of each diagnosis is essential, as it allows for standardized approaches to research, which can then contribute to clinical decision-making and policy development.

2.2.2 Name Changes, Reorganization and Thinking Outside (and About) the Box

Psychiatric diagnosis has been criticized as lacking in diagnostic certainty and scientific rigor [16]. This view seems overly harsh, given the complexity of the brain, and the relative newness of neuroscience as a discipline, and the rigorous efforts of disease classification systems such as the DSM and ICD. By standardizing diagnostic criteria, DSM and ICD provide a reliable means for determining "caseness," which is currently foundational for anxiety disorder research, as it provides a common language through which to communicate about and investigate their causes and consequences [3, 4, 17].

The development and eventual release of the DSM-5 in 2013, after intensive and prolonged international collaboration, allowed for an update of psychiatric diagnoses and disorder groupings, including the anxiety disorders. There have been relevant criticisms of the final document, and ongoing debate has the potential to strengthen the field and future versions [16, 18, 19]. Changes relating to the anxiety disorders include new clustering of disorders, as well as new diagnostic criteria [7]. Most notably, when compared to DSM-IV, obsessive-compulsive disorder and posttraumatic stress disorder (PTSD) are now grouped separately from the anxiety disorders in the "Obsessive Compulsive and Related Disorders" and "Trauma- and Stressor-related Disorders" chapters, respectively. There is divided opinion on the justification for these changes, particularly in relation to PTSD [20, 21]. A potential advantage, however, may be new research pathways for these disorders, which may in turn clarify the underlying neurobiology and allow progress towards more targeted treatment [22]. Further reorganization involving anxiety disorders includes the placement of separation anxiety disorder and selective mutism within the

anxiety disorder section, rather than in disorders usually first diagnosed in infancy, childhood or adolescence. For separation anxiety disorder, this change was made because a significant number of people only experience separation anxiety after the age of 18 years, while selective mutism was moved because of the high likelihood of significant anxiety in children who are selectively mute [7, 23].

Apart from this regrouping, the DSM-5 also includes a number of other changes, including to names and diagnostic criteria. Panic disorder and agoraphobia are now regarded as separate conditions, even though it remains clear that there is considerable comorbidity, and there is now a panic attack specifier that can be applied to any mental condition [7]. For agoraphobia, specific phobia and social anxiety disorder, the person no longer needs to recognize that their anxiety is excessive or unreasonable; instead it is now up to the clinician to determine that symptoms are out of proportion to reality [7]. For social anxiety disorder, the term social phobia falls away, and symptoms must now have been present for more than 6 months across all age groups, while a "performance only" specifier has been added.

Though many may have hoped that the DSM-5 would be a paradigm shift in how mental illness is conceptualized, the changes to the anxiety disorders are an example of how it has been a more iterative process, with a paradigm shift not yet possible [24–26]. Still, these changes may represent a worthwhile refinement of thinking about anxiety and related disorders [22].

The imminent release of the ICD-11 will provide further fuel to the debate about disease classification, especially relating to mental illness. Overall, efforts have been made to harmonize the ICD-11 and DSM-5, so as to allow for crosstalk for those using both systems and to allow meaningful integration for statistical purposes. The ICD-11 aims to emphasize clinical utility, so complementing DSM-5 [16, 18, 27], which focused on diagnostic validity—though both systems clearly strive for both aspects. Even though the changes expected in the ICD-11 for the anxiety disorders are broadly in line with those in the DSM-5 [27, 28], it remains important that clinicians and researchers review both classification systems to assess the extent to which they can inform practice, and facilitate research, with the goal of further development and refinement [29].

While categorical systems such as the DSM-5 and ICD-11 are currently indispensable in clinical and research psychiatry [3], the limitations of these approaches indicate the need for new ways of conceptualizing mental illness and making diagnoses [16, 18, 19]. The Research Domain Criteria (RDoC) project initiated by the National Institute of Mental Health in the USA is a leading example [18, 30]. The goal of the RDoC is to move towards "precision medicine for psychiatry" [18] by developing a robust biological basis for psychiatric diagnosis and treatment though the rigorous exploration of five research domains, namely, negative valence systems—including fear and anxiety, positive valence systems, cognitive systems, social processes and regulatory and arousal systems [17, 30]. Each of these domains is further extrapolated into subconstructs, and research is ongoing on the genetic, molecular, cellular, physiological, behavioural and systems levels [30].

The RDoC project, while clearly a valuable long-term initiative which builds on many years of neuroscience research, is still at a very early stage. So, while there

has been some discussion of whether the RDoC may represent the beginnings of a paradigm shift for the anxiety disorders [31], it has yet to have a major impact on clinical management. Nevertheless, it may usefully serve as a stimulus for clinicians and researchers to remain flexible and inquisitive, to seek to not only think outside the "box" of diagnostic categories and conceptualizations but also to think about the box itself, and whether or not there is, or even should be, a box at all. Though the final outcomes of the RDoC initiative are some way off, there is already a large body of research on the neurobiological underpinnings of anxiety disorders, which we will now review.

2.3 The Anxious Brain—What's Going on in There?

In the past two decades, neuroscience research, both in humans and animal models, has expanded [17, 32, 33], with ongoing development and refinement of methodologies at both the "macro" level (especially structural and functional neuroimaging) and "micro" level (especially genetics and molecular biology). The result has been steady headway in deepening our understanding of the neurobiology of psychiatric illness [34, 35]. We present here an overview of the cognitive-affective neuroscience of anxiety, in order to inform diagnosis and treatment.

2.3.1 Anxiety Circuits and Systems

The signs and symptoms of anxiety disorders are diverse, including cognitive features such as prominent rumination and attentional difficulties; emotional aspects, including fear and dysphoria; and physical changes and experiences such as breathlessness or tachycardia [7]. This indicates that multiple brain regions and systems are implicated in both the vulnerability to anxiety and in its acute manifestation, and the neuroscience literature confirms that anxiety is a "whole brain" problem involving cortical, limbic and brainstem structures and networks [10, 33, 36, 37].

A key circuit thought to underlie experiences of anxiety and the anxiety disorders themselves is the "fear circuit" [10, 36], which is involved in *fear conditioning* (the development of fear in response to a stimulus), *fear extinction* (the diminution and disappearance of fear in response to a previously fearful stimulus) and the *fear response* itself (the physiological and overt manifestations of fear). This circuitry was initially delineated in animal work, mostly in rodents, but because of the preservation of fear-related systems through evolution, an analogous system exists in humans, the understanding of which guides clinical applications [10, 38–40].

Critical brain structures initially implicated in fear conditioning and fear extinction in humans include the amygdala, hippocampus and prefrontal cortex (PFC) [10, 36]. Other work suggests a role for the insula cortex and anterior cingulate cortex (ACC) [17, 41]. These regions interact to process fearful stimuli received through afferent connections from multiple other brain structures and then

coordinate the fear response via efferent connections especially with the hypothalamus and autonomic nervous system control centres in the brainstem, which are involved principally in the expression of fear [10, 17, 39]. The amygdala and hippocampus play central roles in the acquisition of conditioned fear, while the prefrontal cortex has a top-down modulatory function over amygdala activity levels, which regulates GABAergic connections between the amygdala and brainstem, thus regulating fear expression [36, 38]. In addition, it is postulated that while the amygdala is responsible for the "positive" features of fear (such as hyperarousal), the hippocampus may govern the "negative" symptoms (such as avoidance), a separation that may reflect different evolutionary origins, with the amygdala's role reflecting an implicit process that likely evolved earlier, while the hippocampus mediates a more explicit process relying on memories of past fearful stimuli [10]. Relying on the same circuitry, fear extinction (achieved, e.g. through graduated exposure) involves upregulation of PFC inputs and thus reduced output from the amygdala [36, 40].

The system described above evolved in response to the realities of the evolutionary environment, and when triggered in response to appropriately threatening stimuli remains adaptive, and as a result has been preserved across evolution [10, 39]. In the anxiety disorders, however, the structures and circuitry malfunction, with the result that problematic symptoms arise that can be usefully conceptualized as different types of "false alarms" [10]. It remains difficult to determine if the abnormalities in the fear circuitry detected in anxiety disorder research are causal, or the consequence of some other as yet unrecognized factor, but understanding the changes remains valuable in explaining the symptoms of anxiety, as well as the mechanism of action of established and novel treatment approaches.

In individuals with high trait anxiety and those with anxiety disorders, there may be dynamic imbalance between the amygdala and the PFC, with amygdala hyperresponsivity, and insufficient recruitment of prefrontal input, resulting in alterations in attentional, associative and interpretive processes in response to threatening or potentially threatening stimuli [36, 38, 40]. Hyperactivity of the insula may compound this [17], with the overall result that those with anxiety disorders have a "threat-related processing bias" or "negativity bias" [17, 36], with selective attention to threatening stimuli and resultant poor performance and distressing symptoms. In research paradigms exploring this, the threatening stimulus need not have reached conscious awareness for it to have an impact, i.e. even fleeting stimuli can be significant [36, 38]. In addition, those with anxiety disorders are also more likely to misinterpret neutral or ambiguous stimuli as threatening [10, 36, 42]. Combined this enhancement/exaggeration of threat evaluation mechanisms in anxiety disorders results in more frequent perceptions of threat and the associated activation of the fear response, with an increased likelihood of fear conditioning, and a reduced likelihood of fear extinction [40]. This potential runaway cycle may be involved in both the aetiology and maintenance of anxiety and anxiety disorders [36].

These changes appear to be relevant to the anxiety disorders as a group [40], with research in individual disorders confirming this and highlighting more disorder-specific aspects. PTSD in particular, while no longer grouped with the anxiety

disorders in DSM-5, is nevertheless mediated by fear circuitry mechanisms [40]. Panic disorder, agoraphobia and specific phobia, which revolve around fear conditioning experiences and impaired fear extinction, also appear to stem from dysregulation of this system, particularly relating to the balance between amygdala and PFC activity [10, 17, 40]. In social anxiety disorder (SAD) and generalized anxiety disorder (GAD), the insula component of the fear circuitry is also implicated [38], and ACC hypoactivity and insufficient connectivity between the ACC and amygdala during processing of threat stimuli also appears significant in the manifestation and maintenance of anxiety [17]. In addition, the over-interpretation of social cues, which may contribute towards anxiety in those with SAD, may be more specifically linked with dorsolateral PFC (DLPFC) and dorsal ACC hypoactivity [10], while the chronic worry and rumination characteristic of GAD (which is in contrast to the more focused experiences of fear and anxiety present in the phobic disorders and panic disorder) may stem from additional dysfunction in a "cognitive control circuit" including the DLPFC, ACC, dorsal parietal cortex and precentral gyrus, representing a form of "cognitive overdrive" [17].

Despite these important advances, which bring clarity to the neurobiological processes underlying the anxiety disorders, there is much still to be determined. Particularly, the circuitry underlying specific symptoms of anxiety, and further details of the unique features present in the different disorders, as well as which features are transdiagnostic, need elaboration. As mentioned in the discussion of classification, it is likely that current anxiety disorders do not map neatly onto discrete neurobiological processes [18]. Further work on the cognitive-affective neuroscience of anxiety has the potential to move the field towards a biological basis for understanding symptoms, and for assisting with the determination of diagnosis, classification and treatment. The RDoC project is an example of a coordinated effort towards this end, and the negative valence system domain may be particularly likely to provide insight for understanding anxiety [30]. Broad-based, longitudinal research projects exploring anxiety symptoms by combining neuroimaging and symptom measures in diverse subjects, and relating this to behaviour and functioning, are currently underway [17].

2.3.2 Anxiety-Related Genes and Molecules

Intensive research is also focused on what is happening at the "micro" level within the anxious brain. This includes both animal and human studies focusing on endocrine pathways (especially the hypothalamic-pituitary-adrenal axis), neurotransmitter systems (including monoamine pathways, as well as glutamatergic and GABAergic functioning), an increasing number of neuropeptides and, at a fundamental level, the role of genetic factors in the vulnerability towards anxiety disorders—all of which align with the goals of the RDoC project [30, 32, 35, 38, 43, 44]. This research agenda compliments the larger systems-level work already described, with the potential to deepen the understanding of the neurobiology of anxiety, and assists in developing possible diagnostic biomarkers, clarifies the effects of

established treatments and lays the foundation for identifying novel treatment targets and therapeutic agents [44, 45]. Though the available literature in this area is extensive, and interested readers should refer to more in-depth reviews [34, 35, 38], what follows is a summary of key points to inform the later discussion of treatment.

2.3.2.1 Hypothalamic-Pituitary-Adrenal Axis (HPA Axis)

The HPA axis is central to the bodies' response to stress, and HPA axis dysfunction may be present in a subset of anxiety disorders [38]. The neuropeptide corticotrophin-releasing factor (CRF) is a key regulatory factor for the HPA axis and has a neuromodulatory effect with specific relevance to anxiety, including via anxiety-related targets outside the axis itself, such as the amygdala [35, 38, 45]. Brain areas involved in anxiety show high expression of CRF receptors, especially the frontal cortex, hippocampus and amygdala, and CRF receptor antagonists are an intense focus of research as possible therapeutic agents, with some encouraging early findings [38, 45]. While CRF overexpression has been most clearly linked to anxiety in rodents [45], behavioural inhibition in children—a risk factor for SAD and panic disorder—is associated with CRF gene polymorphisms, though CRF-related findings in specific anxiety disorders are inconsistent and are not a uniform abnormality [38]. In addition, in panic disorder there may be reduced sensitivity to CRF (specifically a reduced HPA axis response to its release), which may in part explain the intense anxiety symptoms characteristic of the disorder [38].

Finally, besides CRF itself, there are other endogenous ligands of the CRF receptor that may be relevant, including the neuropeptides urocortin 1 and 2, which appear to be involved in adaptive stress recovery processes, and dysfunction within this system may increase vulnerability to stress, including development of anxiety disorders [45]. This is an example of the extensive interconnections that exist between the various molecular subsystems relevant to anxiety.

2.3.2.2 Monoamine Systems with a Focus on Serotonin

The role of monoamines (including serotonin, noradrenaline and to a lesser extent dopamine) in the aetiology of anxiety disorders has been recognized for some time [10, 38] and rests in part on the fact that pharmacological agents targeting monoamine pathways are effective anxiolytics [46], as well as the extensive monoaminergic projections present throughout the fear circuitry [10]. The relevant research has been reviewed at length [35, 47, 48]. An important recent stream is the sustained focus of interest on the serotonergic receptors and the serotonin transporter, as they are believed to underlie the benefits of the selective serotonin reuptake inhibitors (SSRIs)—currently the first-line medications for anxiety disorders [2, 46]. This line of enquiry unites genetics and molecular biology and highlights the value of translational approaches across animal and human research, with the potential to clarify the mechanism of effects of SSRIs and other anxiolytics targeting this system [46]. There is already clear evidence of a role for the 5HT1A receptor in modulating anxiety in animal models, and while initial attempts at developing effective receptor agonists as therapeutic agents in humans were unsuccessful, it remains an active

interest area [46, 47]. Additional work in humans highlights the distribution of the 5HT1A receptor in key components of the fear circuitry (prefrontal cortex and hippocampus), and the association of 5HT1A receptor gene polymorphism with amygdala reactivity, indicating a likely effect on anxiety expression [46].

Alongside the 5HT1A receptor, the 5HT2 group of receptors (most notably 5HT2C) are implicated in the aetiology of anxiety and may be a mechanism for the effectiveness of anxiolytics [35, 46]. In animal models, 5HT2 antagonists augment the effect of SSRIs, though human trials have not yet demonstrated any benefit [46]. The existing agent agomelatine, which apart from its melatonergic effects is also a 5HT2C receptor antagonist, has been shown to be an anxiolytic in those with GAD, and this may be due to its influence on this receptor [49]. In addition, there appears to be a functional interaction between 5HT2 receptors and CRF that may have a role in modulating fear extinction, and the 5HT2A receptor has coactivity with $GABA_A$ receptors at certain sites [46]—interrelationships which exemplify the complexity of the molecular basis of anxiety.

The serotonin transporter (5HTT) is probably the most widely studied component of the serotonergic system, in large part because it is a key mechanism for the effects of the SSRIs [46]. Particular 5HTT gene variants have been suggested as a risk factor for anxiety traits and disorders and possibly a reduced ability to tolerate or adapt to stress [36, 46]. This may be due to an effect of these gene variants on amygdala activity, a change specifically relevant to SAD [10]. As a further example of the interaction between the various molecular subsystems involved in anxiety, there is some indication that 5HTT and the functioning of the neuropeptide oxytocin may be intertwined [46]. In animal genetic models, knock-in and knockout approaches have confirmed a role for 5HTT in anxiety, which may be the early beginnings of genetically targeted treatments for anxiety disorders [46].

This has been only a brief glimpse of serotonergic research, but what is obvious, is that, despite its central place in anxiety research, this system doesn't operate in isolation [48]. Apart from the connections already described, the serotonergic system also has important reciprocal relationships with the opioid and GABA systems [46, 50], and the fact that a significant number of those with anxiety disorders do not respond to serotonergic treatments is an important reminder to keep other molecular subsystems in mind too [45].

2.3.2.3 Glutamate and GABA

Apart from the monoamines, the classical neurotransmitters glutamate and gamma-aminobutyric acid (GABA) also have important and intertwined roles in anxiety [44, 51]. Glutamate is the main excitatory neurotransmitter, while GABA is the main inhibitory neurotransmitter, with the dynamic balance between them essential to effective brain functioning. GABA inhibitory interneurons are a core component of the fear circuitry within the amygdala [36], with a prominent role in the expression of anxiety, including as the intermediaries for the top-down control exerted by the PFC in the downregulation of the amygdala, a process that is dysfunctional in anxiety disorders [36, 40]. Psychotherapeutic interventions involving exposure are thought to upregulate PFC input to the amygdala and achieve their benefit in part by modulating these GABAergic neurons [36].

The central importance of GABAergic neurons in anxiety is confirmed by the fact that they are the molecular targets of the benzodiazepines, which are effective anxiolytics [46, 52]. There is also some evidence of a role for GABA-related genes in increasing vulnerability to anxiety disorders, though this is likely a polygenic effect, the importance of which is still being determined in human research [46]. The GABA system is a highly attractive target for pharmacological agents, and several agonists/analogues are already in clinical use or development [2, 46, 53]. Research priorities include determining the effects of targeting different subunits of the receptor and whether there are ways to reduce the concerns about tolerance and abuse relating to these agents [46]. Besides its inherent role in anxiety, the GABA systems interact not only with the glutamatergic system but also with serotonergic and opioid systems, which may account for some of the anxiolytic effects of agents targeting all three of these systems [46, 50].

Research on glutamate is another key focus for deepening our understanding of anxiety and is revealing important insights [38, 51]. Glutamatergic neurons are widely distributed throughout the fear circuitry of the brain, and variability within this system is regarded as highly likely to contribute towards the development of anxiety disorders [38, 44]. Glutamate is central to synaptic plasticity processes relevant to learning and memory and to hypothalamic regulation of the acute stress response [44, 51]. Through effects on ionotropic and metabotropic (Mglu) receptors, glutamate regulates multiple intracellular processes, and agents acting on the glutamatergic system, such as memantine, pregabalin and riluzole, have already been shown to be effective anxiolytics [38, 44]. Novel Mglu receptor agonists have shown particular promise in preclinical studies and may have a similar role to benzodiazepines without tolerance and dependence risk, while Mglu antagonists and selective antagonists may also be valuable, in part because these receptors influence other anxiety-related systems (including the HPA axis, serotonergic system and BDNF) [38, 51].

Conditioned fear acquisition has also been shown to depend on glutamate NMDA receptor-mediated neuroplasticity in the amygdala, and manipulation of this receptor through the administration of the partial agonist D-cycloserine has been shown to augment exposure therapy in producing fear extinction in humans [40, 44, 54]. This exciting finding is an example of how preclinical neuroscience research has contributed directly to therapeutic approaches. Ongoing preclinical and clinical work on interventions which target the glutamatergic system and the important interactions between GABA and glutamate are likely to result in improved understanding of and treatment for anxiety disorders [51].

2.3.2.4 Neuropeptides

A growing list of neuropeptides has a role in the aetiology and possibly the management of anxiety. Neuropeptides are short-chain fatty acids that act as neurotransmitters in various brain circuits [38], and those for which there is the most robust evidence of a role in anxiety include substance P, neuropeptide Y, oxytocin and galanin.

Substance P is the endogenous ligand of neurokinin 1 (NK1) receptors, which are distributed in the amygdala and hippocampus, and may be a mechanism for the production/expression of anxiety [45]. Animal models involving receptor gene knockouts or administration of receptor antagonists have shown promising anxiolytic effects, with additional evidence that this ligand-receptor complex may have a beneficial influence on BDNF-dependent signalling and hippocampal neurogenesis similar to that induced by antidepressants [38]. There have been mixed results in human trials, but a NK1 receptor antagonist may reduce symptoms in SAD [38, 45].

Neuropeptide Y (NPY) is widely expressed in the central nervous system including hippocampus and amygdala, suggesting broad involvement in physiological processes [38, 45]. It interacts prominently with CRF/HPA axis to regulate the stress response and likely has a modulatory role in stress adaptation, especially to chronic stress, which is a recognized risk factor for anxiety [38, 45]. In animal models, reduced NPY following acute stress is associated with increased anxiety, and pharmacological intervention studies support a role for NPY in moderating anxiety—with the injection of NPY reducing anxiety, while NPY gene knockout results in increased anxiety [45]. The bulk of research on NPY at this stage is preclinical, but intranasal NPY has been trialled as a rapid-acting anxiolytic [38].

Oxytocin is active in key nodes of the stress circuitry including the amygdala and hippocampus, whereby it regulates the stress response and stress-related behaviours [45]. Its effects on the amygdala include inhibiting excitatory outflow to the brainstem and modulating complex social behaviour [38]. In animal studies, administration of oxytocin appears to reduce anxiety levels, and oxytocin-deficient rodents show increased anxiety, with heightened HPA axis activity [45]. Human research appears to support this, with polymorphisms of the oxytocin receptor gene resulting in increased vulnerability to stress [45]. Human fMRI studies, on the other hand, showed reduced amygdala activation in response to fear-inducing faces and reduced amygdala-brainstem coupling, after intranasal oxytocin administration [38]. Oxytocin analogies have been trialled in depression with promising results, suggesting further trials in anxiety disorders are warranted, with SAD thought to be the disorder most likely to benefit [38, 45].

Galanin targets receptors in the amygdala and hippocampus and influences the serotonergic and noradrenergic systems, suggesting a high likelihood of involvement in stress and anxiety [45]. Animal models show galanin antagonists to have both acute and chronic anxiolytic effects, in part due to a modulation of the usual inhibitory effects of galanin on the serotonergic system [38]. The galanin system may also be upregulated in chronic stress, a finding which was reversed by antidepressants [45]. Recent large-scale genetic studies have identified an association between galanin gene polymorphisms, anxiety disorders and increased HPA axis activity in female patients, though the significance of this, and any role for galanin as a clinical treatment target in anxiety disorders, remains to be clarified [45].

From this brief overview of several of the neuropeptides, there are indications that they may be amongst the various mechanisms for vulnerability to anxiety, and that they will inform new drug discovery, with multiple compounds targeting these systems currently being investigated [38, 45]. It may also be that an improved

understanding of the role of the various neuropeptides in the aetiology of anxiety can contribute to the development of a biologically based diagnostic and classification system for anxiety disorders [18, 45].

2.3.2.5 Genetics

The final "micro" level to consider in attempting to understand the neurobiology of anxiety disorder is that of genetics. Anxiety disorders are strongly heritable, and there is growing direct evidence that genetic factors play a key role in vulnerability to and development of anxiety disorders [46, 55]. This role for genetics is evident in the preceding discussion of the molecular subsystems involved in anxiety, including the value of genetic manipulation studies (such as animal gene knockout approaches) in exploring these systems [56]. Nevertheless, translating findings at the genetic level into clinical applications such as novel diagnostic and treatment strategies remains a challenge [46, 55]. Genetic vulnerability for anxiety disorders likely stems from the influence of multiple genes, each with a small effect, as well as complex gene-environment interactions and ongoing epigenetic processes [35, 46, 55].

Still, multiple genes with relevance to anxiety disorders in humans have been identified including those coding for COMT, cholecystokinin, 5HT1A and 5HT2A receptors, serotonin transporter (5HTT), monoamine oxidase A and BDNF—all of which may contribute towards the development of novel anxiolytic agents in the future [43, 46, 55]. Two genetics research approaches which will likely produce important findings over time include genome-wide association studies (GWAS) and endophenotypic studies. GWAS, which survey the whole genome as a broad approach to identifying abnormalities contributing towards anxiety disorders, are currently underway, and while several associated genes have been identified, this research is at a very early stage in terms of its clinical utility [57]. Endophenotypic studies, on the other hand, are intermediate studies which investigate the genetic component of common behavioural or neurobiological traits identified in those with anxiety and may contribute to transdiagnostic understanding [46, 55, 58].

On this background, a key strategy, which may promote continued advancements in understanding the genetic basis of anxiety disorders, is the development of robust, bidirectional translational models, whereby discoveries in both animals and humans can be developed and tested using the full range of neuroscientific methodologies [46, 55, 56].

Having briefly reviewed the interesting findings emerging from the neuroscience of anxiety disorders, it is clear that there is extensive overlap between the larger brain circuits and systems, and the distribution of the molecular pathways and genetics aspects just described, which may indicate they are amongst the proximal mechanisms whereby those larger systems mediate their effect on anxiety [43, 44, 51]. Secondly, it is obvious that there are extensive interconnections between the various molecular subsystems [50], indicating the complexity of the challenge of determining the neurobiology of anxiety, and thus the importance of further research in clarifying any clinical applications [18, 46, 51].

Neuroscience research provides a valuable framework for understanding anxiety disorders in terms of pathogenesis, vulnerability and symptom production, as

well as highlighting the mechanisms by which established treatments may have their effects, and helping with identification of possible new diagnostic and classification biomarkers and treatment targets. Nevertheless, clinical research is just as vital to assess how to make the best use of existing treatments in the management of anxiety disorders in real-world settings—the focus of the final section of this chapter.

2.4 Treating Anxiety Disorders—Current Practice and Emerging Approaches

In the context of their epidemiology, the ongoing debates regarding their classification and conceptualization, and the promising but still incomplete neuroscience perspective, the practicing clinician must determine how best to manage anxiety disorders. Several recent international guidelines and related literature exist to guide treatment strategies and highlight emerging approaches [2, 52, 59–61]. This section is a practical introduction to this literature and will aim to integrate information from the preceding sections in a unifying way, while pointing out where further research is needed.

2.4.1 Considerations in the General Approach to Anxiety Disorders

Important general considerations for successfully managing anxiety disorders start with appropriate screening for these conditions, especially in high-risk groups, establishing the presence of comorbid psychiatric and physical illness (which is highly likely) and determining the severity of symptoms and their functional impact on the individual. Once the correct diagnosis has been made, and the need for treatment established, the choice of particular treatments depends on research evidence, specific clinical characteristics (which may be differentially targeted by the various treatment options), comorbid illnesses and other medications being used (which may constrain the pharmacological options), as well as the preferences and past treatment experiences of the patient (including tolerability of medication) and, finally, the local availability of the various possible interventions [2, 52].

The clinician can then select from a range of psychological and pharmacological options in formulating an individualized treatment plan. Psychological treatments include supportive counselling, interpersonal therapy, exposure therapy, traditional cognitive behaviour therapy (CBT), psychodynamic therapy and newer transdiagnostic CBT and mindfulness-based approaches [2, 52, 62, 63]. Evidence-based pharmacological options include several different categories of medication: SSRIs and SNRIs, other antidepressant drugs, benzodiazepines, alpha2delta ligands (specifically pregabalin) and other agents such as buspirone, antipsychotics and antihistamines, with several new agents in active development [2, 60, 62]. This broad range of treatments allows for considerable flexibility [2, 52, 60, 62].

While recommendations vary for individual disorders, an important initial decision is between psychological and pharmacological management. Research, including meta-analysis, suggests that patients often have a strong preference for psychological treatment, and that it is beneficial both acutely and for relapse prevention [2, 64–66]. Psychological treatment likely achieves its effects via modification of the brain circuitry described in Sect. 2.2, particularly via effects on the interaction between the PFC and the amygdala [10, 40, 42]. While the efficacy of psychological and pharmacological treatments for anxiety disorders has usually been regarded as broadly similar [2], a recent meta-analysis indicates that medications may be superior [62]. Efficacious therapeutic modalities include mindfulness, CBT, exposure therapy, relaxation training, psychodynamic therapy and eye movement desensitization and reprocessing [62]. CBT and exposure therapy are particularly widely practised and show equivalent benefit across disorders, except for SAD where CBT appears superior [67]. An often-stated advantage of psychological treatment over medication is that psychotherapy does not have side effects, though this claim has been refuted [68, 69]. An important disadvantage compared with medication is reduced availability due to therapists needing special training and the reality of treatment waiting lists, given that between 8–20 hour-long treatment sessions may be required [2, 62].

The reality of psychotherapy side effects notwithstanding medication side effects (including for antidepressants the FDA black box warning regarding increased suicidality), as well as drug interactions, discontinuation syndromes and, in some cases, addiction potential, is significant [2, 62, 70]. In addition, further large-scale, pragmatic, industry-independent trials are needed [71]. Nevertheless, the existing pharmacological options clearly target various components of the fear circuitry and molecular subsystems described above [38, 46], suggesting a strong theoretical basis for their use. The advantage of medications over psychological treatment, apart from greater efficacy [62], may be their ability to produce more rapid relief of symptoms, and that they require less clinician time [2]. Furthermore, they may be the more obvious choice for initial treatment of severe symptoms and severe comorbid depression [2].

Depending on the response to either psychological or pharmacological treatment, clinician's may need to determine if combination treatment should be offered. This is an area of active research interest, and while it remains uncertain if a combined approach is superior in the long term, there is some evidence that the addition of medication can enhance the efficacy of CBT in the short term, which may be valuable [2, 72–74]. A pragmatic and resource-conscious approach, given uncertainty in the literature about the comparative benefits of these treatment modalities alone or in combination, is the stepped care approach advocated by the National Institute for Clinical Excellence [61]. This proposes comprehensive screening and assessment, psychoeducation and active monitoring (step 1), followed if needed by low-intensity psychological interventions (including self-help; group support—step 2), progressing to high intensity psychological interventions (such as CBT) *or* medication treatment (step 3) and, finally, the combination of psychological and medication treatment, including inpatient treatment when needed (step 4).

Considering that anxiety disorders are frequently undiagnosed, and/or are inappropriately or under-treated, it is important to emphasize again the heavy disease burden associated with these conditions [1, 4, 12]. Given the range of treatment options, it is usually possible to develop a care plan that addresses the needs of the individual. In support of this, the advances in neuroscience described earlier are contributing towards the identification and development of biomarkers (including neuroimaging and molecular features) which can predict response to specific treatments and thus guide treatment selection and sequencing [75, 76]. In addition, further large prospective cohort studies, RCTs and meta-analyses of the medication and psychotherapy options will continue to refine treatment approaches [1, 2, 62]. Following from this, recommendations for the individual disorders will now be described.

2.4.2 Treatment Recommendations for Specific Disorders

Generalized Anxiety Disorder In line with the stepped care approach, psychoeducation and psychological interventions such as CBT should be considered. Evidence-based medication options include a range of antidepressants (SSRIs, SNRIs, TCAs, agomelatine and trazadone), pregabalin, benzodiazepines, buspirone, antipsychotics (notably quetiapine) and the antihistamine hydroxyzine [2]. For most patients, an initial trial of an SSRI is recommended, and there is some evidence for the superiority of sertraline and fluoxetine [61, 77], though meta-analysis suggests that SNRIs may in fact be the most efficacious [62]. Consistent with positive systematic reviews and meta-analysis, pregabalin is emerging as a valuable first-line agent, with the advantage of more rapid onset than antidepressants and the ability to assist in relieving associated depressive symptoms when used as monotherapy [53, 78]. While benzodiazepines can provide rapid relief in the short term, including while initiating antidepressant agents, there are concerns regarding tolerance and dependence, and long-term use should be avoided [61]. For non-response to a first-line option, trials of alternatives from different classes and with different neurotransmitter receptor targets should be attempted, e.g. switching from an SSRI to an SNRI, TCA or pregabalin [2, 60]. There is only limited evidence for dosage increase as a strategy, though higher doses of pregabalin may be the exception [2, 53]. Combination treatment should be considered in resistant cases, aiming to extend the breadth of neurobiological systems targeted, e.g. combining an SSRI or SNRI with pregabalin or buspirone or CBT [52, 60, 72], and there is evidence that the addition of CBT may be particularly valuable [72]. Further strategies, such as the addition of low-dose antipsychotics or regular benzodiazepines, are also described, though given the disadvantages as well as inconsistencies in the literature, these should likely be regarded as a last resort [2, 52]. Once a beneficial response has been achieved, there appears to be substantial ongoing benefit from staying on active treatment over the long term [2, 52, 60].

Panic Disorder and Agoraphobia The involvement of the fear circuitry and fear conditioning processes in producing anticipatory anxiety and avoidance in panic

disorder and agoraphobia [10, 17, 40] indicates the value of CBT and exposure therapy, which modify these processes [40, 42]. There is good evidence for the value of these psychological interventions, and they should be considered first-line, but they are not clearly superior to medication monotherapy [2, 52]. It is important to note that while these two conditions frequently co-occur, the DSM-5 clearly recognizes their independence [7], though there is little known on the best treatment approach for agoraphobia in the absence of panic disorder [2]. For first-line medication treatment, it is reasonable to consider similar antidepressants to those used for GAD, with the MAOI phenelzine, the RIMA moclobemide and mirtazapine being additional options [2, 52, 60]. The literature is inconsistent on the relative advantages of the different antidepressants, and they are likely equivalent in terms of both efficacy and tolerability [2]. As alternatives, there is some evidence for monotherapy with the anticonvulsants gabapentin and sodium valproate [2]. Several widely used agents, notably buspirone, bupropion and the beta-blocker propranolol, lack obvious efficacy and should not be utilized [2, 52]. Benzodiazepines are efficacious and may offer particular value in easing the heightened anxiety which can occur during initiation of antidepressants in those with panic disorder, but there is strong tolerance and dependence potential with longer-term use [2, 60]. If there is inadequate response to initial treatment, higher-dose monotherapy is worth considering [2, 60], as is switching between medication classes and combination treatment with agents from different classes, though antipsychotics do not appear to add value for acute treatment [2, 52]. Switching from medication treatment to psychological treatment is also evidence-based, and the combination of CBT and antidepressants also appears superior to either given alone for achieving an acute response, but there is no clear benefit of this combination for relapse prevention when compared to monotherapy [2, 52]. An important new development is the effectiveness of augmenting exposure therapy with the administration of the glutamate receptor partial agonist D-cycloserine, which may hasten and increase the overall response to therapy—discussed in more detail below [54, 79]. Finally, long-term treatment is beneficial, and though the optimal duration of treatment for relapse prevention is uncertain, durations of as long as 3 years have shown value [2, 60].

Specific Phobia This is the most common anxiety disorder and the one most comparable neurobiologically to fear-related responses in animals, highlighting the value of animal models [10, 17, 40]. Though this disorder has been under-researched in comparison with the others discussed here, there is clear benefit from multisession, exposure-based psychological treatments [2, 80]. In vivo exposure is regarded as most efficacious, but some interesting new work suggests the feasibility and value of computer-based virtual exposure—discussed in more detail below [81, 82]. The majority of patients respond to psychological approaches, and these should be first-line, but the addition of medication, particularly the SSRIs escitalopram and paroxetine, is evidence-based, especially for those who initially struggle to tolerate exposure [2]. There is no clear benefit for the addition of benzodiazepines as adjuncts to exposure therapy itself, but there may be some value for intermittent dosing to allow patients to tolerate feared but unavoidable situations, such as medical procedures [2, 52].

Social Anxiety Disorder There is the risk that SAD can be dismissed as mere "shyness" and not treated, an approach which can be avoided through careful screening [2]. This can be a debilitating condition, including high comorbidity with depression and substance use disorder [8, 11], but it may respond well to treatment. Psychological intervention is recommended, and in contrast to specific phobia and panic disorder, CBT is regarded as superior to exposure therapy [2, 67, 83], though there is emerging evidence for the augmentation of exposure with D-cycloserine [54]. There is proven efficacy for a range of antidepressants, including most SSRIs, SNRIs, phenelzine and moclobemide, while the benefits of TCAs are unclear [2, 83]. Alternatives include benzodiazepines, anticonvulsants (including gabapentin and pregabalin) and olanzapine, with higher-dose pregabalin now regarded as a first-line option [2, 52, 84, 85]. Importantly, neither buspirone nor beta-blockers are effective for generalized SAD as monotherapy [2]. There is still no final consensus on the relative benefits of any particular intervention. In terms of medication, SSRIs and SNRIs may be the best choices [83], while some evidence indicates that the combination of CBT and the SSRI escitalopram is superior to CBT alone [74]. A recent meta-analysis suggests, however, that individual CBT monotherapy is most effective [83]. For initial non-response, higher-dose antidepressant treatment is not evidence-based, but higher-dose pregabalin may be advantageous [2, 84, 85]. Switching to an alternative agent from another class and combination treatment are also recommended strategies, though the evidence of benefit is relatively weak [2]. Longer-term treatment is indicated, as the proportion of patients responding to treatment increases steadily over time, with ongoing benefit from staying on active treatment for up to 6 months after response [2, 60].

2.4.3 Pharmacological Advances: Further Thoughts on Alpha2delta Ligands

As already described, the alpa2delta ligands pregabalin and gabapentin are recognized treatments for a range of anxiety disorders, with especially pregabalin regarded as a first-line choice for GAD and SAD [2, 53]. While both these agents were originally developed as anticonvulsants [86], they are given special mention here as an example of the valuable influence of basic neuroscience and data gathered in other research spheres on modern treatment approaches for anxiety disorders. Alpha2delta ligands target voltage-gated calcium channels, thereby modulating the release of neurotransmitters from nerve terminals, essentially acting as analogues of GABA, the main inhibitory neurotransmitter, and thereby reducing neurotransmission in excited neurons [86]. Having been effectively used for epilepsy, it appeared that they had additional benefits, including for neuropathic pain and anxiolysis [86]. Based on this, and the robust preclinical research indicating a central role for the GABA system in the neurobiology of fear and anxiety [36, 46], extensive further preclinical and clinical investigation of these agents has been undertaken with regard to their potential to augment GABAergic pathways in the fear circuits and thereby treat anxiety disorders [53]. Gabapentin has shown some value

in panic disorder and social anxiety disorder, though admittedly as a second- or third-line agent only [2, 52]. Pregabalin, on the other hand, has emerged as an evidence-based first-line monotherapy treatment for both GAD and SAD [52, 53, 78, 84, 85, 87]. In GAD, there is additional evidence for adjunctive benefit when added to SSRIs in those who have not responded to monotherapy, as well as a direct effect in improving comorbid depressive symptoms [53, 88], and in SAD, long-term pregabalin may reduce relapse rates [89].

In comparison with other first-line treatments, pregabalin appears to offer equivalent efficacy and a more rapid onset of action than the SSRIs [90], though it is not more efficacious than CBT in SAD [83]. It does however offer a favourable side effect profile and lower risk of tolerance and dependence than benzodiazepines [53, 78, 87]. Nevertheless, discontinuation symptoms following withdrawal of pregabalin can occur, and there have been reports of abuse of pregabalin, especially in those with a history of other substance abuse [2]—concerns which warrant further investigation. Still, while further pragmatic, head-to-head studies between pregabalin and other first-line medications are required to confirm comparable efficacy, and direct comparison trials of pregabalin and psychological treatments are a notable gap in the literature, this is an agent increasingly being used in the modern pharmacological management of anxiety disorders.

2.4.4 Psychotherapy Advances: Focus on Exposure Augmentation and Mindfulness

Two relatively novel treatments which are gaining momentum in the psychological management of anxiety disorders include exposure augmentation strategies and mindfulness-based interventions (MBIs).

Though still largely employed in the research setting, augmentation of exposure therapy with the glutamate NMDA receptor partial agonist D-cycloserine has already been mentioned as beneficial in the management of panic disorder, specific phobia and SAD [2]. D-cycloserine administered just prior to exposure increases the likelihood of fear extinction, resulting in a more rapid response to exposure therapy, though does not appear to increase the total degree of response when compared to a full course of standard therapy [38, 40]. Theoretical justification for the use of D-cycloserine is based on the distribution of glutamatergic neurons throughout the fear circuitry and the role of NMDA receptors in fear conditioning processes relying on synaptic plasticity as described previously [38, 44]. This is a valuable example of how translational neurobiological research contributes towards successful clinical management. Importantly, while a recent meta-analysis confirmed the benefit of D-cycloserine for augmenting CBT-based exposure therapy for a range of anxiety disorders (panic, SAD and specific phobia) [54], a Cochrane review could not conclude in favour of D-cycloserine, though the authors commented that this was largely due to the poor quality of the evidence, and they recommended further large-scale studies [91]. Apart from D-cycloserine, other agents have been trialled to augment exposure therapy, including cortisol, catecholamines, yohimbine and oxytocin, with

partial research support for these approaches, though specific treatment strategies (dosages, timing of administration, etc.) and overall recommendations remain to be determined [79].

Mindfulness, on the other hand, is a rapidly growing wave that is sweeping through both psychiatry and broader society. There is significant "hype" surrounding mindfulness-based treatment approaches, and while due caution is advised in assessing their value and potential role, as should be the case with any new therapeutic approach, there is growing evidence of substantial benefit for treating anxiety disorders [92, 93]. Originating in eastern philosophical and spiritual practices based around meditation to develop attentional skills and awareness of present moment experience, mindfulness practices allow a shift towards equanimity and a non-judgmental attitude [94, 95]. In addition, there is a decentring from overidentification with arising thoughts and sensations, which has obvious application in relation to ruminative worry and physical symptoms of anxiety [94, 95]. The modern mindfulness movement, in the form of mindfulness-based stress reduction (MBSR), was initially focused on supporting those with chronic physical illness cope better with their symptoms [96]. It has since gained ground as a component of various treatment approaches, most notably mindfulness-based cognitive therapy (MBCT), dialectical behaviour therapy (DBT) and acceptance and commitment therapy (ACT), for a range of psychological and psychiatric conditions, including anxiety disorders [93, 94, 97, 98].

Clinical trials and systematic reviews show both an acute and sustained beneficial effect of MBCT, ACT and MBSR for a range of anxiety disorders including panic disorder, SAD and GAD [92–94, 99]. In terms of possible mechanisms of benefit, there are sound theoretical justifications to indicate that enhancing mindfulness may augment exposure and facilitate fear extinction [95]. While this still needs to be comprehensively tested, it is an intriguing possibility with special relevance to the anxiety disorders. These findings are promising, but it is important to note that MBIs have not consistently been shown to be superior to standard treatment [62, 94, 100], and there are important methodological concerns relating to the research conducted so far, most notably around satisfactory control groups, to determine if it is mindfulness itself (rather than some confounding variable) which is responsible for the apparent benefit [94]. Further research with larger study groups, active controls and longer-term follow-up are needed to clarify the true value of MBIs in anxiety disorders, while neuroscience research continues to clarify the neural mechanisms involved [101]. Pending this, mindfulness appears to represent a reasonable adjunctive or alternative treatment for specific patient subgroups (Arch 2013), or when first-line approaches have been unsuccessful, though it is likely to gain in prominence with time [92–94].

2.5 Conclusions: What's on the Horizon?

This chapter has highlighted the significant disease burden associated with anxiety disorders, discussed some of the issues relating to classification and described the fascinating and rapidly advancing neurobiological understanding of these distressing

conditions. Having subsequently reviewed standard treatment approaches, as well as recent pharmacological and psychotherapeutic advances, it remains to consider cutting-edge ideas that can carry the field forwards in the technological age. While transdisciplinary neuroscience is a prominent example of this and will continue to add value [10, 17], direct patient interventions which make effective use of existing technology present a fascinating opportunity which is beginning to be realized.

The wide availability and advanced level of development of smartphones, the speed and ease of use of internet-based platforms and the rapidly expanding world of virtual reality present new heights from which to view the study and treatment of anxiety. For example, the limited availability of trained psychotherapists in any one location is a problem potentially remediated by online therapy [102], while difficulties in ensuring adequate exposure to a feared stimulus in real-world sessions can be resolved using the essentially limitless options and fine-grained level of control provided by virtual reality platforms [81, 82]. Add in the constant presence of smartphones and other handheld interactive devices, and there are powerful tools for the collection of large volumes of individualized, health-related research data, as well as a convenient route for the direct and personalized delivery of therapeutic content anywhere, anytime [102, 103]. Finally, considering that invasive treatment approaches (such as deep brain stimulation, vagal nerve stimulation and transcranial magnetic stimulation), which may directly target the brain circuits involved in anxiety, are already in development or early clinical trials, it is possible that important advances in the treatment of anxiety disorders are on the horizon [40, 104].

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Semiotic Functions of Outsider Art in Counteracting Stigma

3

Ekaterina Sukhanova

Abstract

The article introduces a semiotic theory approach to explore the notion of aesthetic norm as applied to the field of outsider art. It establishes the connection between the semiotic mechanisms of art production and perception that underpin the potential of art to counteract stigma. All creative activity is a communicative process relying on a dynamic mediation between autonomy and connectedness. The dialogic potential of art may be seized upon to break the stigmatization cycle by preventing a market to be loaded with negative content as well as by improving the artist's self-esteem. The use of outsider art thus may be instrumental in changing the context in which mental illness is experienced and promoting reintegration.

Art perception relies on a dialogical communication between the artist, the audience, and the cultural context, which allows for new interpretations to be made and new meanings to be generated. Inherent in all artistic activity, these dialogical mechanisms become particularly striking in outsider art and can serve as a basis for fighting stigma. All artistic creation is a bridge to the social: artworks can exist only among other artworks and must be preceded by them. "An isolated text is incapable of generating meanings; like any dynamic generating system, a text requires input

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of outside information, which in this case implies an interaction with other texts and cultural environments" [1].

The aesthetic value of an artwork does not depend on the fulfillment of the norm. In nonartistic communication, it is not the language but it is the content that carries information: we do not pay attention to the shade of red used on a stop sign. While this aspect of communication remains present in art, it is not exclusive nor is it necessarily the primary one. Although in a nonartistic communication it is precisely the adherence to the rules that ensures adequate transmittal of a message, in a work of art, this proves insufficient and often even detrimental. Simple adherence to a set of rules will not yet create aesthetic value. "If we dealt only with a strict system of rules, each new work would represent an exact copy of a previous one, redundancy would prevail over entropy and the artwork would lose its informational value" [2]. Kitsch is an example of artwork that copies existing models unquestioningly, without adding a meaningful change that could alter the interpretation.

If mere adherence to the norm does not yet create artistic value, neither does the complete destruction of the norm. The long-standing popular misconception of outsider art, going back to Jean Dubuffet's first coinage of "art brut" (which is still being most commonly rendered in English as "outsider art," in spite of many attempts to find a less value-laden term), presents outsider art as being free from—or unsullied by—existing conventions, social or aesthetical. This romanticized notion of the outsider artist as the modern-day "noble savage" is easily challenged in an age when access to the Internet is widespread and long-term institutional isolation is rare. More importantly, this contradicts the nature of artwork as a semiotic structure.

Indeed, art without any cultural or social context is impossible. Limitless choices, absence of any rules, and absolute freedom from any imposed limits are not the ideal state but the death of communication: this is why a reader facing a text produced in an unfamiliar writing system perceives it as a random collection of symbols. All art represents a dynamic relationship between following an existing aesthetical norm and deviating from it. At a deeper level of analysis, a work of art exists at the intersection of many concurrently active aesthetic norms. The unique nature of art consists in establishing relations among a wide variety of languages and codes present in a culture and transforming these languages from a tool into an object of their work.

Art production allows a maximum freedom of choice for the individual artist while at the same time providing a connection to existing rules, conventions, and structures. The greater the number of potential choices available to the artist, the more valuable will be the information represented by a particular choice. The audience's assumptions of the author's intention and accountability play a particularly big role in the interpretation of outsider art. The greater the awareness of an existing artistic convention to which the new work is responding, the more acute is the audience's perception of the unique qualities of this work. The individual and the universal are no longer isolated but, on the contrary, require each other.

In the words of Joseph Brodsky, a Nobel Prize Laureate for Literature, "the more substantial an individual's aesthetic experience is <…> the freer <…> he is" [3].

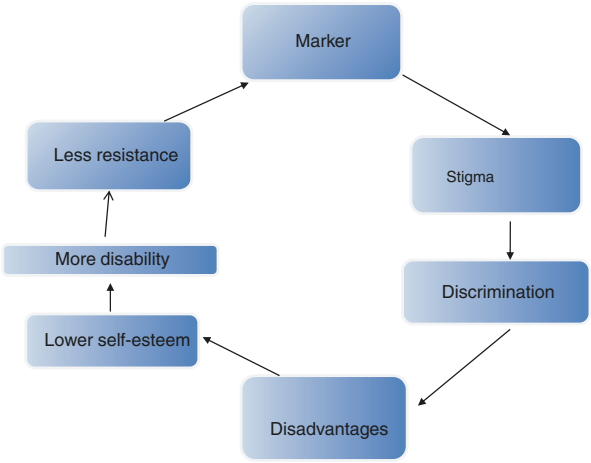

Fig. 3.1 Cycles of stigma (after Norman Sartorius [4])

This is even more true in the case of patients struggling with mental illness, who often find themselves constrained both by the reality of their medical condition and by the social stigma surrounding it. To help visualize the potential of art for combating stigma and promoting inclusion, we will turn to the conceptual model of "vicious circles" of stigmatization as formulated by Sartorius [4]. According to this concept, a marker that allows a person to be identified with it can be loaded with negative contents by association with existing stereotypes and prejudices. Once a marker is negatively loaded, it becomes stigma, and the individual who bears it will inevitably be stigmatized. The experience of discrimination leads to impaired functioning and reinforces stigma, establishing a vicious circle (Fig. 3.1).

Art can counteract stigma by weakening or breaking this vicious cycle in two parts. First, the dialectical mechanisms of art may be built upon in order to prevent a marker from becoming associated with stigma. Stigmatization has at its root the objectification of the other that is denying him or her the right to be an independent agent in the communication process. It also involves rejection of any new information that may lead to altering existing constructs. In sum, stigmatization is a breakdown of communication. Art affords us an alternative: a model of dialogue in which the other is accepted as an equal partner in the communication process. "I cannot become myself without the other; I must find myself in the other, finding the other in me (in mutual reflection and perception)" (Fig. 3.2) [5].

Further, art allows for critical distance, retrospection, and vast opportunities for individual choice and thus may be conducive to an improved self-image and self-esteem. In producing art, the artist interacts with his or her internalized objects. The creative act can become a therapeutic tool, extending from verbal experiences into nonverbal and preverbal experiences across all stages of psychological development: while providing a path for a validation of an artist's own experience, the creative act is also intrinsically linked to abstraction or the ability to see the universal in the individual.

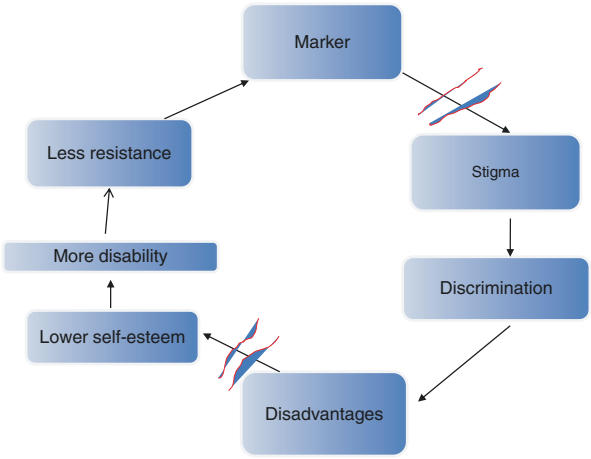

Fig. 3.2 Art's potential to interfere with the stigmatization cycle

The twentieth century critical theory made much of the art's ability to show things anew for the reader or viewer, be it Brecht's "alienation" (*Verfremdungseffekt*) or Shklovsky's "estrangement" (*ostranenie)*, but it was Bakhtin who focused specifically on the critical distance that is being created between the artist and his or her immediate experience. This phenomenon, for which Bakhtin coined the term of "being outside," is sometimes translated as "outsidedness" or "exotopy" (*vnenakhodimost*). After the initial fusional stage where the artist and the character merge, the artist has to disengage from the character's affective state and establish a boundary in order to complete the creative work: "Aesthetic activity begins properly only when one returns into oneself at one's place, outside of the one suffering <…>" [5]. For Bakhtin, this mental distancing is a necessary prerequisite for artistic expression. Regardless of whether a narrative character is meant to be purely autobiographical (or the visual artwork is meant as a self-portrait)—although this is very common in outsider art—the artist has to transcend self-identification with the created image and assume an external point of view.

The creative process acquires therapeutic properties as it aids the artist to cease being engulfed by emotions and start developing an integrated identity. Capitalizing on the intrinsic properties of the artistic process reaffirms the artist's dignity and helps counteract not only social stigma but self-stigmatization as well: "The patient's particularized, broken, fragmented self must fit into a more manageable flow. Then, the patient eases his/her way into a slow process of identity change. <…>Self-transformation is the objective of all art, and the [patient] artists <…>no less than others" [6].

Aesthetic function arises at the intersection of a highly individual activities and established cultural codes and structures. Any art object is saturated with values and must be analyzed in relation to its surrounding society in order to understand how it is perceived. It is the human collective in a given time and place that may or may not perceive the aesthetic function as the dominant one (e.g., objects that had practical or religious significance at the time of their creation may be perceived primary as

artistic objects today). The same artistic object might have multiple functions, ranging from the aesthetic to the therapeutic, social, and ceremonial, which might vary both diachronically and synchronically: "Stabilizing the aesthetic function is a matter for the collective and is a component in the relationship between the human collective and the world" [7]. The more the viewers are aware of an existing cultural convention to which the artwork is responding, the stronger they perceive the individuality and uniqueness of the new creative approach.

No longer isolated, the individual and the universal require each other in art. The unique nature of art consists in establishing relations among a wide variety of languages and codes present in a culture and transforming these language from a tool into an object of their work. The interaction between norm and innovation functions as a mechanism generating new messages or meanings. This dynamic relation between autonomy and connectedness underpinning the processes of art creation and perception is akin to Ricoeur's dialectic notion of identity. Ricoeur sees the notion of selfhood (*soi-même*) as created through a dynamic mediation between the two poles of personal identity, the pole of "sameness," (*la mêmeté*), understood as a set of innate or acquired attitudes and capacities that enables a spatiotemporal coherence, and the pole of "self-sameness" (*la laipséité*), understood as the most concrete and particular core of a subject that enables initiation of new things [8].

The creative act can therefore be considered as unconscious repairing of the body ego, conducive to increased individual psychological stability (feeling connected to oneself) and collective inclusion (the capacity to be connected to others). Erikson [9] also suggests that the individual gains a "sense of reality from the awareness that his individual way of mustering experience, his ego synthesis is a successful variant of a group identity," and this is understood as conferring "status and stature" on the individual [9]. Connecting spectators to meaning just as it connects the authors to collectivity, art fosters cooperative communication in which dignity and individuality of a mental health patient may be reaffirmed.

One of the most common genres in outsider art across cultures and time periods is the self-portrait and the portrait in general. The portrait relies on body image as a frame of reference for all cognitive functions and a key element in emotional functioning. Oscillating between a metonymical representation of a human being and a projection of certain cultural and social assumptions, the portrait has been referred to as "…the most philosophical painting genre. It is built on the juxtaposition of that which human beings are and that which they ought to be" [2]. Situated between semantic oppositions, portraits have a particularly high communicative intensity. "A portrait is akin to a double mirror: through it, art is reflected in life and life is reflected in art. It is not only the reflections but also the realities which switch places" [2]. The borderline between the reflected and the reflection is not a fixed one: a binary unit is transformed to a multidimensional construction. The reconstruction of the body image in portraiture may be an anchorage point in allowing the artist to perceive heterogeneity as empowerment.

Art has the capacity of changing the structural self-orientation not only of the artist but also of the viewer and, over time, the larger sociocultural context as well. "In the realm of culture, outsidedness is a most powerful factor in understanding.

It is only in the eyes of another culture that foreign culture reveals itself fully and profoundly (but not maximally fully, because there will be cultures that see and understand even more)" [10]. To continue evolving, any living culture relies on constant exchange between the peripheral and mainstream, archaic and innovative, and "insider" and "outsider" cultural production, a dynamic which parallels the construction of an individual's notion of self through interaction with cultural others. Asymmetry and ongoing productive exchange between central and peripheral realms are more than simply a desirable change of pace: it is the very mechanism that assures the continuation of a semiotic system. When this dynamic is interrupted, e.g., in isolated or totalitarian societies, the resulting loss of intersubjectivity leads to cultural stagnation that is inevitably fraught with decline and obliteration. Just as an individual deprived of outside stimuli, a culture deprived of exchange with other cultures is at a risk of becoming dysfunctional. Culture as such is polyglossal.

Historically, scholarly interest in outsider art first arose out of a specific clinical task, using patient art to confirm a mental health diagnosis. The use of patient art is no longer limited to differential diagnostics, however. Because all artistic activity is also a communicative act, working with patient art may aid the clinician to gain a better understanding of the preserved aspects of a patients' personality, beyond the pathological syndromes, and build a better rapport. In this way, art is a resource for the clinician in effective planning of specific medical and social rehabilitation strategies. At the community level, public exhibitions of psychiatric art, as promoted by the World Psychiatric Association and its section on Art and Psychiatry, may also be an effective tool in anti-stigma campaigns. These exhibits serve a greater purpose than merely disrupting the historic association between mental health and art in institutional space: they counteract negative social stereotypes of mental illness as well as undermine the cultural mechanisms for stigma. For many of the artists, allowing their work to be seen might effectively be the only meaningful form of communication with other individuals or with the outside world at large. The process of participating in a creative act already engages artists in a conversation, and many are proud to have their art exhibited and their message finding resonance with others. This communicative value of art does not hinge on any formal official recognition or even on an opportunity to socialize with peers; although these positive experiences are desirable, their absence does not yet efface the dialogical dynamics.

Stigmatization has at its root the turning of the other into an object, effectively denying him or her the right to be an independent active partner in the communication process. The psychological basis of stigma is the destruction of communication. Art, relying on the opposite mechanism, may be instrumental in changing the context in which mental illness is experienced, thereby reducing stigma and promoting reintegration. With its powerful potential for changing both the self-regard of the artist and the externally imposed identity, "art is the anti-destiny," to use an expression of Malraux [11]. The dialogical potential of art allows us to better grasp the origins of vulnerability as well as the cognitive, emotional, and behavioral issues critical to improving the experience of self.

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How the Brain Creates Art and Dreams

4

Hans-Otto Thomashoff

In the following article, I would like to address some fundamental questions:

Why does the brain produce art? What are the influences of the brain onto the art production? How do biology and psychology jointly form art and dreams? How does the art reflect the self-perception of the artist?

The task of the brain is to produce an image of the outer reality which (usually) allows for a reasonable coping mechanism. Each living creature depends on keeping a balance of its bodily functions; without such balance, it dies. While in plants the direct contact from cell to cell is enough to assure the distribution of water and nutrition, animals already at the level of the first multicell organisms began to develop a nervous system as a coordination system for the tasks needed for survival. In the beginning, this was very primitive. Its only task was to assure the supply with oxygen, water, and food. With evolution progressing, its tasks expanded: sex for the preservation of the species, stable body temperature, breathing, and hormonal systems, just to mention a few. All these functions depend on a central regulation.

Human beings so far have the most elaborate nervous system. Headed by the brain, its activity has become so complex, that we have gained a consciousness and define ourselves as humans largely by the results of the brain's activities. Consecutively the main criterion for the death of the person is the end of all brain activity.

While most of the numerous brain functions never become conscious to us, some tasks demand purposeful actions and depend, at least to some extent, on conscious decision-making. Finding water, food, or sex partners implies active behavior in the world we live in. By means of the hormonal systems, the brain processes imbalances which result in sensations like hunger, thirst, or sexual lust and strongly demands actions to reinstall the original balance. We have to actively drink to quench our thirst and maybe even do something to find water to start with. (Personally I love the strategy of the Kalahari bushman in the Jamie Uys film

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"Animals are Beautiful People": He catches a baboon, feeds it with salt and then lets it sit and wait all night bound to a tree. The next morning the poor animal is so thirsty, that when the bushman lets it free, it nonstop runs to its hidden source of fresh water leading its torturer to it). Also finding food can depend on various more or less creative activities, even if you are not French, not to mention the satisfaction of our sexual desires.

At some point the increasing complexity of thinking resulted in an expansion of its tasks beyond simply securing the basic physical needs. Fantasy and with it a psychological reality evolved. Even though inevitably linked to the body, the psychological system developed needs on its own. Without external stimuli as mental nutrition, we cannot exist.

Imagine you are offered a job where the only thing you have to do is nothing. In exchange, you receive a generous salary. Would you say no? Sounds tempting, doesn't it? Canada, 1954: Long lines of people were waiting outside to be able to participate in a psychological experiment which exactly demanded of them to do nothing. They just had to rest in bed with their hands and legs loosely tied and their eyes focused on the ceiling. Foods and drinks were served as desired, and at any point in time, they could resign.

Most of the participants took the chance to sleep. When they woke up again, they started to sing or whistle after a while. Or they started talking to themselves. After a couple of hours, they began to feel discomfort. Even though it meant waving their salary, the first ones stepped out. Those who stayed within 24 h all began to hallucinate. The experiment had to be terminated prematurely. The participants who stayed until the early end were not able to resign themselves; they all were acutely psychotic [1]. Deprived from external stimuli, our psychological balance is disturbed as is our physical balance without food and water.

Not only a severe deterioration of our physical stability leads to death but also a massive disturbance of our psychological demands. As a result suicide is the eighth most common cause of death in human beings; in the age group between 15 and 24, it is even rated second. In the United States alone, each year 30,000 people commit suicide; that is one in every 18 min [2]. But what evolutionary benefit do we get from a brain that makes us dependent and creates an enormous risk for survival?

A tremendous one! The organism's capacity to adapt to an ever-changing world was multiplied and sped up almost indefinitely. Our dependency from outer stimuli is the basis of our ability to learn and therefore to adjust ourselves apart from the classic biological laws of mutation and selection. But that is not all. When language was introduced step by step, the learnt knowledge could be passed on to the next generations, even more so with the invention of writing. Recently the Internet has created a pool of information accessible to everyone and unlimited in time and quantity.

If we consider all that, is it then still a surprise that one of the constant constructive processes in the brain is art? If constant production is the way the brain works, is it then not more surprising that, within all the creative overflow, still (most of the time) the outcome also includes an image of the outer world that sufficiently resembles it to assure the survival in it?

It is exactly this constant production of content on the base of formerly stored experience dating back to the first prenatal impressions which is the root of creativity, be it manifested in dreams, in art, in hallucinations, or in any other mode. Dreams, as Freud already suspected, most openly reveal and yet at the same time conceal the constructive process on the base of the formerly stored experience. Due to their free connective creation, they seem to derive from a different world, but nevertheless they are based on the brain structure to the date they are generated.

Yet, interestingly enough, the integration of our current scientific knowledge of the brain's functioning into understanding the psyche still is massively suppressed by subconscious forces, especially irrational denial.

If we look at how the connective structure of our nerve cell system evolves, we easily observe two very simple and efficient rules: Only where there is a stimulus, a structure is built, and every existing structure tends to be used again resulting in its reinforcement. It is like a street that is being built by driving on it, with a tendency to use it again, each time adding a new line.

Even though well proven and rather simple in nature, the consequences of this scientific basis are widely ignored. We learn about the impact of the genes on who we are, but if you look at the facts, their importance must be rather limited. The number of our genes is about 22,500. All human beings share 99.9% of them. Nevertheless we show a huge variety of differences. So we have to look at the genes like at letters of an alphabet creating our features under the influence of the environment. It is the number and order of them being activated resulting in the language of who we are.

Similarly, crucial influences onto the creation of our brain structures, to date, even though obvious, are completely ignored. If a connection between two brain cells depends on an outer stimulus, all information in the brain has to be rooted in such stimuli until the complexity of the brain structure itself allows it to create its own inner stimuli—the starting point of abstract thinking. As a result the first information to create our brain structure unquestionably is that of our prenatal life in the uterus.

Neurology offers a strange observation which easily is unveiled as a proof for this statement. The sensory representation of our bodily surface in the brain provides the evidence (Fig. 4.1). It is distorted. Not just are hands and lips bigger than in the actual body (because of their higher sensitivity more stimuli originate from them), but also lips and hands are in close proximity to each other, as are feet and genitalia, representing the position of the fetus in the uterus and thus, in opposition to Freud's concept, resulting in a rather profane explanation for foot fetishism. The way the stimuli arrive in the cortex, they create its structure.

From this understanding a new light is shed on our concept of paradise. We all have been there. All our brains have a stored experience from a time when we never suffered from hunger, from thirst, from cold, from loneliness, and, probably most importantly of all, from fear. Subconsciously a force in us wants to return to this lost paradise—and for moments we actually can, for example, through meditation. Religion promises us that we will ultimately return. Indeed we do yet unfortunately just for seconds and not for eternity.

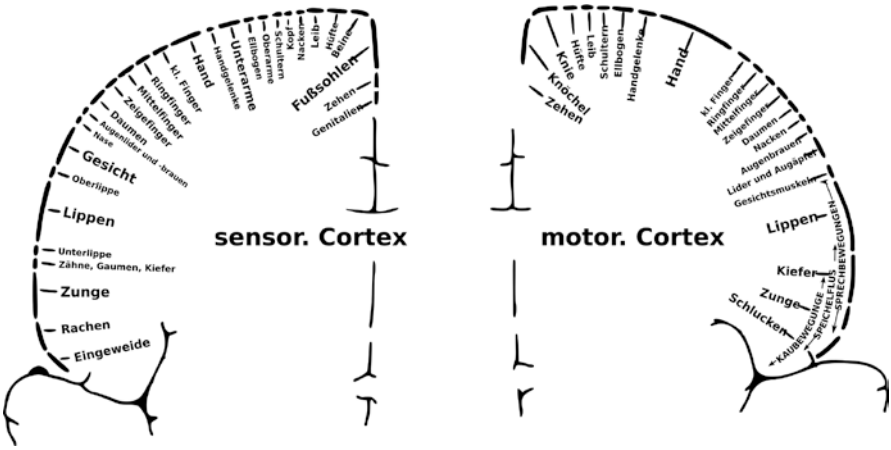

Fig. 4.1 Homunculus, source: Internet

An Alzheimer patient loses his memory starting with his short-term memory. The earliest experiences remain stored in the memory the longest. A brain that is switched off in the process of dying therefore will lose the youngest stored information at first, then go backward in time, and in the final moment return to the earliest stored experiences, those from birth (people who survived having entered the process of dying describe the tunnel they entered) and from the life before birth—the completely sheltered paradise. Here we find a biological explanation for the supposed proof of its existence somewhere out there.

Immediately after birth, the newborn starts to connect with the outer reality. The most determining factor in this conquest of the world is other people, as the brain reliably distinguishes between living and nonliving objects, mainly through its mirroring cell system.

While in the beginning the other is only present in his role in the here and now, resulting in different concepts of partial object relations, the evolution of the capacity to store the image of the other over time is the first step toward an integration of the object.

Many of the earliest impressions which a brain perceives and which lead to its structure thus still are unknown and seem mysterious to us. In part this is because the first impressions are not verbally represented but do consist of physical sensations as well as of auditory and visual impressions. This is why they seem to be strange and foreign to our more or less adult way of thinking. At the same time, resistance toward the earliest memories may add to their repression. Maybe the early paradise was too good to be abandoned and its loss traumatic.

Yet it is the essence of these first perceived impressions which constitute what Freud named the unconscious. I am convinced that looking at the biological buildup of the brain, no other explanation is possible but to understand also the hidden traces of the unconscious as a result of early experiences, mainly of those from inside the

uterus as well as of those from inside the own body of the growing embryo and fetus with needs and drives evolving within. Only if one claims a force outside of our perceivable existence, like a god, an alternative to this explanation may be stated. Yet, even though common, there is no logical argument to support this alternative view of the world, which is something I will come back to.

For now let us look in detail at those influences building up the structure of the brain and thus being the roots of all its creations including art. Brain activity alone does not automatically result in the creation of art—this statement hardly needs an illustration. The knowledge which was created by a generation also needs to be passed on to the next to be accessible for transformation. Cold-blooded animals lack that ability—reptiles live without culture—which was only developed in warm-blooded creatures. Only their brains have special areas, which are sensitive to hormones like cortisol, which directly affect the activation of genes and therefore the development of certain traits, so that, for example, stress leads to an emotional reaction and a learning process which through changes in behavioral patterns then is passed on onto the next generation. The capacity to adapt no longer depends on the rare chance of a beneficial mutation but directly is able to react to environmental changes.

Because of this enormous advance in adaptability, it is thanks to our brains that humans live in the most diverse surroundings, be it the jungle near the equator, the jungle of our cities, a remote island in the South Pacific, a high mountain region in the Himalayas, or the icy world of the polar region. Even more so, people are able to adapt to situations which at first glance seem unable to cope with. They adjust their behavior to roles like that of torturer and prisoner [3] to that of slaughterer and martyr and tend to pass these perverted roles on to the next generations (which is one of the major likely causes of the perpetuation of wars and homicide in some parts of the world).

The deep-rooted effects of transmitted thinking in the creation of societies and within it onto its art can lucidly be observed in Christian medieval art, which was inevitably dominated by religion. Medieval art had to serve Christianity. Tradition demanded this self-limitation of content and style until the Renaissance revolutionized the perception of the world and liberated art from its tight boundaries.

Strangely enough in recent years, Christian fundamentalists in Western societies intend to turn back the clock and reintroduce the dominance of religious belief onto their societies and cultures by implementing a so-called “intelligent design” concept according to which there supposedly is scientific evidence of a planning power (a god) behind the evolving beauty of evolution.

In his recent book *The God Delusion*, neo-Darwinist author Richard Dawkins sums up contrary arguments. For example, he states that the nonexistence of a god cannot be proved but neither can the nonexistence of flying teapots or spaghetti monsters in space, claiming that it is not assumptions but scientific methods which define science. He also presents a list of the crimes that were committed in the name of faith to support his antireligious agenda. Furthermore he states that also without the creation of a fictional “god,” the world can be explained from a scientific point of view including the evolution of moral guidelines for human interactions. He

considers religion a by-product of evolution which according to him is transmitted like a virus between people.

In my view, Dawkins is right, yet his arguments are not new and often somewhat superficial. I doubt that the simplification he gives is able to explain the deep roots of human religious needs. I prefer to understand religion from a psychoanalytic point of view linking it to scientific evidence of our psychological development: Once we become self-perceptive during our early years of life, we start to ask existential questions. As the answers to those inevitably have to remain frustrating, we have created the phenomenon of a god to try to explain the unexplainable. Consecutively it is not a coincidence that the image of god evolved parallel to the evolution of the psyche and to the evolution of societies. The early gods were part of nature explaining things mankind did not understand like lightening and other natural phenomena. On the next level, gods were transformed into a family which had obvious parallels to ordinary family life—or doesn't the Zeus family remind you of Denver Clan?

Parallel to the process of psychological integration which any child goes through in normal development, also the concepts of god then became more integrated resulting in the single patrimonial figure of monotheism. Again this new one and only god reflected the circumstances of its creators. The early Jewish god was as dangerous as was the everyday life of the Jewish people. Dawkins provides us with a shimmering caricature: "The God of the Old Testament is arguably the most unpleasant character in all fiction: jealous and proud of it; a petty, unjust, unforgiving control-freak; a vindictive, bloodthirsty ethnic cleanser; a misogynistic, homophobic, racist, infanticidal, genocidal, filicidal, pestilential, megalomaniacal, sadomasochistic, capriciously malevolent bully" [4].

Later in the New Testament, the god concept gained kindness and then was linked to a pantheistic experience of unity with the universe. At the same time, human emancipation allowed the option to fully abolish the need for a god, as Woody Allen put it in his film "Scoop": "I was born into the Hebrew tradition, but when I got older, I converted to Narcissism."

Parallel to the psychodynamic development of each individual psyche (in societies where a high level of psychological integration has been reached), religion underwent fundamental changes as did the creation of art, both embedded in the progress of the joint wisdom of mankind which still is by no means evenly distributed to date (resulting in different concepts in different societies and even within them to explain the world).

But in addition to those learnt traditions that reflect themselves in the art, are there also biologically inborn traits? Do we have artistic genes?

At this point it is certainly too early to answer this question. Also the existence of certain genes does not guarantee that they are necessarily activated. Yet, first results make it likely that there are some genetically determined inborn esthetic priorities all human beings share.

"Symmetry is beautiful." Psychiatrist Manfred Spitzer tells us why: "A symmetrical body is a healthy body. This rule not only is in force in humans, but also in animals. The reason for it is simple: Infections, parasites, deformities and other illnesses

of the body most commonly are not evenly affecting both arms, legs, eyes or ears. Illness, whatever its cause may be, therefore commonly leads to asymmetry" [5].

Cultural history, especially the abundant heritage of classical architecture, states proof for this observation from the natural sciences. But still there are other factors of beauty than symmetry alone. One may relate to Freudian concepts of round forms or other characteristics of gender, or one may take a stroll to the shopping malls of our cities to observe how shiny objects attract the eyes of many of our fellow citizens—an effect which obviously is not limited to tribal cultures which gave away precious belongings in exchange for some glittering glass pearls. The mental root of this sometimes disadvantageous behavior may likely be our dependency from water. Stone Age people had to search for water with their eyesight in the savannas they lived in (I mentioned the still fashionable Kalahari strategy earlier on) and were not like, for example, cats able to sniff it. Similarly we are attracted by light, by the shining flames of the warming fire (which may be linked to the other humans likely to be encountered nearby), unless its dimensions are threatening (burning disasters).

Due to our social nature, our eyes tend to wander to any live object; the more human, the more attracting it is (not necessarily attractive). Other eyes are like magnets to our own visual system; our attention is immediately drawn toward them. Anything resembling a human being or another live object is in the center of our perception. This is even stronger in baby schemes. Inevitably we sympathize with anything that resembles an infant, yes, even with cars, although any rational thinking would contradict that. Carmakers like Volkswagen (Beetle) and Mazda without hesitation make use of our weak spots.

Key stimuli force their power upon us. We react like a warbler with a baby cuckoo in his nest—the bigger the stimulus, the more we adore it. For the little warblers, this means jumping over the edge of the nest (because the baby cuckoo's bill is brighter); for us the consequences vary. Usually they are linked to our basic needs, to food or sex. Art psychology has collected the evidence of those traps of our perception, which still await being likely linked to some genetic source some day ahead. We hardly resist oversized breasts, legs, eyes, shoulders, etc. [6].

We can assume that all these influences also find their way into art. Yet, the characteristics that decide whether we like a work of art or not tend to be rather simple. In order to appeal to our taste, we need to recognize some familiar aspects in an artwork (which makes it dependent on our artistic education), and at the same time we want to be surprised by something new.

Interestingly enough this "law of art taste" has been proven in animals as well: "A vervet monkey and a chimpanzee were given dies with colorful ornaments. They were allowed to choose some of them to play with. They preferred regular forms (avail or radial symmetry) over irregular ones. Also the color preference of the animals followed certain aesthetic criteria. After a few turns the monkeys and apes tended to switch their color of choice, as do people following the trends of fashion" [6].

Taken this into account, it will no longer surprise us that some artists reach their fame long after their death. Van Gogh's stylistic inventions depended on the

acceptance of impressionism to make their pictorial complexity understood and have their individual language of beauty integrated into the context of the art historical ideal.

It is not culture alone that creates its impact onto the oeuvre of an artist, which also becomes visible in the following phenomenon: A brain has to mature, leading to stylistic phenomena in certain ages. When my 3-year-old daughter is drawing a person, she tends to focus on the head and then add legs and arms. The skipping of the trunk of the body is typical for her age. Curiously enough this basic stylistic oddity is characteristic for the art of children aged between 2 and 4, but it is also found in tribal art as well as in the drawings of severely ill psychiatric patients, mainly those suffering from chronic schizophrenia and dementia (Fig. 4.2). Consequently we seem to be confronted with a minor observation leading to major assumptions. Obviously the "tadpole figure" person reflects a developmental stage of the psyche, respectively, of the brain. Given the fact that early cultures produce the same stylistic features as young brains, there must be a parallel between the evolution of psyches and the evolution of cultures. On the other hand the fact that psychiatric illness results in a transformation of thinking processes (visible in the drawing style) resembling those of children can be seen as an evidence of the regressive potential of certain psychiatric conditions [7].

Despite all these biological influences mentioned, art is not simply an inborn capacity. It has to be elaborated by the cultural tradition it is developed in. Yet even then it is not culture alone but also the life experience of the artist apart from his or her artistic training which leaves traces in the art. Just on the basis of the given biology and the stored biographic experience, the artist starts to interact with the culture.

How subtle the psychodynamic influence on an art can be, the oeuvres of several artists especially those from expressionism clearly reveal. As an example I give you two self-portraits of the German expressionist Ernst Ludwig Kirchner from 1926 (Fig. 4.3) and 1917 (Fig. 4.4) representing the highly changing self-perception of

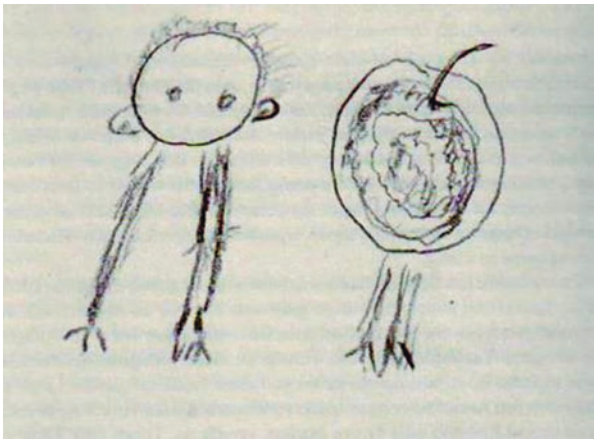

Fig. 4.2 Anonymous: Figures, cited from [6]

Fig. 4.3 Ernst Ludwig Kirchner: Self Portrait, 1926

the artist due to a narcissistic personality disorder he suffered from and which was a major cause for his suicide in 1938 [8].

After thus having also focused on the various noncultural aspects which influence the creation of a work of art, the last remaining question is: How does an artwork become recognized as such, and how does it become integrated into the temple of appraised art history? The answer is: It is the same rules of interwoven biological, psychodynamic, and cultural influences that lead to its creation, which also determine the interpretation and with it the attributed artistic value to a work of art.

As an anecdote goes, Andy Warhol once was asked by a young artist what he should do to get onto the cover page of Andy Warhol's influential art magazine, which would have made him an imminent success. The simple answer was: "Sleep with me." Usually it is not that easy to explain the course of an artistic career. More commonly it is different strategy that opens the gate of the temple of fine arts. An artist whose individual psychodynamic connects with the stylistic tradition of the

Fig. 4.4 Ernst Ludwig Kirchner: Self Portrait, 1917

culture he is in creates an oeuvre in which his subjectivity reaches out to an interindividual level and transcends toward meaningfulness for society. This does not necessarily have to coincide with the artist's intention. For example, the German Ludwig Meidner in 1912 painted apocalyptic scenarios of burning cities and people in panic which later were interpreted as visionary intuitions of the upcoming disasters in the First World War.

Similarly art brut was not accepted within the frame of the concepts of art until Dubuffet and others integrated its stylistic particularities into the field of the fine arts resulting in a reciprocal acceptance of previously rejected artworks. They were not created within the tradition of the academic art, but the tradition changed and incorporated what had been brought to life outside of its former boundaries. Nowadays, the drawings from the Prinzhorn Collection, the paintings of Aloise, and many more

have entered museums and the art market on an equal level as others. Nevertheless these evolutions of traditions do neither progress evenly within a society nor between different societies. Another anecdote may reveal this: A bathtub which had been filled with grease and other things by Joseph Beuys was first used to cool beer and then laboriously cleaned by an eager cleaning woman who thus faced charges of destroying a highly valuable work of art.

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Co-morbidity in the Severely Mentally Ill: Cardiometabolic Risk Factors, Prevention and Intervention

5

H. L. Millar, I. Salloum, and M. T. Abou-Saleh

Abstract

Co-morbidity represents one of the greatest challenges for twenty-first-century medicine. A high prevalence of co-morbidity in the severely mentally ill (SMI) has been well established leading to a significant impact on quality of life, life expectancy and premature death by 15–20 years. The major recognised contributor to excess death is cardiovascular disease.

Known risk factors include smoking, obesity, alcohol and drug misuse and diabetes. The field of knowledge of the linkage between common psychiatric disorders and cardiometabolic risk is growing with a focus on common pathophysiological and inflammatory processes in addition to the already well-recognised cluster of risk factors which have been described in the past as 'metabolic syndrome'.

International/national guidelines and consensus statements provide the guidance and evidence to optimise screening for and management of risk factors with increasing emphasis on early intervention with lifestyle changes and treatment review.

In this chapter, we have prepared a narrative review of the relevant literature complimented by the authors' experience of providing holistic care for the SMI. Also we refer to the evidence for shared pathophysiological mechanisms and cardiometabolic risk factors contributing to the high levels of co-morbidity

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in this population. Finally we make recommendations for screening and treatment outlining effective interventions to improve quality of life and life expectancy.

5.1 Epidemiology of Co-morbidity in the Severely Mentally Ill

Non-communicable diseases (NCDs) and mental disorders account for a high proportion of worldwide morbidity and mortality. The four NCDs are diabetes, cardiovascular disease, chronic respiratory disorders and cancers. Over the last 20 years, there has been a shift of disease burden, measured as disability-adjusted life years (DALYs), from communicable diseases to NCDs, with neuropsychiatric disorders contributing to 28% of the overall disease burden.

The WHO pronouncement that health was a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (WHO 1948) and the slogan 'no health without mental health' highlighted the importance of the need for an overall sense of well-being before a person is considered healthy [1].

Co-morbidity, or the coexistence of several chronic disorders in one individual, has therefore become a major public health concern and a challenge to the current model of health care. With the increase in the prevalence of co-morbidities, the current challenge of the NCDs is only more evident especially with diabetes now considered a global epidemic.

Studies demonstrate that NCDs share common modifiable risk factors, namely, poor diet, physical inactivity, smoking and harmful use of alcohol, which are all exacerbated by mental health problems. About 60% of the excess mortality in the mentally ill population is attributed to co-morbid physical health problems, predominantly cardiovascular diseases, in addition to an overall increased risk for completed suicide [2].

Evidence consistently demonstrates that people with long-term physical health problems are two to three times more likely to suffer mental health problem than the general population and overall 30% of those with long-term physical conditions have mental health problems [3].

Studies have shown a clear link with deprivation and excess co-morbidity/multimorbidity and mental illness. The Scottish cross sectional study by Barnett et al. showed that the 10% most deprived Scottish population has life expectancies 13 years shorter for men and 9 years for women compared to those in the most affluent 10%. The onset of multimorbidity occurred 10–15 years earlier in those living in areas of high deprivation with socioeconomic deprivation associated with multimorbidity that included mental illness. The presence of mental health problems increased with the number of co-morbid physical health problems and was reported as more prevalent in deprived areas [4].

With co-morbidity, there is a substantial increase in costs due to health service utilisation. International studies have demonstrated the financial impact of mental

health co-morbidity. Depression is associated with increased total medical costs for people with chronic conditions such as diabetes, asthma and congestive heart failure. Several studies have demonstrated that after controlling for the severity of the physical health condition, co-morbid mental health problems are associated with a 45–75% increase in health-care service cost. In addition to the costs of medical care, co-morbid mental health problems have wider economic consequences. Individuals with coexisting mental health problems are less likely to work, and the productivity of those in employment is reduced. Higher levels of absenteeism are reported in those with diabetes and co-morbid mental health problems than in those with diabetes alone [3].

Quality of life in this population has been examined using the health-related quality of life scores demonstrating a clear reduction in quality of life in those with coexisting mental and physical conditions [5]. Mental health can compromise an individual's ability to cope and manage a physical health condition and therefore lead to an overall reduction of functional ability, prognosis and quality of life. This is highlighted in diabetes and depression with depression estimated at two to three times more likely in those with diabetes leading to more complications in managing the physical condition including worse glycaemic control due to poor compliance with pharmacotherapy and dietary/activity regime. In addition weight management becomes increasingly difficult due to poor motivation and non-adherence to lifestyle interventions [6].

Overall therefore people suffering from long-term physical health problems are at an increased risk of developing mental health problems and vice versa with three to four times greater mortality than the general population due to cardiovascular disease.

Epidemiological studies have shown an increasing trend that co-morbidity is a common phenomenon particularly in the elderly population and has become the 'norm' and not the exception in those over 65 years of age. Although it is more common in the elderly, it is now becoming increasingly common in the younger population, in those with mental health problems in areas of socioeconomic deprivation and in low-income countries [7].

Although individual diseases are still the focus of health-care delivery systems, medical research and education, it is clear that people with multimorbidity need a much broader care approach including good co-ordination and integration to ensure a more collaborative, safe and effective service delivery. Our current health-care systems are designed to manage individual diseases in a single disease model of care. To meet the current and escalating demands with the increase of chronic coexisting diseases, health systems need to meet the challenge of co-morbidity.

5.2 Redefining the Metabolic Syndrome: Cardiometabolic Risk Factors

Major mental disorders, schizophrenia, bipolar disorder and severe unipolar depression are associated with many traditional cardiovascular disease risk factors, elevated blood pressure, obesity, dyslipidaemia, diabetes, alcohol misuse, smoking and lack of exercise.

These associations are linked to the development of what has been described in the literature as ‘metabolic syndrome’. The metabolic syndrome is highly prevalent in those with mental disorders such as schizophrenia and depression. De Hert et al. (2011) reported high levels of metabolic syndrome in people with severe mental illness. Studies have shown levels between 19 and 68% in those with a diagnosis of schizophrenia. In addition people with bipolar disorder and schizoaffective disorder have shown high prevalence levels of 22–30% and 42%, respectively [7, 8].

Co-morbidity was originally introduced by Feinstein in 1970 to signify the coexistence of two or more diseases in the same patient. This definition includes any relevant phenomena requiring clinical attention which may not be related to the index disease. Grumbach then suggested that the term co-morbidity should relate to the coexistence of two or more pathological conditions when one is predominant. Starfield suggested the term for the simultaneous presence of multiple health conditions when there are a clear index condition and other unrelated conditions. Other researchers have defined co-morbidity as the simultaneous presence of diseases which are associated with one another through pathogenesis or more frequently than by chance in contrast to multimorbidity which refers to the presence of two or more conditions within one person without defining an index disease. Goldberg was the first to coin the term co-morbidity to describe the existence of a physical condition in someone with mental illness [6].

The concept and clinical value of the term ‘metabolic syndrome’ have come under critical scrutiny recently attracting increasing debate between endocrinologists, diabetologists, cardiologists and other specialists in the field. As a result the term metabolic syndrome has been replaced by the terms co-morbidity and multimorbidity attributed to conflicting and incomplete diagnostic criteria, general lack of consensus over definition and the principal underlying factors (Appendix 1).

The concept of physical co-morbidity and cardiometabolic disorders dates as far back as 250 years ago when the Italian physician, Morgagni, described the associations between visceral obesity, hypertension, atherosclerosis and high levels of uric acid in the blood and frequent respiratory disorders [9].

By the middle of the twentieth century, adiposity of the superior part of the body had been identified as a risk for diabetes mellitus and cardiovascular disease. Towards the end of the 1980s, the assembly of glucose, insulin metabolism, obesity, dyslipidaemia and arterial hypertension received the name ‘X syndrome’.

In 1988, Reaven, an endocrinologist, took the bold step forward interpreting the association between diabetes, obesity, dyslipidaemia and arterial hypertension by their common pathogenesis through peripheral insulin resistance. He named it ‘X syndrome’—underlining the doubts that accompanied the new concept. The overarching concept being that the metabolic syndrome represented a complex disturbance of metabolism connecting insulin secretion disturbance influenced in turn by the sensitivity/resistance to insulin [10]. Further research in the field considered that the spectrum of metabolic disturbances was wider. Zimmet and Serjentson coined the phrase ‘plus X syndrome’ addressing the association with hyperuricaemia, sedentary lifestyle and old age [11].

More formal definitions of metabolic syndrome emerged from 1998 onwards with the WHO group studying diabetes outlining the presence of type 2 diabetes or altered glucose tolerance at the heart of the syndrome with at least two other factors (hypertension, increased level of blood lipids, obesity and microalbuminuria) [12].

The EGIR (European Group for the Study of Insulin Resistance) proposed a further change in 1999 establishing that insulin resistance is the main cause of the syndrome [13].

In 2001 NCEP-ATP III (the National Cholesterol Education Program, Adult Treatment Panel III) introduced alternative clinical criteria for defining metabolic syndrome which did not require the demonstration of insulin resistance [14]. In 2003 the American College of Endocrinology revised the NCEP-ATP III criteria redirecting the definition to insulin resistance [15].

In 2005 concerns led to the American Diabetes Association and the European Association for the Study of Diabetes to issue a joint statement identifying major concerns on the use of the metabolic syndrome as a term in clinical practice. The paper recommended the need for more research in the field to resolve fundamental issues about the construct itself. The recommendations emphasised that clinicians should evaluate and treat all cardiovascular risk factors whether a diagnosis of metabolic syndrome was present or not. Interventions should include lifestyle modification and treatment of frank disease treated in accordance with recommended guidelines. The paper emphasised that there was no clear evidence for specific medication interventions that benefit those with metabolic syndrome, and until such times further research was completed, there could be no recommendations for use of specific pharmacological therapies or use of medication to treat insulin resistance in those with metabolic syndrome [16].

In 2005 the IDF (International Diabetes Federation) modified the ATP III definition publishing new criteria. The IDF suggested the key element as central obesity which closely correlated with the metabolic syndrome with cut-offs for men and women and ethnic groupings with =/>2 of the parameters [17] (Appendix 1).

In 2005 the AHA/NHLBI statement, in contrast to IDF, maintained the ATP III criteria except for minor modifications. This decision was based on the conclusion that ATP III criteria was simple to use in a clinical setting and had the advantage of avoiding emphasis on a single parameter. The majority of studies were supportive of the structure of ATP III criteria at the time. It should be noted that the threshold for IFG was reduced from 110 to 100 mg/dL; this adjustment corresponded to the modified American Diabetes Association (ADA) criteria for IFG. Otherwise, the statement maintained that continuity with the original ATP III definition.

By 2009 various diagnostic criteria had been proposed by different organisations. In attempt to harmonise the risk factors, the IDF, the American Heart Association and the National Heart, Lung, and Blood Institute met to address the main differences concerning the waist circumference as an obligatory component in the International Diabetes Federation definition, lower than in the American Heart Association/National Heart, Lung, and Blood Institute criteria, and ethnic specific. It was agreed that there should not be an obligatory component, but that waist measurement would continue to be a useful screening tool. Three abnormal findings out of five would qualify a

person for the metabolic syndrome. A single set of cut points would be used for all components except waist circumference, for which further work is required. In the interim, national or regional cut points for waist circumference were used.

Controversy and the lack of agreement regarding the definition of metabolic syndrome have continued. Hence the symptoms of metabolic syndrome remain ill-defined and the effects unclear. The parameters are clearly interconnected, but it is still not absolutely certain how they became the decisive factors. Although the metabolic syndrome has been viewed by some in the field as the most important medical problem in the twenty-first century, the reality is that it remains difficult to estimate because of the numerous points of view globally regarding the elements needed for the diagnosis.

In conclusion it appears that the analyses to date indicate that too much critically important information is missing to warrant its designation as a 'syndrome'. Until much-needed research is completed, the literature suggests a more pragmatic approach in clinical practice. Therefore clinicians should assess and evaluate all cardiovascular and metabolic risk factors and not only those that specifically meet the criteria for a diagnosis of the 'metabolic syndrome'.

5.3 Co-morbidity in the Severely Mentally Ill: Modifiable Risk Factors and Pathogenesis

Sources of risk for cardiometabolic disorders are multifold and complex in the mentally ill population.

There is clear evidence of disparities in overall health care demonstrating that those with mental health problems seeking help for physical conditions such as diabetes are less likely to receive standard care. Potential barriers to obtaining the appropriate care at the right time can be attributed to a variety of reasons. For the person with mental health problems, it can be related to poor motivation and/or cognitive impairment along with the mental health symptoms themselves. People with mental health problems are less likely to seek out help early on for the treatment of a physical health condition [18].

Difficulties in understanding the health-care system and engaging early on with interventions can lead to more complications and worse outcomes as a result. The other concern is that psychiatrists and family doctors at times do not feel adequately experienced and trained to deal with the complexities of multimorbidity and the associated polypharmacy including the adverse effects/interactions of antipsychotic medication and other prescribed medications.

There are a number of clear modifiable risk factors identified including diet and lifestyle which play a fundamental role in the well-being of the mentally ill and in determining the outcome of coexisting medical conditions. Socioeconomic issues may contribute to the overall unhealthy lifestyle of this population as individuals

with mental health problems are more likely to have less financial resources to fund healthy diets and access facilities for exercise.

Diet is a major modifiable risk factor for cardiovascular disease. A poor diet may lead to an increase in insulin resistance, dysplidaemia and hypertension. Apart from the risk of obesity due to high calorie intake, a diet rich in saturated fats and low in unsaturated fats is associated with increased LDL cholesterol and insulin resistance. High calorie intake in the form of carbohydrates especially refined sugars is related to high fasting triglyceride levels and low HDL cholesterol. Poor consumption of fruit and fibre is associated with increased food intake and reduced control of sugar homeostasis and plasma lipid levels. High salt intake may be related to an increased risk of hypertension.

Obesity levels are associated with the basic lifestyle factors such as the imbalanced diet as described and the lack of exercise in this population. It is well recognised that those with severe mental illness have a higher risk of obesity and therefore have shorter life spans. The extent of obesity varies with diagnosis. For example, studies have shown that those with schizophrenia have a 2.8–3.5 times increased likelihood of being obese compared to those with major depression who have an estimated 1.2–1.5 increased likelihood. Clinical research has suggested that those with a diagnosis of bipolar disorder are up to 68% overweight or obese [8].

A recent systematic review on the assessment of diet in those with schizophrenia concluded that subjects with schizophrenia have an unhealthy diet, rich in saturated fats and poor in fibre and fruit. These patients also show a high caloric intake [19].

The review explains the linkage between both high saturated fat intake and low fibre and fruit consumption with high levels of inflammatory markers, especially tumour necrosis factor-alpha (TNFα), interleukin-6 (IL-6) and C-reactive protein (CRP), which in turn may promote the development or the worsening of the cluster of risk factors known as ‘metabolic syndrome’ in genetically or metabolically predisposed individuals. This is particularly concerning for those with schizophrenia, who show an elevated oxidative stress, high levels of pro-inflammatory cytokines and several metabolic abnormalities at the onset of the illness [19].

Osteoporotic changes are more common with schizophrenia, schizoaffective disorders and major depression along with bipolar disorder. This may be due to the disease itself but also poor diet including vitamin D deficiency as contributing factors along with excessive smoking, calcium deficiency and alcohol abuse [8].

Physical inactivity is now recognised as a global pandemic within the general population. The Lancet (2016) published a series highlighting the requirements for governments as well as all sectors of the society to step up to an increased activity in a bid to solve this escalating problem. Better-quality research is required to support evidence-based interventions, but more importantly the authors emphasise the need for a joint effort on the part of all sectors of government and society to tackle this epidemic [20].

On a neurochemical and physiological level, a number of acute changes occur during and following exercise, and several long-term adaptations have been linked to regular exercise.

Exercise has been found to normalise reduced levels of brain-derived neurotrophic factor (BDNF) and therefore has neuroprotective or even neurotrophic effects. Animal studies have found exercise-induced changes in different neurotransmitters such as serotonin and endorphins, which relate to mood, and positive effects of exercise on stress reactivity (e.g. the hypothalamus-pituitary-adrenal axis). Finally, anxiolytic effects of exercise mediated by atrial natriuretic peptide have been reported [21].

Potential psychological changes can occur including learning and health attitudes/behaviours, social reinforcement, experience of ownership of well-being, shift of external to more internal locus of control, improved coping strategies or simple distraction.

The lifestyle for those with mental health problems is more likely to be sedentary with less exercise or any physical activity which can be due to the mental illness itself, socioeconomic problems and possible adverse effects of medication such as sedation.

Studies investigating the prevalence of cancers overall in the SMI population have demonstrated conflicting results. The discrepancy in results may be due to the lack of early intervention, screening and diagnosis in this population. For example, those with SMI are less likely to visit their general practitioner for investigation or attend referral appointments to secondary services for cancer screening.

An important breakdown of cancers has found that obesity-related cancers such as endometrial, renal and bowel cancer occur more frequently in the SMI population and hence contribute to the increased premature mortality.

Due to the controversial evidence for the role of prolactin in breast cancer rates, it had been assumed that exposure to prolactin-raising dopamine antagonists would result in an increase in breast cancer rates in this population. Conflicting results have emerged, and studies of the effects of typical antipsychotics showed no increased risk for breast cancer apart from a cohort described by Wang et al. [8].

People with mental health problems are more likely to smoke and smoke more heavily than the general population [22].

Smoking rates amongst patients with a serious mental illness are significantly higher, estimated at around two to three times the general population, and hence smoking is considered to be a major risk factor for cancer, respiratory disease and circulatory disease which are all major causes for premature mortality amongst this population [8].

In addition to smoking more heavily, people with mental illness are more likely to be to nicotine-dependent and have smoked for longer than smokers in the general population. There is also evidence that nicotine has a greater effect on cognitive performance in those with mental health problems [23].

The risk of many diseases, in particular respiratory and cardiovascular disease, in people with mental health problems could therefore be preventable by appropriate support to stop smoking. This would significantly improve physical health, life expectancy and well-being.

Oral hygiene and health in this population is poor with lack of attention to dental care. In addition medications including antipsychotics and antidepressants all cause xerostomia leading to caries, gingivitis and periodontal disease.

Sexual dysfunction in this population has received little attention with few systematic reviews in people with schizophrenia. Although there are few studies, we do know that sexual dysfunction is more frequent in people with schizophrenia compared to the general population—affecting 30–80% of women and 45–80% of men. Dysfunction can be secondary to the disease itself but also due to physical co-morbidities or adverse effects of antidepressant or antipsychotic medication with up to 70% of those with depression describing sexual dysfunction [8].

With substance misuse, there is higher risk of sexual behaviour which contributes to the higher risk of hepatitis C, HIV and reduced immune function in the SMI population [8].

A significant number of people with schizophrenia misuse alcohol. Heavy use of alcohol increases the risk of cardiovascular disease, hypertension, cardiomyopathy and various cardiac rhythms. The potential increase in calorie intake also increases the risk of obesity. Heavy drinking and binge drinking also increase the risk of diabetes, but low consumption could reduce risk [24]. Light and moderate drinking may be protective for cardiovascular disease for some, but studies have recently confirmed that the general alcohol-related harm outweighs any cardiovascular benefits [25].

5.4 Non-modifiable Risk Factors

5.4.1 Genetic Factors

Genetic associations have been reviewed in a substantive systematic review of genes implicated in the development of metabolic syndrome in people with schizophrenia by Malan-Muller et al. (2016). Relevant extensive databases were accessed, and a review of published studies was conducted. Several genes showed a strong association with metabolic syndrome in those with schizophrenia including the fat mass and obesity gene (FTO), leptin and leptin receptors genes (LEP, LEPR), methylenetetrahydrofolate reductase (MHTHFR) gene and serotonin receptor 2C gene (HTR2C).

Genetic associations have proved to be very complex due to the multifactorial nature of cardiometabolic problems. Recommendations from the systemic review include the need for further longitudinal large sample studies including healthy controls. Ultimately in the future, these findings could allow for early risk prediction of metabolic syndrome in schizophrenia and patient-specific interventions tailor-made to minimise cardiovascular risk, co-morbidities and premature mortality in this population [26].

5.4.2 Hypothalamic Pathway and Stress

Drug-naive patients have allowed the opportunity to study patients without the effects of antipsychotic medication to influence the picture. The findings of cardiometabolic problems in first-episode patients have been hypothesised to be related to

high levels of stress and the hyper-activation of the hypothalamic-pituitary-adrenal axis which in turn enhances circulating cortisol and glucocorticoid resistance leading to an increase in the deposition of visceral fat altering leptin signalling, insulin resistance and glucose intolerance.

Repeated episodes of psychological distress in both childhood and adulthood have been reported by those with schizophrenia, and at the time of or just before the first episode of illness. These stressful episodes may induce a chronic inflammatory process with an increase in inflammatory markers such as C-reactive protein (CRP) which in turn may lead to further metabolic disturbance [27].

5.4.3 Inflammation and Oxidation in Schizophrenia

A landmark study by the Schizophrenia Working Group of the Psychiatric Genomics Consortium identified 108 schizophrenia-associated genetic loci. Many findings provide potentially new insights into aetiology, but associations at *DRD2* and several genes involved in glutamatergic neurotransmission highlighted molecules of known and potential therapeutic relevance to schizophrenia and are consistent with current pathophysiological hypotheses. Independent of genes expressed in the brain, associations were enriched amongst genes expressed in tissues that have important roles in immunity, supporting a possible link between the immune system and schizophrenia [28].

Research has now emerged over the past decade adding to the literature suggesting a relationship between a state of subclinical chronic inflammation in this population characterised by abnormal pro-inflammatory cytokines, obesity, insulin resistance, type 2 diabetes in amongst activation of a network of inflammatory pathways suggesting a link between inflammation, acute coronary syndromes and metabolic syndrome. In the presence of obesity, the adipose tissues produce pro-inflammatory cytokines in excess. Inflammation and immune system dysfunction have been described in those with schizophrenia. Miller et al. [29] added to the growing body of literature demonstrating that given the high prevalence of elevated CRP, metabolic syndrome and premature cardiovascular mortality, the measurement of blood CRP levels may be relevant in the clinical care of patients with schizophrenia and related disorders [29].

Although acute inflammation is an adaptive process, the long-term consequences of inflammation and immune system activation are not beneficial. Prenatal infections and maternal immune changes have been implicated as potential increase in the risk of schizophrenia and schizophrenia-related abnormalities [30].

Researchers have started to explore specific inflammatory markers in those with schizophrenia. Naudin and colleagues have reported that patients with schizophrenia have significantly higher levels of TNFα and interleukin 6 than healthy controls. Whilst CRP has been associated with worsening symptoms of schizophrenia, TNFα, interleukin 6 and CRP are all well-recognised inflammatory markers that play a part in insulin resistance, type 2 diabetes and metabolic syndrome [31, 32].

Oxidative stress reactions in those with schizophrenia have been implicated in the side effects of antipsychotic medication. This increased oxidative stress reaction can

lead to tissue damage and stimulate an inflammatory response. Walss-Bass et al. identified proteins that are irreversibly oxidised by clozapine. These proteins are enzymes implicated directly in energy metabolism. It is considered that this may be the mechanism for second-generation antipsychotics inducing metabolic syndrome [33].

5.5 Cardiometabolic Disturbance and Antipsychotic Medication: Weight Gain, Diabetes/Glucose Regulation and Dyslipidaemia

5.5.1 Weight Gain

With the shift to atypical antipsychotics, this was a further advancement in pharmacotherapy for the treatment of those with severe mental health problems, but second-generation drugs present different challenges in terms of adverse effect profile. The older medications primarily caused movement disorders along with the physical effects of hyperprolactinaemia, i.e. galactorrhea, gynaecomastia and infertility amongst other adverse effects.

The atypical medications are a heterogeneous group of drugs, each with its own weighting of adverse effect profile in terms of cardiovascular and metabolic problems. Weight gain liability has been a concern with some of the second-generation drugs.

Included in the higher risk agents for obesity are clozapine and olanzapine with intermediate-risk agents risperidone and quetiapine, and asenapine, amisulpride, ziprasidone and aripiprazole are classified as lower-risk agents. This may relate to the partial agonism effect at certain serotonin receptors and/or partial agonism at dopamine D2 receptors (DRD2).

Certain antidepressants, such as the tricyclic and SSRI groups, carry a risk of weight gain due to an increased appetite and sedation. Mood stabilisers such as sodium valproate and lithium also have a propensity for weight gain.

Whilst drugs substantially vary in their effects on body weight and other metabolic factors, individual responses considerably vary. Some people rapidly gain weight, whilst others treated with the same medication are unaffected. Lifestyle and diet as discussed also have a contribution, but in addition it appears that genetic factors are also important.

Candidate genes have been investigated for the association with weight gain when receiving antipsychotic medication in those with chronic schizophrenia. Strong candidates for the pharmacological mechanisms that could be responsible for the weight gain include antagonism at serotonin 2C (5HT2c) receptor although other receptor sites such as histamine H1 provide alternative additional mechanisms. Both of these receptors are involved in hypothalamic mechanisms in controlling food intake and can disrupt normal hormonal regulation in the system. Leptin has been identified as a hormone that increases with second-generation antipsychotics and is seen as a consequence of the medication-induced weight gain although leptin resistance has been reported.

Other implicated regulators include dopamine D2 (DRD2) at which all antipsychotics act and which also have involvement in hypothalamic mechanisms and appetite.

There are several other genes possibly at play including the pharmacological targets of antipsychotics including alpha 2 adreno-receptors, in genes involved in the hypothalamic control of food intake and body weight and other genes emerging from genetic studies for obesity and metabolic problems.

Genetic factors also influence the rate of weight loss after a drug treatment and in those who have developed metabolic syndrome following commencement of antipsychotic medication.

These genetic factors associated with drug-induced weight gain and metabolic risk may provide opportunities in the future for more personalised medicine with predictive screening as part of the psychiatric assessment for metabolic risk with antipsychotic medication, diabetes mellitus and glucose dysregulation [34].

5.5.2 Diabetes/Glucose Regulation

In terms of glucose regulation, people with schizophrenia have a higher prevalence of glucose abnormalities, insulin resistance and type 2 diabetes leading to the increased risk of metabolic syndrome. This effect is greatest in those prescribed second-generation antipsychotics than typical ones.

Clozapine, olanzapine and risperidone are viewed as high risk for diabetes mellitus, whilst others such as quetiapine amisulpride and aripiprazole show no significant increase. The higher individual variability in medication-induced weight gain suggests that there are genetic factors at play. For example, studies have shown that HTR2C and LEPR polymorphisms are genetic predictors of weight gain. Although the results are promising, this area requires further research for practical application.

People with schizophrenia have an overall twofold risk of diabetes mellitus. Again the aetiology is complex with a combination of genetics, diet, lifestyle and the disease-specific treatment factors. It is now recognised that the risk of diabetes increases in those treated with multiple episodes of relapses compared to those with a single episode.

Certain antipsychotics are likely to increase the risk of diabetes as this increases weight gain which in turn increases insulin resistance. However this does not explain the whole story as there is a subgroup of people on antipsychotic treatment who do not gain weight but develop diabetes mellitus. Changes in glucose regulation have been shown in those people with schizophrenia without diabetes taking antipsychotic and independent of adiposity. Henderson and colleagues [34] have demonstrated that shortly after commencing clozapine and olanzapine, glucose abnormalities are evident; hence, it is unlikely that weight gain is the reason behind the development of metabolic adverse effects [34].

A possible explanation is that clozapine and olanzapine may restrict the capacity of pancreatic β cells to secrete appropriate amounts of insulin. Another explanation is that clozapine and olanzapine would affect glucose metabolism at a cellular level

by interfering with the glucose transporter proteins and inhibit glucose uptake. Another mechanism is that second-generation antipsychotics may affect insulin production and resistance by blocking the muscarinic receptor (M3R) signalling pathways in the brain.

Impaired fasting glucose levels have been associated with insulin resistance measured by homeostatic model assessment-insulin resistance (HOMA-IR). Studies have reported the increased HOMA-IR induced by chronic treatment with second-generation antipsychotics.

Hence to date the research shows that antipsychotics may affect glucose metabolism through different mechanisms which increase insulin resistance, type 2 diabetes and metabolic syndrome [35].

5.5.3 Dyslipidaemia

Dyslipidaemia is one of the most important risk factors for cardiovascular disease. Dyslipidaemia has been linked to second-generation antipsychotics especially olanzapine and clozapine. People with schizophrenia given second-generation antipsychotics show increased levels of LDL cholesterol and triglyceride and decreased HDL cholesterol.

Antipsychotics vary in weight gain propensity suggesting that that the level of lipid abnormality may be related to weight gain and adiposity.

Obesity is associated with insulin resistance which stimulates more insulin secretion leading to hypersecretion of very low-density lipoproteins and triglycerides. Some evidence shows antipsychotics can increase triglycerides without much in the way of weight gain suggesting a direct effect on lipid metabolism through an unknown mechanism.

Hence the evidence shows that the molecular mechanism of antipsychotic drug-induced lipid dysregulation remains unclear but an important contributor to the cardiac risk and mortality in this population [34].

5.6 Current Models and New Approaches: Assessment and Interventions for Co-morbidity in the Severely Mentally Ill

Co-morbidity is perhaps the single area of medicine that clearly demonstrates the inadequacy of prevailing models of care. There is clearly a recognition of the challenges posed by co-morbidity especially with mental illness and the limitations of the current model of care which focuses on the assessment, acute care and management of a specialised, single disease.

Consensus statements and guidance have been published over the years, and studies have outlined the requirements for a cardiovascular risk assessment for this population. Whilst there are variations on the specific assessment tools, broad principles and a better consensus have emerged as a result of good medical practice.

The following broad monitoring parameters reflect the cluster of cardiovascular and metabolic risk factors outlined in the various definitions of metabolic syndrome.

Cooper et al. [35] compiled an up-to-date guidance from a consensus meeting with experts in the field on the management of physical risk factors and recommendations for interventions after a review of trials of interventions including consensus data based on good clinical practice standards [35].

5.6.1 Assessment and Monitoring for Physical Health Risk Factors

It is now universally agreed that monitoring of the physical health risk factors in the mentally ill should be assessed as early on as possible and preferably prior to the commencement of any antipsychotic medication to provide key baseline measurements. This is the ideal situation but at times not possible due to the practicalities of the clinical situation and the requirement for emergency treatment.

BMI is considered a good measure of weight gain during the early stages of treatment and should be carried out weekly in the first instance for the first 4–6 weeks and 2 weekly for up to 12 weeks and then assessed at 6 months and annually as a minimum thereafter. Ethnicity needs to be taken into account when recording the BMI.

Blood sugar should be monitored in the long term using the glycated haemoglobin, but in the early weeks, fasting blood glucose or random may provide a measure of glucose control. Glucose should be measured at 6 months and annually thereafter. Lipid profile should be completed at 12 weeks, 6 months and then annually.

Cardiovascular risk should be measured using an algorithm such as the QRISK2 cardiovascular risk model. QRISK2 is the most up-to-date version of QRISK using traditional risk factors (age, systolic blood pressure, smoking status and ratio of total serum cholesterol to high-density lipoprotein cholesterol) along with body mass index, ethnicity, measures of deprivation, family history, chronic kidney disease, rheumatoid arthritis, atrial fibrillation, diabetes mellitus and antihypertensive treatment to measure cardiovascular risk. A QRISK2 over 10 (10% risk of CVD event over the next 10 years) indicates primary prevention with lipid-lowering therapy (such as statins) should be considered. In the UK, current National Institute for Health and Clinical Excellence (NICE) guidelines recommend using QRISK (as opposed to the Framingham Risk Score) [36].

Blood pressure should be monitored at 12 weeks, 6 months and annually. If antipsychotic medication is changed, the above need to be revisited.

Smoking and alcohol use should be monitored and interventions offered when required.

5.6.2 Interventions for Co-morbidity in the Severely Mentally Ill

In terms of interventions, overall it is emphasised universally in all the guidelines that people with mental health problems should receive the same standard of care as

the general population and hence national standards for specific risks and diseases should be followed for the mentally ill.

The National Institute for Health and Clinical Excellence (NICE) recognised that many people in the UK were living with long-term health problems such as high blood pressure, diabetes, heart disease or arthritis and mental health problems such as depression and anxiety. As a result, a guideline for health-care professionals was created for 'multimorbidity'. 'This guideline covers optimising care for adults with multimorbidity (multiple long-term conditions) by reducing treatment burden (polypharmacy and multiple appointments) and unplanned care. It aims to improve quality of life by promoting shared decisions based on what is important to each person in terms of treatments, health priorities, lifestyle and goals. The guideline sets out which people are most likely to benefit from an approach to care that takes account of multimorbidity, how they can be identified and what the care involves'. [37].

5.6.3 Obesity

Various global guidelines have been developed over the years recommending lifestyle interventions to increase basic physical activity, improve eating behaviour, quality of a person's diet and reduce energy intake. Programmes describe a range of basic interventions including education on diet and lifestyle skills, exercise initiatives, smoking cessation and counselling on alcohol and substance misuse. NICE (2010) sets out the broad guidance for managing cardiovascular risk in the general population which was reviewed in 2014 with no new evidence to add. This tool should be used for the SMI population to manage cardiovascular risk taking into account any additional risk factors [38].

Lifestyle studies are usually of a behavioural nature with most of the approaches reported for short or intermediate timeframes of up to 12 weeks with exceptions of a maximum of 24 weeks. In broad terms, lifestyle interventions are recommended as they appear to have an overall positive effect as a first-line intervention and therefore should be continued in addition to other interventions. Studies to date have demonstrated a reduction in weight of 3 kg on average and can minimise the weight escalation in the early stages of first-episode individuals.

Difficulties have been repeatedly identified in studies of how to tackle the issue of improving engagement with such programmes, and as a result, the maintenance of effect data is limited. Overall it appears that programmes combing individual and group activities are the best approach designed specifically to meet the needs of the individual.

Switching of antipsychotic medication to a lower-risk agent should also be considered as another thread to the strategy with the following appearing to have the lowest weight gain: haloperidol, aripiprazole, ziprasidone, lurasidone and amisulpride and asenapine.

RCTs have examined switching for the purpose of weight reduction. These studies included switches from olanzapine to either aripiprazole or quetiapine demonstrating a 3 kg reduction compared to no change.

In the switch to a lower-risk agent, careful consideration must be given to the risk of relapse, chronicity of illness and ongoing psychotic symptomatology. Adjunctive aripiprazole is recommended as a possible addition for weight gain associated with clozapine and olanzapine.

Other medications have been considered for adjunctive treatment.

Metformin has been recommended for high risk of diabetes groups to slow down or reduce weight gain following commencement of antipsychotic medication.

Studies recommend that before consideration of such medication, all lifestyle interventions as above should be considered. Metformin has been compared to lifestyle interventions in a large 3-year cohort with an increased risk of diabetes demonstrating that it can have modest benefits in the short term but that over the long term, lifestyle interventions are more effective. NICE guidance supports the use of metformin in those with high risk of diabetes [39].

> 'This guideline covers how to identify adults at high risk of type 2 diabetes. It aims to remind practitioners that age is no barrier to being at high risk of, or developing, the condition. It also aims to help them provide those at high risk with effective and appropriate intensive lifestyle-change programme to prevent or delay the onset of type 2 diabetes. The 20 recommendations in this guideline can be used alongside the NHS Health Check programme' [40].

Short-term studies of those taking antipsychotics have shown that metformin can be beneficial and can moderate weight gain in those with first-episode psychosis, although metformin is not within adverse effect and monitoring must include renal function tests and vitamin B12. Orlistat has been studied for weight loss in the general population. Data from long-term use is limited due to discontinuation. Topiramate has also been used with those on antipsychotic medication, but benefits appear to be outweighed by adverse effects. Other medications such as reboxetine, glucagon-like peptide, amantadine and melatonin have either very limited evidence or failed to show benefit. To date bariatric surgery as an intervention in the mentally ill has not been studied adequately.

In terms of management of cardiovascular risk, a useful resource created by the late Professor Helen Lester has been adapted in the UK. This provides a tool for clinicians to address the risks and monitor risk. It provides a practical guide to monitoring clinical risk, monitoring clinical parameters and implementing interventions [41].

The management of weight gain is essential to overall improve cardiovascular function. Promotion of exercise is appropriate through either the mental health teams or primary care depending on local arrangements. People with hypertension and dyslipidaemia should be referred to their family doctors for treatment as usual and adhere to recommended national guidance for the general population. All people should receive advice about their diet, exercise and weight management along with smoking cessation. A cholesterol-reducing agent should be considered if lifestyle management is not effective.

5.6.4 Diabetes

National diabetes standards/guidelines should be followed in relation to the general population. In the UK, the NICE tool for the general population should be followed (www.nice.org.uk/guidance/ng28/resourcesendocrinal--nutritional-and-metabolic-conditions/diabetes).

It is important that those with mental illness receive the same standard of care as the general population. Consideration needs to be given to engagement of this population given the additional challenges in terms of motivation, learning and cognitive function.

A programme including advice and education on diet and exercise requires to be implemented to optimise lifestyle interventions in the first instance. Medication review including consideration of the lowest-risk agents for treatment is essential given the potential extra burden of antipsychotic medication, and switching may be required to a lower-risk agent. Other weight-reducing agents may be considered thereafter.

5.6.5 Smoking/Alcohol and Substance Misuse Interventions

Tobacco smoking has been identified as a major risk in those with mental illness and is a risk factor for diabetes and cardiovascular disease. Referral to smoking cessation services should be the first port of call. The use of nicotine replacement in those with psychosis is supported in the literature as effective. A recently reported UK pilot of a bespoke smoking cessation programme for people with psychosis compared to usual care suggested better outcomes with a full-scale trial to follow [42].

Studies with bupropion are limited and suggest only modest benefit. Therefore overall the literature supports NRT remains the treatment of choice.

Alcohol misuse and the use of other substances are particularly harmful in those with mental illness on medication and require careful assessment and treatment where appropriate. Despite this common problem in this population, studies remain limited and the challenge for clinicians difficult given the lack of evidence base.

Various studies including both first- and second-generation antipsychotics have examined potential benefits of one antipsychotic over another in the treatment of co-morbid substance abuse in those with psychosis with no firm conclusions.

There is little evidence for relapse prevention in those with psychosis. For the non-co-morbid dependent population, acamprosate and naltrexone have been used with disulfiram as second line. In those with psychosis, acamprosate and naltrexone have been safely used. However disulfiram is contraindicated in those with psychosis due to concerns of an increased risk of worsening symptoms. Overall there is no robust evidence to support psychosocial interventions over usual management. Optimisation of medication in the first instance to treat the primary mental health problem is important to reduce the use of substances, with clozapine considered potentially useful in reducing the use and improving psychosis.

Naltrexone and acamprosate can be useful in alcohol dependence and relapse prevention in keeping with NICE guidance.

In terms of substance misuse and severe mental illness, NICE published a comprehensive overview of the models of service and evidence-based interventions [43].

5.7 Global Models of Care: Co-morbidity and the Severely Mentally Ill

The WHO Global Action Plan (2013–2020) has determined that the prevention and control of the NCDs are a priority. There are nine targets outlined for the successful implementation of the Global Action Plan with establishment of 80% of affordable technology and medicines to treat NCDs and the other eight targets directed at the modifiable risk factors: 50% preventative therapy for heart attacks and stroke, reduce obesity and diabetes, 30% reduce salt intake, reduce harmful use of alcohol by 10%, reduce CVS deaths, cancer, diabetes or chronic respiratory disease by 25% , 10% reduction in prevalence of insufficient physical activity, 30% reduction in smoking and 25% reduction in prevalence of high blood pressure. Overall the aim is to reduce the most common NCDs by 25% by 2025. It has now been clearly recognised that there are common chronic disease determinants for the NCDs and mental disorders resulting in a high disease burden and socio-economic impact.

Globally health-care systems need to adapt to manage the shift in morbidity and mortality caused by the common modifiable risk for NCDs [44].

An integrated response to mental disorders and NCDs has been outlined by the WHO [45] which has been developed as a response to the fundamental connection between mental disorders and other chronic health conditions and the implications for mental health care being integrated with general health care. The new approach emphasises the challenge as not simply scaling up health-care systems but the need for the transformation of health-care systems by implementing evidence-based approaches for integrated, effective and efficient care along the life course. The promotion of healthy living is key through a person-centred model to co-ordinate and enhance continuity of care for those with mental disorders and other chronic disorders. The overall principles include a public health approach focusing on disease prevention, health promotion as well as delivery of health services under an umbrella of sound governance, appropriate resourcing and timely information [45].

This approach only emphasises the person-centred model of care and the consideration of the totality of the health status of the person presenting for care, including ill health as well as positive aspects of health and well-being including the contributors to health (ill and positive health) in a bio-psycho-social framework. It aims at empowering the therapeutic relationship by viewing the health-care process as a partnership between the person presenting for care, significant others and other health stakeholders and the health-care providers. It emphasises

health preservation, health prevention and health restoration at the individual and community levels. The integrative person-centred diagnostic model operationalises this paradigm shift into a usable diagnostic model articulating the integrative and dynamic interplay amongst the different domains of the health status and the diagnostic process [6].

We need innovative solutions that empower individuals to manage their own health care. Growing evidence and experience have already shown that when people engage fully in a more integrated collaborative approach, outcomes are better. When patients have chronic multimorbidity, it is even more crucial that communication is effective to enhance coping strategies, discuss treatments and help provide and customise resources leading to better outcomes.

Given the limited resources in our current health-care systems, this approach requires innovation in the whole system service design to provide comprehensive person-centred care encompassing early detection, co-ordinated multidisciplinary working across specialities as well as between primary and secondary care with easy access to basic healthy lifestyle care programmes [46, 47].

Locally driven pragmatic health screening programmes for those with severe mental illness and coexisting physical health problems have been evolving with the plethora of guidelines and consensus statements in the field.

Developments of health screening and lifestyle programmes have been pioneered to meet the demands of local populations using a pragmatic approach based on the availability of other services in the area and limited resources. The Dundee Health Screening Clinic was such a venture to address the needs of a deprived community population of Scotland by monitoring physical health parameters and providing follow-up to ensure that any physical health problems were being treated. Simple cardiometabolic tests/measurements were completed on attendance at the clinic and recorded and the information communicated to primary for interventions to be initiated if required [48, 49].

5.8 Conclusions

Co-morbidity in medicine is now viewed as one of the major challenges in the twenty-first century in terms of prevention and treatment. It is now well established that those with severe mental illness suffer increased co-morbid conditions and a reduced life expectancy due to predominantly co-morbid cardiovascular problems. Co-morbidity in the context of mental illness has now been established as the norm not the exception causing a massive disease burden globally in both personal costs and larger-scale economic consequences.

Evidence in the field has accumulated to understand the complex associated genetic factors, common pathogenesis and interaction with the known cluster of modifiable risk factors. Controversy has dominated the debate regarding the definition of metabolic syndrome, but a consensus has now emerged that all individuals with mental health problems require an assessment of cardiovascular risk whether they fulfil a metabolic criteria checklist or not.

The monitoring of modifiable risk factors with the aim of early intervention is key to prevention and improving long-term outcomes. Engagement in healthy lifestyle interventions remains a key challenge to sustain any meaningful improvements. Lifestyle interventions must be considered in the context of regular reviews including medication reviews to consider switches to the lowest-risk agents.

Fragmentation in the health-care system and the current single disease model only exacerbate the problem of effectively helping people experiencing co-morbidities and especially co-morbidities involving both mental and physical conditions.

The gap between the current single disease model of care and the dynamic model of service required to manage co-morbidity in the mentally ill is growing, whilst the trend of the burden of disease has developed to epidemic proportion. It is now recognised that a dramatic shift in health-care provision is required to effectively address the requirements for this growing population with co-morbidity with the expectation of longer life expectancy.

It is only by delivering a more integrated person-centred model of care that we can enhance communication and seamless care to improve health outcomes and quality of life for this population.

New ways of thinking are required to redesign health-care systems to enable clinicians to deliver cost-effective early health checks and interventions to treat coexisting conditions in the mentally ill and improve health and social outcomes.

Appendix 1: Metabolic Syndrome Diagnostic Criteria[1]
Criteria for Metabolic Syndrome (MetS) Definitions in Adults

World Health Organization Criteria (1998)

Insulin resistance is defined as type 2 diabetes mellitus (DM) or impaired fasting glucose (IFG) (>100 mg/dL) or impaired glucose tolerance (IGT), plus two of the following:

- Abdominal obesity (waist-to-hip ratio >0.9 in men or >0.85 in women, or body mass index (BMI) > 30 kg/m^2. There should only be a gap of one line only under this sentence in keeping with other bullet points. i.e. these are 4 consecutive bullet points.
- Triglycerides 150 mg/dL or greater, and/or high-density lipoprotein (HDL)-cholesterol <40 mg/dL in men and <50 mg/dL in women.
- Blood pressure (BP) 140/90 mmHg or greater.
- Microalbuminuria (urinary albumin secretion rate 20 μg/min or greater, or albumin-to-creatinine ratio 30 mg/g or greater).

[1] Adapted from: Kassi et al. Metabolic syndrome: definitions and controversies. *BMC Medicine 2011* ***9****:48* doi:https://doi.org/10.1186/1741-7015-9-48 www.biomedcentral.com

European Group for the Study of Insulin Resistance Criteria (1999)

Insulin resistance defined as insulin levels >75th percentile of non-diabetic patients, plus two of the following:

- Waist circumference 94 cm or greater in men, 80 cm or greater in women.
- Triglycerides 150 mg/dL or greater and/or HDL-cholesterol <39 mg/dL in men or women.
- BP 140/90 mmHg or greater or taking antihypertensive drugs.
- Fasting glucose 110 mg/dL or greater.

National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII) Criteria (2001)

Any three or more of the following:

- Waist circumference >102 cm in men, >88 cm in women.
- Triglycerides 150 mg/dL or greater.
- HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women.
- BP 130/85 mmHg or greater.
- Fasting glucose 110 mg/dL* or greater.

* In 2003, the American Diabetes Association (ADA) changed the criteria for IFG tolerance from 110 to 100 mg/dL.

American Association of Clinical Endocrinology Criteria (2003)

IGT plus two or more of the following:

- BMI 25 kg/m^2 or greater.
- Triglycerides 150 mg/dL or greater and/or HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women.
- BP 130/85 mmHg or greater.

American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) Criteria (2004)

Any three of the following:

- Waist circumference 102 cm or greater in men, 88 cm or greater in women.
- Triglycerides 150 mg/dL or greater.

- HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women.
- BP 130/85 mmHg or greater (or use of medication for hypertension)
- Fasting glucose 100 mg/dL or greater(or use of medication for hyperglycaemia)

International Diabetes Federation (IDF) Criteria (2005)

Central obesity (defined as waist circumference but can be assumed if BMI > 30 kg/m^2) with ethnicity-specific values,* plus two of the following:

- Triglycerides 150 mg/dL or greater.
- HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women.
- BP 130/85 mmHg or greater. (or use of medication for hypertension)
- Fasting glucose 100 mg/dL or greater. (or use of medication for hyperglycaemia)

*To meet the criteria, waist circumference must be: for Europeans, >94 cm in men and >80 cm in women; and for South Asians, Chinese, and Japanese, >90 cm in men and >80 cm in women. For ethnic South and Central Americans, South Asian data are used, and for sub-Saharan Africans and Eastern Mediterranean and Middle East (Arab) populations, European data are used.

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Unconventional Therapies

6

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Abstract

Unconventional treatments are a group of diverse medical and healthcare practices arising from varying schools of thought, different cultures, and world regions. Often practiced in developing countries, these treatment modalities are heterogeneous, multicomponent (as in yoga), and often used along with other conventional treatments. Current evidence recommends these treatments as adjuvants rather than primary intervention strategy. Whether the evidence protocol suggested in modern psychiatric practice can be utilized in studying the unconventional treatment methods is yet to be answered.

6.1 Introduction

Pluralism is widely prevalent in the management of psychiatric disorders across the globe. The word *conventional* is reserved for treatments that are widely understood, common in literature and widely taught in medical schools. Unconventional treatments are a group of diverse medical and healthcare practices arising from varying schools of thought, different cultures, and world regions. These practices are widely used even in developed countries and do fill a major gap in mental health service delivery. Many unconventional treatments especially biologically based therapies using herbs, foods, and vitamins took origins from diverse medical systems, spiritual-meditative practices, creative outlets (e.g., dance), and "energy medicine"

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(Qigong and Reiki and cranial electrotherapy stimulation). Most of the unconventional therapies come under the frequently used term—the complementary and alternative medicine (CAM).

6.2 Why Do People Select "Unconventional" Methods?

The treatment gap for psychiatric disorders in developing countries is huge (even to the tune of 70% in some countries) due to the inaccessibility to standard treatment [1]. Around 40% of individuals with a mental disorder receive treatment, but of these, only 32% get adequate treatment [2]. Treatment resistance due to comorbidity, nonadherence, treatment inadequacy, and "true resistance" occurs in one-third of patients.

Gureje [1] has suggested that an appeal to the wisdom of nature is a defining metaphor in traditional treatments. That might be one of the reasons why 20–80% of patients with psychiatric disorders opt for CAM as monotherapy, as add-on therapy, or as a part of "pathway of care." The other reasons include etiological and diagnostic concepts rooted in culture, religion, or the diverse systems of medicine, less stigmatization, high popularity and perceived "user satisfaction" [3], individually tailored treatment designed to the whole person than targeting psychopathological symptoms alone, nonavailability of mental health resources, inadequate knowledge about modern concepts, inadequate response and side effects of psychotropics, and the humanistic and empathy fostering attitude of the practitioners of CAM.

The diagnostic category for which treatment is sought includes depressive illness, anxiety disorders, somatoform disorders, cognitive decline, substance use disorders, and psychotic disorders (rarely). As a desperate remedy, unconventional strategies are adopted by patients with chronic and refractory illness.

6.3 What Is the Scientific Rationale?

6.3.1 Exercise, Meditation, Breath Regulation, and Spirituality-Based Therapies

Although yoga practice is known in folk traditions, Indus Valley Civilization, Vedic and Upanishad heritage, and Sage Patanjali structured it to eight rungs—yama, niyama (behavioral level), asana, pranayama (physical level), pratyahara, dharana (cognitive level), dhyana, and samadhi (spiritual level) [4, 5]. Yoga is a healthy practice intended to maintain an equilibrium of fluctuating mind. Patanjali Ashtanga yoga focuses mainly on direct contemplative practices like meditation with or without movements, whereas equal weightage is given for movements, breath regulation, and meditation in Hatha yoga.

The neuroscience involved in the multicomponent yoga practice and meditation is very complex. Multiple brain networks and low-order brain mechanisms are

involved in yoga experience [6]. Supervised postures may reinforce the premotor and parietal mirror neuron system with the resultant improved social cognition and empathy enhancement [7]. Yoga practice may produce a parasympathetic overdrive followed by a balanced autonomic system functioning.

Meditative practices improve neurocognition and mentalizing abilities through refinement of lateral and medial prefrontal brain networks. During deep meditation, the striatum, the left insula, and the anterior cingulate are functionally active, whereas the lateral prefrontal and parietal cortex show reduced activation. The interaction between internal awareness network (posterior and anterior cingulate, precuneus, and medial orbitofrontal cortex) and external awareness network (posterior parietal cortex, dorsolateral prefrontal cortex) underlies mindfulness meditation. Meditation, while reducing norepinephrine and cortisol, may increase arginine vasopressin, gamma-aminobutyric acid, melatonin, serotonin, endorphin, and brain-derived neural growth factor. Exercise, breath regulation, and mentalizing components improve neuroplasticity, alter the expression of genes associated with cellular metabolism and oxidative stress, and reduce proinflammatory signaling [8, 9].

Tai Chi and Qigong are traditional Chinese exercises involving body movements, breath coordination practices, and meditation. Tai Chi and Qigong have been shown to augment immune function and baroreceptor sensitivity [10]. Dance involving kinesthetic and emotional perception as well as expressive and sociocommunicative skills may enhance empathy. It also helps in motor learning through the action-observation network.

6.3.2 Biological Treatments (Herbs, Nutrients)

Herbal medicine and nutraceuticals include St. John's wort, *Crocus sativus*, passionflower, valerian, sage, *Withania somnifera* (ashwagandha or Indian ginseng), *Convolvulus pluricaulis* (shankhpushpi), *Bacopa monnieri* (Brahmi), SAM-e (S-adenosylmethionine), omega-3 fatty acid, folic acid, myoinositol, N-acetylcysteine, glycine, *Ginkgo biloba* extract EGb761, and curcumin (*Curcuma longa*). The proposed mechanisms include antioxidant, immunoregulatory, and anti-inflammatory with modulation of various neurotransmitters, neurosteroids, and cytokines. These herbs and nutrients are used primarily for mild depression, anxiety, insomnia, and cognitive decline.

6.3.3 Acupuncture and Cranial Electrotherapy Stimulation

Acupuncture is a traditional Chinese therapeutic tool using needles (including press needles). Various acupuncture protocols have been used with multitude mechanisms including vagal stabilization [11]. Cranial electrotherapy stimulation (CES) is a noninvasive electromedical treatment using a weak electrical current (less than 4 milliamps), given to the ears or scalp for 20–30 min. CES causes cortical deactivation, increases alpha activity, and decreases delta and beta activity. The

neurochemical alterations include increased levels of endorphin, adrenocorticotrophic hormone, serotonin, melatonin, norepinephrine, and decreased serum cortisol levels [12].

6.4 What Is the Current Clinical Evidence for "Unconventional Treatments?"

Many systematic, evidence-based reviews [13–23] have evaluated the role of CAM in psychiatric disorders and reported level 1 evidence (meta-analysis or replicated double-blind (DB), randomized controlled trial (RCT) that includes a placebo condition) for only a few treatments, which cannot be recommended as a primary intervention. Spiritual augmentation of cognitive behavioral therapy has also been shown to be effective in demoralization and depression [24].

Most treatments have only level 2/3 evidence (level 2 at least one DB-RCT with placebo or active comparison condition; level 3 prospective uncontrolled trial or case series or high-quality retrospective studies). The methodological issues and side effects including drug interactions limit recommendation for wider use. Yet, these treatments may be used as adjuvants in selected cases.

6.5 Why Is There a Dearth in Evidence-Based Research in CAM?

Practitioners of CAM use different diagnostic categories to classify patients with mental illnesses, negligible public demand for "proof of effectiveness" because of wide popularity and perceived better quality of life, lack of government or pharmaceutical support, inadequate training in research methodology, use of combination of treatments, highly individualized and tailored treatments based on patient's feedback, multicomponent strategies (e.g., yoga), heterogeneity of clinical study designs, methodological lacunae (small sample size, randomization and blinding issues, lack of active comparison group, etc.), variability of assessment tools, and the wide disparity in defining primary outcome variables. Many natural products are marketed as dietary supplements containing diverse active ingredients which are not scientifically analyzed for proven efficacy or toxic effects.

6.6 What Should Be Done in Future Studies?

The proposed stepped approach for mind and body research requires proof of concept, intervention refinement and standardization, pilot testing for feasibility and acceptability, efficacy or effectiveness studies with active comparison group, and further studies which can guide for wider use [25]. In herbal and other unconventional biological treatment research, the active ingredient has to be evaluated like any modern psychopharmacological agent with probable pharmacologic

mechanism of action, the safety profile, and specific clinical targets. Well-designed, adequately powered clinical trials incorporating suitable controls are needed for any recommendation for wider clinical use. Although designing and validation of a yoga-based intervention is attempted in schizophrenia and obsessive-compulsive disorder [26, 27], future studies of CAM should evaluate electrophysiological, neuroimaging, and neuroendocrine parameters to unleash any specific biomarker.

Conclusion

Kienle and co-workers [28] have commented on the reverse research strategy employed in CAM vis-à-vis conventional drug therapy. Conventional medicine mandates preclinical studies followed by clinical studies before a drug is approved in clinical practice, whereas CAM adopts a model of clinical wisdom and experience translated to clinical practice before any preclinical studies are done. Regulatory decision-making requires randomized controlled studies, the backbone of evidence-based medicine. Although today's evidence may be discarded in future, it is important in scientific wisdom to analyze the efficacy/effectiveness, the biological targets, and the benefit-risk ratio. Current evidence suggests that most of the CAM approaches cannot be recommended as primary intervention yet may be used as adjuvant depending on the patients' preference. However, currently employed evidence-based requirements focusing on technical rationality and marginalizing clinical expertise and patient's autonomy may not fit to evaluate the unconventional treatment modalities as the practices are heterogeneous, multicomponent (as in yoga), and often used along with other conventional treatments. Good clinical practice recommends respect to autonomy, better benefit, and less harm, honoring personal and cultural dignity and employing evidence-informed (if not evidence-refined) treatment to offer the "best treatment" if patient is taken as a whole.

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Dual Disorders: Addiction and Other Mental Disorders. Integrating Mental Health

7

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Abstract

Understanding dual disorders (DDs) implies recognizing that an addiction is a mental illness and therefore a brain disease. There are common brain areas involved in both addictions and other mental illnesses; it could explain the high comorbidity between drug use and other psychiatric disorders. Factors increasing the vulnerability to develop an addiction include family history, early initiation of substance use, socially stressful environments and suffering from a mental illness. In addition, lifetime diagnosis of any mental illness has been found to be associated with higher prevalence of transition from substance use to substance use disorder. Social influences are critical factors that promote experimentation or initiation which, combined with an individual vulnerability, may lead to a substance use disorder development. Historically, there has been an artificial separation between services treating addiction disorders and services treating other mental illnesses. The new paradigm of addiction, which indicates that DDs are a brain disease, highlights the need to reconsider this model.

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7.1 Introduction and Definitions

Despite mounting scientific evidence and advances in knowledge regarding the common neuroanatomical and neurofunctional basis of mental illness and concurrent substance abuse, the conceptualization of dual disorders (DDs) has been relatively ignored or denied for years. Nevertheless, recent research has increasingly supported the view that addiction is an acquired disease of the brain, explaining how a voluntary drug use can interact with environmental and genetic factors to result in addiction in some persons but not in others [1].

The history of defining DDs has evolved over time. It has been 40 years since clinicians began to name the condition of patients with substance use disorders (SUDs) associated to other mental disorders, and "dual diagnosis" emerged as an initial term which became useful [2]. However, many other terminologies have been applied to name the same concept: mentally ill chemical abusers, chemically addicted mentally ill, co-occurring disorders, or comorbid disorders [3, 4].

During the effort to define the relationship between substance misuse and other mental disorders, the term "comorbidity" has also been used [5]. In our opinion, this expression could lead to a problematic misinterpretation as it merely refers to an association in time, but it does not establish a causal relationship [6], which is the terminological wealth of "dual disorders".

This novel terminology (and also concept) has allowed addictions to be currently within the scope of mental health. Whereas it could seem obvious nowadays, this idea is relatively recent though, since addictions were once misunderstood as lack of willpower, psychiatry has not always paid attention enough to this field, which led to stigmatization of those who suffered from them [7].

So, the critical point is if we are describing two independent and categorical DSM different entities or just multiple clinical manifestations of a single etiology. Clinical practice demonstrates that, both in substance use disorders and other mental disorders, we can identify innumerable phenotypes receiving the same DSM diagnostic category [8]. Therefore, current diagnosis classifications are simplifying real phenomenology, which is probably the handicap of every categorical procedure in medicine.

On the other hand, symptoms that do not reach the diagnostic established threshold might impact severely on individual's functionality. Thus, using a dimensional approach instead of categorizing or dichotomizing increases the possibility of understanding the case and designing an accurate global therapeutic intervention [9–11]. However, we are too used to categorical criteria to eliminate them, and they also offer advantages for common approaches to diagnosis. Integrating models have been purposed for amplifying categorical definitions with a dimensional component in a way that is evolutionary and not disruptive to the existing taxonomy [12]. This new context probably reflects that we are moving from the categorical diagnostic system to a more personalized and precise psychiatry.

Personalized medicine is based on the assumption that the average response to treatment is not necessarily representative of the response of each individual [13].

Even using a categorical model which presupposes relatively homogeneous groups, they should constitute an initial step for developing more accurate risk prediction models. Thus, it will promote the development of personalized evidence-based approaches for heterogeneous syndromes such as dual disorders.

Another conceptual misinterpretation, which brought about confusion in this field, has been to distinguish between substance-induced (mental) disorders (SID) and dual disorders. Only a comparatively small proportion of psychiatric illnesses appears to be possibly attributable to substance use, whereas an important proportion of substance use seems possibly attributable to psychiatric illnesses, and many mental disorders have their onset prior to the emergence of the SUDs [14, 15].

Thus, for example, depression levels are associated with increased likelihood of lifetime use of tobacco, marijuana, alcohol, inhalants, prescription painkillers, and other substances [16]. On the other hand, the NESARC study [17] demonstrated that purely substance-induced depressive disorder (SIDD), despite its importance in DSM-5, accounts for a very small percentage of mood disorders among all those individuals with SUDs [18]. However, there are similar patterns of comorbidity and common risk factors between SIDD and major depression among people using substances, which suggest that both conditions may share underlying etiological factors [19]. Therefore SIDD, from a descriptive point of view, could be over-dimensioned leading to the wrong admission door for DDs patients.

Recognizing the relevance of this new integrative paradigm, on November of 2011, the World Psychiatric Association's (WPA) Executive Committee approved the creation of a specific section on dual disorders, whose significance was definitely supported during the WPA General Assembly on 2014.

7.1.1 Addictions Without Substances

Researchers and DSM-5 have recently agreed to recognize that certain behaviors resemble substance addictions [20]. Core features include continued engagement in a behavior despite adverse consequences, craving that often precedes behavioral engagement and compulsive behavioral engagement [21, 22]. Pathological gambling, kleptomania, pyromania, compulsive buying, but also more contemporary disorders as Internet use/gaming disorders or sexual compulsive behaviors could be included in this category [23, 24]. However, DSM-5 only has reclassified gambling disorder, making it the first (and unique for the time being) behavioral addiction in DSM. Probably Internet gaming disorder will be included soon.

Growing evidence is emerging from neurocognitive, neurochemical, neuroimaging, and genetic research suggesting similar pathophysiology between substance use disorders and behavioral addictions [25, 26]. Accordingly, current research and DSM-5 also suggest neurobiological similarities between obesity, binge eating disorder, and SUDs, suggesting that treatment advances in the field of SUDs may inform advancements in the treatment of eating disorders and vice versa [27].

However, some concerns have been raised about the potential negative impact of being too inclusive regarding behavioral addictions [28].

7.1.2 Relevant Definitions Related to DDs

7.1.2.1 Substance Use Disorder (SUD)

Diagnostic term used in the fifth edition of *the Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) referring to the recurrent use of alcohol, tobacco, or illegal drugs that causes clinically and functionally significant impairment, such as health problems, disability, and failure to meet major responsibilities at work, school, or family. Depending on the level of severity, this disorder is classified as mild, moderate, or severe [1].

7.1.2.2 Addiction

The most severe phenotype chronic stage of substance use disorder, in which there is a substantial loss of self-control, as indicated by compulsive drug taking, despite the desire to stop using the drug. In the DSM-5, the term addiction is synonymous with the classification of severe substance use disorder [1] and sometimes include physiological "dependence" (tolerance and withdrawal). The term also includes behavioral addictions such as gambling, video gaming, some eating disorders, and other compulsive use disorders without substances.

7.1.2.3 Dual Disorders

This is the term used in the mental health field to refer to those patients who suffer from SUDs or an addictive disorder and other mental disorders. They can occur simultaneously or, even more importantly, sequentially throughout their life span [29]. The definition specifies necessarily a relationship, which could reflect common brain factors. It also implies interaction between the two different psychopathological expressions that affect course and prognosis of both [30]. Interactions between both disorders may involve genetic, neurobiological, neurodevelopmental, social, ethnic, environmental, and cultural domains [31]. The term also allows identifying and thinking about these dimensional conditions that highlight the continuum of severity (mild to severe) as a factor in the heterogeneity (different phenotypes) of individuals with DDs.

Other expressions, as co-occurring disorders or coexisting disorders, have been used to describe the same concept and probably have a wider spreading among the USA and Canada. Thus, they can be used interchangeably. Meanwhile in Spanish language, the most widespread and accepted term is "dual pathology" [4, 6].

The aim of this chapter is not only to review the theoretical background and the historical development of dual disorders' concept but also to provide an overview of the epidemiology, neuroanatomic correlations, diagnostic assessments, and treatment guides for dual disorders (Fig. 7.1).

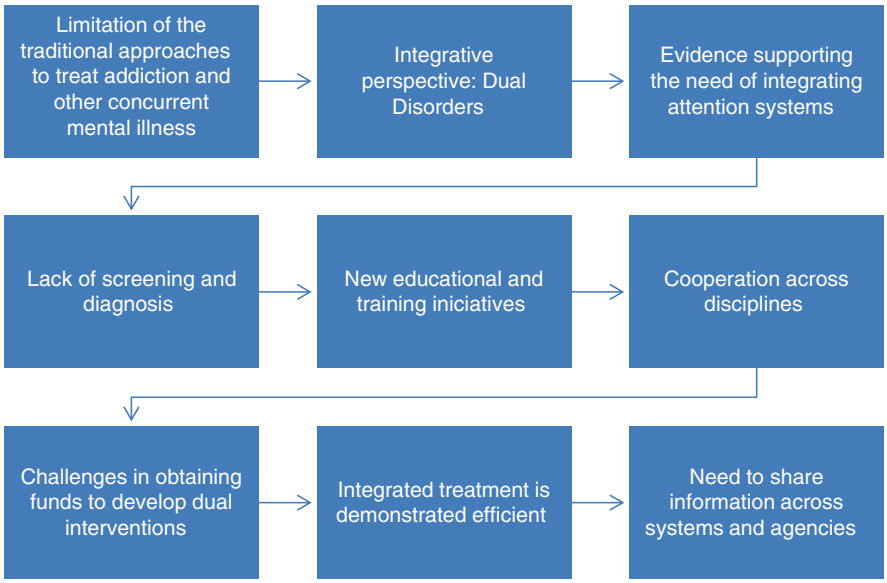

Fig. 7.1 Dual disorders: evolution within the past decades

7.2 Epidemiology of DDs

Only a minority of drug users become addicted, as their vulnerability to genetic, environmental, and developmental factors differ [1]. Factors increasing the vulnerability to develop an addiction include family history, early initiation of substance use, socially stressful environments, and suffering from a mental illness [32]. Thus, drug use before the age of 14 leads to fourfold greater likelihood to develop a substance use disorder in life.

People suffering from any mental illness have a greater risk of suffering from a substance-related disorder as well. The risk has been estimated to be four to five times higher than the general population [33, 34]. Lifetime diagnoses of any mental illness have been found to be associated with higher prevalence of transition from substance use to SUD across most categories of substances [35]. Mental illness' early treatment plays an important role in high-risk population [32]. For example, medication may reduce substance use disorders in children and adolescents with attention-deficit hyperactivity disorder (ADHD), when given before puberty, who are almost three times more likely to develop a SUD compared with other adolescents [36].

Individually, substance use patterns are widely variable. Whereas some subjects face lifelong difficulties with substance misuse, other people suffer phasic symptoms, while others do not have any problematic use. Nonetheless, from a population perspective, there are consistent and predictable epidemiologic patterns [37].

Thus, DDs are so common that they should be expected in the regular clinical practice instead of being considered an exception, as per accumulated epidemiological evidences [38]. In the USA in 2013, 24.6 million of people (9.4%) aged 12 or older were current illicit drug users, 60.1 million (22.9%) were binge alcohol users, and 21.6 million (8.2%) had a past year SUD [39]. Regarding mental health needs in the USA, 43.8 million adults aged 18 or older (18.5%) were estimated to have any mental illness in the past year, and 10.0 million (42.2%) had a serious mental illness. In 2013, 3.2% of all adults aged 18 or older (7.7 million adults) had both SUD and any mental illness. In 2013, 1% of all adults (2.3 million adults) had a dual disorder in the USA. Among adolescents, this proportion increases to 1.4% of the population.

Several major epidemiological surveys have been conducted in the general population to examine the co-occurrence of SUDs and other psychiatric disorders in the USA: the Epidemiological Catchment Area (ECA) Study [40], the National Comorbidity Survey (NCS) [41], the National Comorbidity Survey Replication (NCS-R) [42], and the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [15]. All these epidemiological studies coincide and confirm that DDs are the norm and not an exception. On the other hand, there is a lot of epidemiological evidence, based on clinical population, of the high rates of DDs in patients seeking treatment in the psychiatric clinic or in the drug clinics [4, 43] Furthermore, epidemiological research also indicates a reciprocal contribution to the development of both disorders [42, 44, 45].

Although one in three people with mental illness smoke tobacco, a historical significant deficit has been to minimize or ignore the impact of the tobacco use disorder in this collective [46]. Lifetime diagnosis of any mental illness has been found to be associated with a higher prevalence of transition from tobacco use to tobacco use disorder [35]. According to Sheals et al. (2016), the most commonly held beliefs among mental health professionals were that patients are not interested in quitting (51.4% of mental health professionals) and that quitting smoking is too much for patients to take on (38%) [47]. These attitudes and misconceptions may undermine the implementation of smoking cessation interventions.

Whereas it is still maintained that substance use causes or triggers mental illnesses that otherwise would not have occurred [48], other epidemiological studies do not confirm this hypothesis, because despite the increase, in some cases exponentially, of substance use [49], there has not been an increased incidence of other mental disorders. Thus, causal relationship between substance use and mental illness remains an area without consensus.

Suicidal behavior is a significant problem for people with dual disorders. Up to 40% of patients suffering from dual disorders report a history of previous suicide attempts [50]. Substance use has been identified among the main risk factors for suicidal behavior [51], and it has even been stated that there is a causal relationship between substance use disorders and suicide [52]. However, personality traits (impulsiveness, hopelessness, coping strategies), sociodemographic factors, and comorbid disorders such as depression may modulate this relationship [53–56].

7.3 Neurobiology of Dual Disorders

Understanding dual disorders implies recognizing that an addiction is a mental illness and therefore a brain disease [1]: there is a powerful link between addiction and brain function, impairing the ability to feel pleasure and motivation. Research has repeatedly supported this statement, but it has not always had the desirable impact in the clinical practice, as it would have been expected. The concept of addiction being a complex brain disease supposes a new paradigm that questions drug compulsive abuse as a voluntary and hedonistic act.

DDs have existed so far as orphans of an integrative perspective and have been thought of as an undesirable inclination of some subjects to drug consumption due to a lack of willpower, omitting the neurobiological dysfunctions of systems and brain circuits also involved in other mental disorders [57].

Addiction is characterized by a compulsive drug craving, seeking, and use despite devastating consequences. People suffering from a substance use disorder endure conditioned responses and stress reactivity which drive them to drug consumption in order to avoid negative emotions. Executive functions are involved in these drug-seeking behaviors. Neural regions playing an important role in addictions are ventromedial prefrontal cortex, amygdala, striatum, anterior cingulate cortex, and insular/somatosensory cortices [58–60].

Koob et al. have divided addiction into three recurring stages associated with specific circuits and clinical and behavioral consequences: binge and intoxication, withdrawal and negative affect, and preoccupation and anticipation (craving) [61]. The use of drugs activates rewarding circuits, releasing dopamine, and producing associative learning which drive users to experience desire to take the drug when environmental stimuli appear. For many years, it was believed that chronic drug consumption would increase sensitivity to the rewarding effects of a drug. However, although this theory appeared to make sense, it has been demonstrated that in addicts, drug consumption triggers much lower dopamine than in the general population [1]. After repeated use of a drug, dopamine cells start firing in response to conditioned stimuli itself instead of firing in response to the drug [62]. The responses become deeply ingrained and have been observed to be preserved even when the use has remitted a long time ago [1]. In this new environment, the reward system develops a desensitization of rewards (both substance and non-substance related) [63].

There are common brain areas involved in both addictions and other mental illnesses (depression, anxiety, or schizophrenia) [30]. These changes could explain the high comorbidity between drug use and other psychiatric disorders. Thus, although deficits probably exist before the consumption begins, it may be worsened by the substance use increasing the affectation of brain areas and functions [64].

Substance and behavioral addictions share a neurobiological correlate. Thus, behavioral addictions are also characterized by functional and anatomical abnormalities in cortical and subcortical regions and circuits [64].

Behavioral decision-making and emotional balance are impaired in both substance and behavioral addicts, who show a tendency to immediate reward, altering voluntary behavioral control, which is also abnormal in other related disorders of self-regulation (obesity, Internet gaming, etc.) [1, 58].

Recent research has differentiated between two different neural dysfunctions, which trigger addictions by affecting decision-making. The first one would involve the impulsive system, exaggerating the rewarding drug consumption experience, probably through a hyperactivity of the amygdala. The second way to become an addict would involve a hypoactivity in the prefrontal cortex, impairing the reflective system [58, 60]. Regarding the cognitive control network, during cognitive and behavioral control, attenuated functional and structural connectivity has been observed between the amygdala, the insula, the rostral anterior cingulate cortex, and ventromedial prefrontal cortex structures [59].

Researchers have proposed different neurobiological theories to explain addiction. These conceptual approaches involve multiple systems in the brain, not simply dopaminergic reward centers (which govern the ability to plan, anticipate, and change their behavior, under various circumstances). All psychoactive substances with abuse potential bind to some endogenous system, such as opioid, cholinergic/nicotinic, glutamatergic, endocannabinoid system, etc. [57, 65].

These endogenous systems do not exist for humans to get high but are linked, from an evolutionary perspective, to individual and collective survival of the species. From this perspective, animals would benefit from a neural mechanism (circuitry) that supports an animal's ability to pursue natural rewards (food, water, sex). These circuits are sometimes dysfunctional, leading to various types of disorders as contemporary exposition to substances subject individuals to potent cues, which test their neurobiology [66, 67]. However, it is estimated that only a small proportion of people exposed to substances will develop the most severe forms of substance use disorders (approximately 10%), and even in those who progress to addiction, there will be different severity phenotypic characteristics [68].

A deficit, both inherited and acquired, in these systems and brain circuits, which may be dysfunctional, could explain both addictive behaviors and the concurrence with other psychiatric symptoms, including pathological personality traits [57].

Adolescence is a particular risk period when dual disorders start to appear gradually. Mental illness screening is crucial at this point. A still developing brain is especially sensitive to substances, whereas mechanisms of emotional self-regulation and reward are not mature yet. Early interventions at this point seem to be particularly efficient [32]. Preventive actions should be designed to enhance social skills and improve self-regulation [1].

There is also a biological correlate that links suicidal ideation and dual disorders [51, 69]. Researchers have found abnormalities on the noradrenergic-locus coeruleus system, serotonergic system, and endogenous opioid system in suicidal behaviors and completed suicide. Thus, the use of drugs can alter transmission, which has been involved in suicidal behavior. Future research should also try to integrate findings in the psychological and biological domains.

7.4 Psychosocial Determinants

Psychosocial risk factors may contribute to a better understanding in dual disorders' development. Social influences are critical factors that promote experimentation or initiation which, combined with an individual vulnerability, may lead to a substance use disorder development.

Early initiation of substance use (childhood and adolescence) contributes to higher levels of substance use disorders and DDs later in life. Furthermore, early initiation is also related to more severe social adjustment problems [37].

Although causality cannot be established, mental disorders are risk factors for subsequent development of addiction disorders [30]. Although there is an association between mental disorder and substance use disorder development, this relationship seems to be attenuated after correction for childhood adversity and other substances misuse prior to mental illness onset [70], which appears to be a significant risk factor itself. Thus, DDs are commonly presaged by problems in childhood and adolescence and the early expression of psychopathology [71]. Psychological characteristics which have been associated with substance use disorders include poor self-esteem, low assertiveness, and poor behavioral self-control.

Family factors play an important role in substance use. While aggressive behavior, high levels of family conflict, and poor parental support may contribute to substance use disorders, consistent limit setting, careful monitoring, and communication may promote healthier coping mechanisms and a protective environment. Parental separation, single-parent families, or blended families have been found to be predictors of addiction development [72]. Socioeconomic family difficulties (educational, financial, and social status) have also been suggested as facilitators to drug dependence among youths and young adults.

Childhood abuse and neglect have been associated with drug use, with an earlier initiation and more extensive polydrug use [73]. Results indicate that child sexual abuse is a statistically significant, although general and nonspecific, risk factor for substance problems [74].

Paternal and maternal psychiatric disorders are associated with an increased risk of substance misuse and behavioral and emotional difficulties in their children. Similarly, parental drug or alcohol misuse has been stated as a risk factor for drug dependence development.

Even though some drug users consider substance abuse as a socio-environmental phenomenon embedded in interpersonal activities, solitary substance use appears to be a significant predictor of substance use disorders [75]. Nonetheless, personal relationships, free time activities, and coping strategies are essential to address substance use disorder development and approach.

Behavioral addictions have also been associated with adverse psychosocial development and mental disorders. Dysfunctional familial relationships and poor academic performance are risk factors for behavioral addictions, which appear to arise from composite interactions between personal, familial, and psychosocial framework [76].

7.5 Diagnostic Assessments

Because dual disorders are highly prevalent, all practicing psychiatrist are likely to look after patients suffering from them. However, only a small fraction of people with DDs receive early attention and treatment, delaying the beginning of an intervention up to more than a decade. In addition, only a minority will ever reach specialized care [77].

Psychiatric conditions are syndromes rather than diseases, what makes difficult to disentangle the overlapping symptoms of SUDs and other mental disorders, turning diagnosis into a complex target. Special efforts must be dedicated to people suffering from DDs as an accurate diagnosis is critical to ensure appropriate and effective treatment.

Even though there is a consensus about the need to screen, capacity to report drug use among serious mentally ill patients has been controversial. During Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) survey, assessing mainly schizophrenic patients, a significant proportion (38%) of participants tested positive for drug use on laboratory measures, and more than half (58%) did not report using these drugs. Thus, Bohorik et al. have stated that subjects suffering from schizophrenia, especially those with significant cognitive impairment, tend to underreport the use of substances, which is actually common among these patients [78]. However, other colleagues have questioned their findings and have argued that individuals with schizophrenia can adequately and accurately self-report their substance use [79]. To them, biological tests add little to the accuracy of multimodal assessment protocols [80], suggesting that, overall, self-report is able to garner accurate information regarding illicit drug use among adults with schizophrenia and other serious mental illness [81].

Frequently, mental disorder's diagnosis and treatment are delayed until diagnostic thresholds are achieved. This could increase clinical practice's accuracy, but subclinical symptoms are known to predispose drug use, leading to confusion about what came first. According to Volkow et al., three different scenarios must be considered [30]:

- Scenario 1: Drugs emulate mental illness symptoms among users. This scenario has been known as "substance-induced (mental) disorders" (SID). Cocaine-, marijuana-, or methamphetamine-induced psychoses have been purposed as models to explain this possibility [82].
- Scenario 2: Mental illnesses can lead to drug abuse. People suffering from mental disorders could use substances as a way or self-medication in order to improve their psychiatric symptoms. Thus, mentally ill individuals would use drugs to achieve self-neurobiological regulation. One example is the abuse of stimulants in individuals with ADHD syndrome [83].
- Scenario 3: Interaction between overlapping factors such as genetic vulnerabilities, underlying brain deficits, and/or early exposure to stress or trauma causes both, addictive and other mental disorders [30].

In the purposed model of precise and personalized psychiatry, clarifying symptom heterogeneity is meaningful, as even subthreshold symptoms may impact quality of life and treatment outcome. The use of relatively homogeneous groups can be used as the basis to advance in the development of personalized evidence-based medicine approaches to heterogeneous syndromes such as DDs [13].

It is difficult to combine the development of standardized diagnostic instruments to this perspective, since including individual differences increase complexity and categorical models may not compile the repertory of syndromes and their particularities observed in the clinical practice. The central theme of personalized medicine is the premise that an individual's unique physiologic characteristics play a significant role in both disease vulnerability and in response to specific therapies [84].

The commitment to assess patients individually demands the effort of integrating the evidence-based medicine and the personalized medicine to obtain the best results on each patient. We are moving to function-based framework, including dimensional and categorical aspects, as well as vulnerability and resilience diagnostic elements [85], defining clinical entities by the extent of dysfunction on large-scale neural circuits. This new models could also help to translate neuroscience advances into clinical practice [86].

Therefore, diagnosis on dual disorders should be an individualized assessment, possibly imperfect, bearing in mind different symptomatic dimensions from a longitudinal perspective. The approach must take place as soon as possible, without arbitrary waiting periods, not requiring psychiatric stabilization, based on an integrated longitudinal history [38].

However, assuming the wide spread of the categorical traditional perspective, we can suggest the use of the "The Dual Diagnosis Screening Instrument" (DDSI) [87], a PRISM derivative (Psychiatric Research Interview for Substance and Mental Disorders). The DDSI has shown a high sensitivity (≥80%) and high specificity (>82%) for identifying lifetime depression, mania, psychosis, panic, social phobia, and specific phobia disorders. The duration of its administration makes this interview a realistic useful tool for daily clinical practice.

The Global Appraisal of Individual Needs-Short Screener (GAIN-SS) is another tool with adequate internal consistency, designed to identify and put into groups dimensional psychopathology, distinguishing between "internalizing disorders" and "externalizing disorders" and including substance use disorders and other mental disorders. The substance use disorder subscale has shown adequate sensitivity (88%) and specificity (89%) [88], although psychiatric disorder subscales have been found less efficient.

Anyhow, it has been noticed that many of these instruments fail to identify patients with attention-deficit hyperactivity disorder (ADHD), which is essential in patients with addictions considering its reported high prevalence and its importance regarding treatment approaches [89]. The most relevant and effective tool in the assessment of dually diagnosed patients with ADHD and SUD is a full and comprehensive clinical and psychosocial assessment. Nonetheless, complementary screening tools such as the adult attention-deficit hyperactivity disorder quality of life (AAQoL) scale or the adult ADHD Self-Report Scale v.1.1 (ASRS v1.1), as well as

other semi-structured clinical interviews like Conners Adult ADHD Diagnostic Interview for DSM-IV (CAADID) or Diagnostisch Interview voor ADHD bij volwassenen (DIVA 2.0), can be useful.

7.6 Integrated Models of Treatment

All around the world, historically, there has been an artificial separation between services treating addiction disorders and services treating other mental illnesses, probably based on the belief of the sociogenetic, environmental, and cultural origin of addictive disorders [1]. Due to this theoretical incompatibility, two different treatment networks were created and developed for years. Alcohol and tobacco have even been artificially excluded from the drug system regularly. As a consequence, both networks have not been able to correctly look after the full range of problems presented by people suffering from dual disorders. Professionals' attitudes are among the main barriers to correct integration and effective treatment [90]. The new paradigm of addiction, which indicates that DDs are a brain disease, highlights the need to reconsider the model [29].

In order to treat patients with DDs, it is crucial to understand the limitation of the traditional approaches for the assessment and management of these disorders. The effective integrative treatment requires collaboration across disciplines and also sharing information across systems and agencies [91].

Ignoring or failing to treat DDs can jeopardize a patient's chance of recovery. Growing evidence from research demonstrates that integrating mental health treatment and substance use treatment into a single cohesive model increases efficiency and efficacy. In addition, inpatient (residential) integrated treatment for dual disorders has also shown higher efficacy for individuals who have not responded to outpatient interventions [2].

There is a need to develop and integrate in daily clinical practice meaningful dimensional indicators of improvement and treatment efficacy rather than using substance abstinence as dichotomous outcome [92]. It seems clear that dual disorders share many characteristics with other chronic diseases. Proposed indicators would focus on patient reported measures of functioning and psychosocial benefits. However, health issues and morbimortality must be used as other treatment indicators, especially from a more global perspective (epidemiological).

Successful treatment interventions for patients with DDs should consider both "disorders" as primary, and treatment of both should be integrated and simultaneous, avoiding arbitrary conditions, such as sobriety periods, in order to access assessment and treatment [93]. There is a growing body of research on the effectiveness of psychopharmacological interventions, even when active substance use continues (Table 7.1).

While treating DDs, interactions between pharmacological treatments and substances must be taken into consideration. Beside treatment's safety, medication abuse must be prevented and monitored.

Table 7.1 Specific substances and treatment constraints and clues

Substance	Frequent concurrent disorders	Constraints	Treatment clues
Cocaine and other psychostimulants	Substance-induced psychosis vs schizophrenia Anxiety disorders Depression ADHD Personality disorders	Lower antipsychotic efficacy Higher incidence of antipsychotic side effects Lower adherence	Symptomatic pharmacological treatment Psychotherapeutic approach
Tobacco	Schizophrenia ADHD	Cancer and other major health issues risk factor	Varenicline, bupropion, nicotine replacement therapy
Opiates	Mood disorders Triple diagnosis (HIV/HVC) Borderline personality disorder	Chronic curse Main cause of death related to substances	Opioid agonist: methadone, buprenorphine Antagonist: naltrexone Adrenergic agonist: clonidine Psychosocial approach
Alcohol	Mood disorders Anxiety disorders ADHD Antisocial and borderline personality disorders Gambling Frequent polydrug use	Major impact on physical health Increases suicide risk	Detoxification: thiamine, benzodiazepines, tiapride Aversive: disulfiram Anti-craving/priming: nalmefene, naltrexone, acamprosate Anticonvulsants: gabapentin, topiramate Individual and group therapy
Cannabis	Psychosis ADHD Mood disorders Anxiety disorders Personality disorders	Close association with other substances use Trivialized risk	Symptomatic pharmacological treatment Psychotherapeutic approach

ADHD attention-deficit hyperactivity disorder, *HIV* human immunodeficiency virus, *HCV* hepatitis C virus

Many studies have suggested that combining medication with psychosocial interventions improves dual disorders' treatment outcomes [94]. Psychosocial and motivational interventions have been effective to improve the patient's emotional functioning and to prevent relapses, increasing long-term adherence to the longitudinal care plan. The most consistent evidence recommends the use of cognitive behavioral therapy (CBT) and motivational enhancement therapy for assisting with substance use reduction in dual disorders [95]. Psychosocial treatments must be also individualized to address personal factors and stage of motivation [2].

Early treatments for emotion regulation, which improve prefrontal functioning, may offer efficacy for preventing substance disorders, as the impairment in this

Table 7.2 Pharmacological agents

Property	Main objective	Examples
Antagonist	Receptor blockers. Antagonists do not allow the drug to produce their physiologic action	Naltrexone, naloxone, nalmefene
Agonist	Partially mimic drug's effect, binding the same receptors	Methadone, buprenorphine, amphetamines, varenicline, nicotine
Anti-craving/ priming	Decrease the desire to use a substance	Naltrexone, acamprosate, nalmefene
Aversives	Unpleasant physiologic reactions. Sensitization to the negative effects of a substance when is used combined	Disulfiram

region functioning seem to be the cause of disturbances in emotional regulation that could lead to substance use disorders [60].

However, clinical treatments tend to focus on pharmacological and psychotherapeutic interventions and often ignore other nonmedical interventions, such as housing, employment, social support, etc. [38].

As part of the pharmacological treatment, clinician should consider using pharmacological agents with agonist properties, such as methadone, nicotine, and stimulants or with antagonist properties such as naltrexone, nalmefene, or partial agonists such as varenicline, buprenorphine, and others (Table 7.2).

7.7 Future Challenges

Introducing the concept of dual disorders in clinical practice remains a challenge. Understanding the high rates of substance use among mentally ill people and the increased incidence and prevalence of mental disorders among drug users have taken years, and there is probably no consensus yet. From this point of view, the evolution and prognosis of both disorders are related to their initial development. Therefore there is an urgent need to integrate healthcare networks.

This new paradigm has not only clinical but also research implications and offers promising perspectives to develop innovative approaches both in addiction and other mental illness fields. Despite their high prevalence and severity, the vast majority of pharmacological treatments have not been assessed for dual patients as clinical trials were designed to proof efficacy for just one mental illness.

Specific research in DDs is needed. Clinical trials in population with DDs must be promoted to gain evidence, which would facilitate effectiveness and a rational use of resources.

Implementing this purposed integrative model of treatment for dual disorders faces the challenge of getting funds from stakeholders and clinical directors in order to make possible a combined approach. In addition, there is a need for specific and broad training of professionals working with people suffering from DDs, probably creating specialized teams.

Objective predictors of response must be developed to improve outcomes. Identifying phenomenological subgroups and biomarkers in addiction could probably provide targets for treatment. In addition, standardized and efficient tools must continue developing to integrate empirical approaches in clinical practice.

Nowadays we know that suffering from a dual disorder is a risk factor for other health issues. For instance, dual disorders predispose the HIV and HCV infection. Beside virus acquisition, dual disorders worsen the infection progression and deteriorates adherence to treatments. However, it has been noticed that it will take longer to initiate treatment for people suffering from a dual disorder, and morbidity and mortality are increased among these groups [96]. Thus, some investigators have named this comorbidity as "triple diagnosis" due to its high prevalence (up to 79% of people living with HIV/AIDS) [97]. This example highlights the need of future coordination between dual disorders' professionals and other specialist physicians.

In spite of the major improvements done, many questions remain unresolved.

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Accessible and Cost-Effective Mental Health Care Using E-Mental Health (EMH)

8

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Abstract

The burden of disease due to mental illness has risen dramatically over the last 20 years. Only a small minority of patients globally has access to expert-level care, and the number of trained specialists in some of the mental health profession is declining. This is happening on the background of extremely limited resources for mental health care worldwide, including developed countries where it is the most underfunded area in medicine.

With current health-care paradigms, it will be impossible to address this disparity; mainly the development of new web-based technologies offers the opportunity to approach that problem. E-mental health can contribute substantially to a more accessible and cost-effective system of delivery with higher quality and sustainability of care. It also allows for the reallocation of health-care spending toward a more patient-focused approach.

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8.1 Introduction

The World Health Organization (WHO) refers to mental health as "a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community."[1] Mental health has also been considered an important aspect of societal and economic progress [1, 2]. Unfortunately, in most parts of the world, mental health is not given the same degree of importance as physical health and is instead ignored or neglected [3].

It has been estimated that about 30% of the global population is affected by a mental disorder in a given year [4]. Mental illness alone is expected to account for most of the global burden of disease, followed by cardiovascular diseases, cancer, chronic respiratory disease, and diabetes [5]. Of the 30% affected by mental health problems, over two thirds do not receive adequate care, while access is one of the most important reasons.

Research shows that people suffering from mental issues are typically heavy users of all medical services, including primary care and various types of physical health services. If mental health care and support were available to these patients, it could reduce medical utilization and generate large savings to health-care programs. A study by Lechnyr [6] indicated that individuals in need of, but not receiving, mental health care visited a medical doctor twice as often for no appropriate reasons than persons who receive treatment. The Group Health Association found that patients receiving mental health counseling decreased their nonpsychiatric health-care usage by 30.7% and their use of laboratory and X-ray services by 29.8% [7]. Another study showed that patients who participated in psychosocial interventions decreased their average length of hospital stay by 77.9% and had a 66.7% decrease in hospitalization frequency, a 47.1% decrease in physician office visits, a 45.3% decrease in emergency room visits, and a 4% decrease in the number of prescriptions received [8].

Worldwide, many individuals are victimized for their mental illness and are targets of discrimination and stigma [3]. Untreated mental illness often worsens over time, resulting in increased use of emergency services, which in turn leads to extra cost to the society and economy as a whole [9]. For families, wait times for mental health care can lead to considerable loss of income [10]. This is especially true in cases where there is no insurance to cover the potential lack of income as a result of debilitating mental illness that goes untreated [11]. Despite the fact that mental illness accounts for a significant proportion of the global burden of disease, mental health is the most underfunded area in medicine. This ratio between disease burden and disease spending is unreasonable. Furthermore, more than 40% of countries around the world have no mental health policy, and more than 30% do not have any mental health program [3]. Given that the burden of disease due to mental illness is increasing dramatically, the current model of health-care delivery needs to be revisited. As a result,

[1] Retrieved from http://www.who.int/features/factfiles/mental_health/en/ on 11 October 2016.

web-based solutions have been investigated as alternatives or complementary to the current model of care for the following reasons:

- They can improve the efficacy of health care through increased convenience for the patient in terms of time and treatment location [12], the anonymity of such interventions, the reduced costs for health-care providers, and the ability to bridge gaps in the provision of care [13].
- They can support a more effective use of resources and improve the quality of care through changing paradigms [13].
- They are more congruent with general trends in other industries that are moving toward digitalization and virtualization and are less dependent on brick-and-mortar-style delivery models.

The impact of e-mental health interventions in response to the critical challenges faced by the health-care industry is potentially huge. The situation is critical and requires a paradigm shift to address these challenges. In this chapter we discuss areas that could be improved by the implementation and use of e-mental health interventions.

8.1.1 Reduction of Sick Days and Productive Time

As previously mentioned, the global prevalence of mental health disorders is increasing. This increase is associated with financial costs to the affected individuals, their families, and society as a whole. Mental illness affects the ability to work, which results in negative impacts on productivity in the workplace and limits contributions to the national economy. As stated by Chisholm et al. [14], the significant gap between the need for mental health treatment and its availability "affects not just the health and wellbeing of people with mental disorders and their families, but also has inevitable consequences for employers and governments as a result of diminished productivity at work, reduced rates of labor participation, foregone tax receipts, and increased health and other welfare expenditures" ([14], p. 415).

According to the Institute for Health Metrics and Evaluation [15], mood disorders alone account for 2.5% of the global burden of disease. Direct costs of major depressive disorder, suicide-related costs, and workplace costs (i.e., absenteeism and presenteeism) were estimated at over $210.5 billion in 2010, a 21.5% increase since 2005 [16]. Similarly, in 2010, the average *direct* health-care cost of an individual with major depressive disorder was an estimated $10,379 per year, compared to the $4391 cost of an individual without this disorder [16]. However, for every $1 spent on *direct* costs, $1.9 was spent on *indirect* expenses, such as workplace and suicide-related costs, and an additional $4.9 spent on *workplace comorbidity* costs. This serves to underline that the burden of disease associated with depression is also related to the indirect impacts such as absenteeism and loss of productivity in the

workplace. A study by Lepine and colleagues suggested that insufficient mental care has major consequences on individual's ability to work: over a 6-month period, those with major depression took an average of 13 days off work due to illness, compared with 2.5 days for those without depression [17]. Decreased productivity is particularly an important issue in mood disorders, because they often strike during working age, and when become chronic, they lead to an accumulation of lost productivity throughout a person's working life [18].

8.1.2 Reduction of Long Waiting Times

Barriers to primary and particularly secondary care, such as long waiting times for diagnosis and treatment for patients with mental illness, result in overuse of emergency rooms [19]. For employees who receive mental health treatment, employers will save an estimated $5000–$10,000 (per employee per year) in wage replacement, sick leave, and prescription drug costs [20]. Across Canada, waiting times for assessment in child psychiatric services appear to differ depending on clinical priority level (i.e., perceived severity of illness). For children and adolescents with low clinical priority (e.g., anxiety affecting school performance), waiting times averaged at 105.9 days, while some patients had to wait an entire year for an initial assessment [21]. Children and adolescents with high clinical priority (e.g., suicidal or homicidal behavior) waited an average of 3.4 days, with some children waiting as long as a month for an initial assessment [21].

These findings highlight the substantial wait that is likely for children and adolescents with less severe mental health concerns. In some countries waiting times even for severe cases far exceed these numbers. Mental health problems often negatively affect school performance as a result of loss of productivity and increased sick days, which in turn results in a greater likelihood that the child or adolescent will leave school with fewer or no qualifications, be more likely to be out of work, and be more likely to become homeless [22].

Therefore, a multifaceted approach that allows for quick detection, diagnosis, and treatment of mental illness is necessary to reduce the economic burden of disease resulting from increased sick days and loss of productivity at the workplace and schools.

8.2 How Could E-Mental Health Address This Challenge?

Web-based or mobile solutions can address this challenge in the following ways:

- Redefining the patient/physician relationship—when patients become partners in their own health, and make use of online programs and interventions, it helps change the patient/physician interaction. This can have a positive effect on clinical decision-making, increase efficiency, and improve communication between physicians and patients.

- The availability of online mental health support can provide immediate self-assessment to determine everything from the severity of the mental health problem(s) and the associated warning signs to suggestions of the appropriate direction in which to proceed.
- Online programs and interventions may also help reduce patient waiting times by providing resources such as self-management programs or e-therapies like Beating the Blues and MoodGYM. In some cases, these may provide a viable alternative to traditional face-to-face mental health care [23].
- EMH interventions can be accessed easily from anywhere with Internet access and at any time that suits the user. This in turn may help reduce travel costs and time spent in transit, especially for those living in rural areas.
- The possibility of self-booking of appointments in several settings can make contact management as easy as possible and shortens the way between professionals and patients if capacities are available.

8.2.1 Reduction of Cost for Pharmacotherapies

Health-care spending encompasses a wide variety of health-related expenditure such as prescription drugs. In 2010, $259 billion was spent on prescription drugs in the USA [24]. Across member countries of the Organisation for Economic Co-operation and Development (OECD), pharmaceutical spending accounted for about 20% of total health spending on average in 2013 [25]. The cost of polypharmacy, the prescribing of ineffective medications, and noncompliance are important contributors to these rising costs. According to Bennett et al. [26], approximately 40% of the elderly and nearly 11% of the total US population take five or more prescription drugs at any one time.

8.3 How Can E-Mental Health Contribute to Effective Medication Management?

The opportunities in this critical area are enormous:

- Medication management as part of online health platforms can support informed decision-making and could potentially reduce prescriptions over time.
- Online prescription is already possible (e.g., as a function of a “virtual clinic”). The physician could e-mail or fax a prescription to the pharmacy or the patient especially if the patient is known and/or it is a refill after communicating with the patient online [27].
- Online pharmacies or traditional “brick-and-mortar” pharmacies could send certain types of medication by courier to the patient for convenience. Reductions in travel time, handling time, and waiting time could amount to 1–3 h saved per prescription.
- Lower prices through centralized online pharmacies (such as mycare.de in Germany) could reduce medication costs for the patient.

- Informed decision-making can be facilitated by sharing evidence of the effectiveness of existing treatment approaches on consumer websites.
- An alert system (e.g., addressing polypharmacy or unusual pattern of prescription) could help health-care professionals optimize prescription safety and find more suitable alternatives.
- Improved dosing through outcome monitoring or in case of medication with narrow therapeutic range through recording medication blood levels should be a routine and would empower patients to take control of their health checks and their ongoing treatment [28–30].
- Improved patient compliance with pharmacotherapy can be achieved by helping patients to understand their medication and set realistic expectations about their treatment outcomes, as well as through functions and mobile apps like medication reminders [31, 32].

A framework for better medication management based on web-based systems and EMH needs to become a critical component and an appropriate asset for such an important and expensive part of medical care. The use of clinical decision support systems (e.g., MedTech in NZ), applications that analyze data to assist health-care professionals in making decisions regarding diagnoses and medication prescription, will be in place to support the decision-making process probably first as an adjunct asset to reduce medication errors and implement early warnings to professionals as well as patients.

8.3.1 Reduction of Individual Face-to-Face Time with Experts

Face-to-face interactions are by far the most prevalent form of health-care delivery. However, it is not a necessity most of the time, nor is it the most effective intervention from a user and provider perspective. Face-to-face interactions require more planning, effort, infrastructure, and travel time for professionals as well as patients. This traditional form of health-care delivery is especially inconvenient for individuals in remote areas, with travel time and cost being most negatively impacted.

Both physical and virtual interactions with health-care professionals have advantages, and patients should be able to choose their preferred method of delivery. Sometimes patients prefer online contact, which is often just as effective as face-to-face contact and can come with less of a burden or stigma like sitting in a waiting room of a psychiatrist, etc.

8.3.2 The Potential Impact of EMH

A number of online psychological therapies (e-therapies) have been developed over the last decade, and their effectiveness has been evaluated, with promising results. A systematic review of e-therapy for depression and anxiety in children and young people concluded that computerized CBT shows promise as an effective intervention [33].

With the virtual clinic concept [23], all symmetric and asymmetric communication channels from e-mail and chat to video conferencing can be made available, which reduces the need for face-to-face interaction. Cost reduction is related to the fact that you build capacity through being able to see more patients. Documentations and referrals to online resources could happen in the same process. The whole process can be more effective, care can be more accessible, and online resources can replace direct assessments and interventions in part through adding a virtual clinic concept.

However, it is not sufficient to simply replace face-to-face physical visits with virtual video-based visits. The utilization of asynchronous communication modalities such as secure online messaging can provide a more convenient and accessible means for patients and clinicians to engage with one another. Asynchronous web-based e-visits through the computer or smartphone are much more in line with changing communication culture in mainstream society.

8.3.3 Access to and Cost Reduction of Effective Psychotherapies

Psychotherapies of different kinds are proven to be effective in the treatment of most mental illnesses. In Canada, counseling and other psychosocial interventions are not covered by the medical service plans and are not easily accessible. Even in countries in which psychotherapies are financially covered by the health-care system, accessibility and expertise in complex cases are limited.

The use of online psychotherapies is well researched, and the scientific evidence is growing [34, 35]. Guided Internet-based CBT interventions have been found to be equally effective as face-to-face CBT interventions [12]. Combined with face-to-face contact with a mental health professional, these programs can provide the highest level of care. Developed EMH programs are freely available in some countries like Australia and New Zealand (for an overview of EMH services in Australia, see [36]), and the effectiveness of some of these programs is well documented (e.g., [37]).

Psychotherapies can also be used in a blended model in which online interventions are integrated with face-to-face interactions with a health-care professional. Studies on the effectiveness of blended models have yielded promising findings.

8.3.4 Reduction of Cost for Assessments and Diagnostics

Monitoring and screening are critical for the organization of appropriate mental health care. Psychiatric and psychological assessments enable the application of appropriate interventions and the measurement of health outcomes but also take up a lot of time in the interaction between patients and professionals. Assessments need to be undertaken and recorded, which makes them a significant part of the care process.

Screening and online assessments can be integrated into online platforms. If well organized, they can provide ongoing monitoring of patients' well-being, long-term health overview, integrated feedback, automatic scoring, and online referrals. In some virtual clinic models, pre-assessment to a meeting is integrated into the functions including scoring and documentation (e.g., https://inputhealth.com).

The patient's online self-assessment (e.g., https://www.walkalong.ca) allows ongoing monitoring and self-control as a measure of empowerment and base for informed decision-making.

8.3.5 Prevention of Early Retirement and Burnout

Burnout and early retirement are a major threat for the workforce and productivity in developed countries and have been on the rise for a long time. Between 1993 and 2015, the number of early retirements in Germany rose from 41,409 per year to 74,745 cases, which is an increase of 42.7% [38]. Mental illness is the most important reason for this development. Schofield et al. from Sydney quantified the cost of lost savings and wealth to Australians who retire early (ages 45–64) because of depression or other mental illnesses. They included 8864 people and used an economic model called the Health & Wealth MOD, which contained information on employment, income, and wealth accumulated in savings, property, and other financial investments. Forty-three of the 8,864 individuals were not working because of depression, and 56 were not working because of other mental illnesses [39]. Longitudinal studies demonstrate that improvement in depression is associated with significant increases in ability to find or maintain paid employment and significant decreases in time missed from work due to illness.

This has multiple economic consequences for the individuals as well as for the system. The individuals dropping out of their jobs early may end up in poverty and isolation, which is leading to an increase in health-care needs. For the employer, they lose qualified staff and workforce in all areas. As for the society, it has to pay millions for unnecessary costs of a failed system including the fact that these impacted individuals no longer contribute to transfer cost through tax or pension funds.

8.3.6 How Can E-Mental Health Contribute to Better Support?

Broad access to effective programs allows more coverage and treatment for those who now remain untreated. Mental disorders like anxiety disorders, mood disorders, and substance use disorders are commonly untreated, which leads to burnout and dropping out of the workforce. Health insurance in Germany covers psychoeducational programs for targeted prevention of burnout. Relatively simple programs could contribute broadly through broad accessibility. Virtual clinic models could increase accessibility to support from mental health professionals, particularly in more remote areas [23].

Automated early detection systems can be deployed which link employees to EMH online-based resources before they have reached later stages of burnout, which are more difficult to treat. These detection systems can detect behaviors that would be typical for the early stages of burnout through contextual tracking of activity. For example, if an employees' social engagement is decreased through number of messages sent, phone calls responded to, etc., then intelligent systems can link them to EMH-based programs.

8.3.7 Reduction of Ambulance and Emergency Room Cost

Serious mental illnesses are associated with high rates of medical complications leading to high rates of emergency room care [40]. Ambulances or police are called instead of providing ongoing consultation and outreach in communities. Patients and their families often have to travel to crisis services and wait for several hours without a medical reason. The enormous investment (e.g., into the ambulance and first responder system) could be reorganized far more effectively, e.g., through online consultations. Also evidence suggests that patients participating in psychotherapeutic interventions have 45% decrease in emergency room visits [8].

Virtual care and online platforms could reduce travel time dramatically, particularly for individuals living in remote areas. Online consultations could help assess the acute needs of the individual and make informed decisions on the level of care needed. Availability of such online consultations can potentially prevent many expensive ER visits from happening in the first place. Specifically, findings from a study in New York indicated that communities with access to telemedicine used ER services 22% less than communities without telemedicine access [41]. If there would be an opportunity for online consultation, the number of not indicated ER visits could be reduced.

8.3.8 Reduction of Infrastructure Cost

Major costs in health-care delivery are related to clinic space, medical assistance, and transport cost and clinic infrastructure. Costs in these areas could be reduced significantly through a virtual clinic approach.

Professionals could save costs for office space and other infrastructure. They could also organize the use of existing resources more effectively. The virtual clinic model also allows for better communication and collaboration between professionals at different locations with asymmetric ways of communication.

8.3.9 Structural Reorganization of Clinical Pathways

Health-care delivery is very much focused on crisis intervention, with limited resources invested in prevention and early intervention. This is especially evident in addiction cases, where the time between the first identifiable symptoms and the first professional intervention is about 10 years [42].

How can EMH help change that? Integrated care in the form of EMH can contribute to positive change in two main areas: (1) facilitating early intervention and (2) increasing the sustainability of care.

Even though early detection and intervention strategies are an important discussion topic in mental health, the majority of funds are allocated to crisis services. Patients are calling for a shift toward more effective medicine, since the current system is too reactive and responds just when individuals are sick [43, 44]. In a crisis-driven system, the sustainability of care for long-term conditions is limited. Professional interventions are in most cases limited to short interactions and prescriptions.

Grand Challenges in Global Mental Health initiative has identified priorities for research in the next 10 years that will make an impact on the lives of people living with mental and neurological disorders. One of them was developing mobile and IT technologies (such as telemedicine) to increase access to evidence-based care [45].

The accessibility of mobile resources allows users to pursue information, self-assessment, and coping strategies like never before. The platforms are all in an early stage of development, but the potential is there especially if implemented into existing systems (PTSD coach ref.).

Already simple reminders or automated messages are seen as helpful by patients (https://itunes.apple.com/us/app/start-is-your-medication-working/id1012099928?mt=8). The integration of online resources (https://www.downyourdrink.org.uk) embedded in a virtual or face-to-face approach is (https://www.onlinetherapyuser.ca/etherapists/heather-hadjistavropoulos) a qualitative change and improvement for the whole recovery process.

8.4 Discussion

Even if these measures do not work to their full potential, a significant structural and cultural change with a substantial increase of cost-effectiveness could be realized. The question whether it will be possible to do that has to be answered on a systematic level.

There are unfortunately only limited resources for health care and limited expertise and accessibility of appropriate care for patients, so we need a paradigm shift in how we deliver health care in general.

The number of psychiatrists in the USA is declining [46], and the burden of disease through mental health is increasing dramatically [47]. Also, only about 10% of patients according to the National Comorbidity Survey have access to specialist expertise on a secondary or tertiary level.

Continuing with the current system is not an option. A paradigm shift in the delivery of mental health care is necessary.

The revolution based on the web and mobile technologies provides new opportunities to build capacity with increased accessibility and better quality of care.

However, this will only work successfully based on a smart implementation strategy, a systematic development, and research efforts.

Health care is a structural conservative area with a lot of impact of professional and economic privileges cemented in certain procedures and funding models. This is a substantial obstacle in changing health-care delivery and funding models. This is true for certain dominant professions and businesses protecting their market share, despite its inefficacy from a patient's perspective.

The development in other economic fields also proves that disruptive change followed the technological development over the last few years. The music industry is a good example, where the invention of the "iPod" changed everything in the way music is bought, sold, and consumed. This business model changed the way existing technologies was used. The "revolution" was constituted through both new thinking and innovative use of technologies. It acts as a great lesson for medicine.

Conclusions

E-mental health and web-based solutions, in general, provide strategic opportunities for the future of mental health-care delivery. Its future use is dependent on the health-care paradigms driving technology development and use. The implementation of existing and functional solutions is a critical step, which needs a systematic approach and expertise. In countries where this is acknowledged like New Zealand, it has a measurable effect on the quality of care. E-mental health opens up significant opportunities to improve access, quality, and sustainability of care for mentally challenged individuals in a system with limited resources.

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The Future of Psychiatry: Early Career Psychiatrists

9

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Abstract

Early career psychiatrists (ECPs) are defined as psychiatry trainees and psychiatrists in their first 7 years since finishing specialty training in their respective home countries. Although this may be a critical moment in the careers of new psychiatrists, it also can be an important period for development and achievement. The goal of this chapter is to briefly state the many possible areas of action for early career psychiatrists, to increase awareness of their current importance, and to stress their crucial role in the future of psychiatry.

9.1 Introduction

The journey from finishing psychiatric training to becoming an established psychiatrist can be a long and arduous one. This tends to be the point in their careers where early career psychiatrists (ECPs) sit. The World Psychiatric Association (WPA) defines ECPs as psychiatry trainees and psychiatrists in their first 7 years since finishing specialty training in their respective home countries [1].

Although this may be a critical moment in the careers of new psychiatrists, it also can be an important period for development and achievement. International efforts toward the consolidation of young psychiatrists' networks worldwide have been helping ECPs reach their full potential, of which the foundation of the Early Career Psychiatrists Section within the WPA is an example [2]. ECPs have been increasingly involved in the organization of local, regional, and international events focused on both research and clinical work done by their peers internationally [3]. These kinds of efforts strengthen the skills of ECPs far beyond their development achieved during formal clinical training, extending it to scientific event organization and international collaboration know-how.

The opening of these new avenues for ECP career development also enables the nurturing of a new generation of future senior psychiatrists as well as fostering the interest and passion for psychiatry among current medical students. It is recognized that psychiatry suffers from a lack of human resources, and findings show an increasing number of training spots left unfilled year after year in several countries [4]. As we see more and more ECPs engaging passionately in collaborative work worldwide, it is hoped that this will eventually influence the career choice of more junior doctors toward psychiatry and help diminish this scarcity of new psychiatrists.

Initiatives that increase the involvement of ECPs in mental health services end up creating an engaging environment often by placing them in the center of scientific and collaborative activities as a practical way to generate enthusiasm, inventiveness, and the full expression of their capabilities. Innovation is necessary and the engagement of new players in traditional activities leads to important contributions via the generation of fresh ideas from ECPs.

Many mental health services in national health systems around the world are structured based on the role of ECPs. ECPs tend to be the working backbone of

much of the current mental health system, and as such, more attention should be directed to these professionals. The goal of this chapter is to briefly state the many possible areas of action for early career psychiatrists, to increase awareness of their current importance, and to stress their crucial role in the future of psychiatry.

9.2 Early Career Psychiatrists and Clinical Psychiatry

Clinical work is the primary activity of most physicians and it is no different in psychiatry. ECPs begin their training with the goal of mastering a variety of topics, including interview techniques, psychiatric diagnosis, and both pharmacological and psychosocial treatments. Despite all psychiatry training programs having an organized format and prefixed time length, clinical psychiatry education endures throughout life. A curriculum has to be limited, for obvious reasons, but our comprehension of psychopathology and human behavior, two core concepts of psychiatry, continues to evolve on a daily basis throughout our careers.

This idea of continued learning and of never-ending exploration of the human condition can only be sustained if psychiatrists find constant motivation in daily routine. As ECPs are exposed to several different fronts of psychiatric work during training, they can fine-tune their interests in a specific area of clinical work. Clinical psychiatry nowadays is subdivided in many specific areas of focus, as shown in the Table 9.1.

As demonstrated, ECPs have a wide range of options to find professional fulfillment. Traditional subspecialties of psychiatry are those that already have formal training and are usually recognized in the official national psychiatric training worldwide. Areas of interest described above as "super specialized" are those areas that still are not fully recognized as a proper subspecialty but have a very specific clinical focus, either restricted to a single disorder or to a group of disorders that have shared features. The third part of the table refers to a set of areas that present specific features related either to their setting (emergency) or to the specificities of etiology (after a disaster, during military service, or in the beginning of adolescence).

Beyond the categories described above, ECPs can choose to pursue a career focusing on the specifics of different forms of treatment of psychiatric disorders. The two main categories here are biological/somatic and psychosocial treatment. This division takes into account the biopsychosocial model of psychiatric treatment [5] and can be detailed as shown in the Table 9.2.

9.3 Early Career Psychiatrists and Research

According to the 2003 report of the US Institute of Medicine on "Research training in psychiatry residency: strategies for reform" [6], only 2% of all US psychiatrists considered themselves primarily engaged in research. Research by US psychiatrists seemed to be in "danger of extinction" [7]. Current figures are not available, but it

Table 9.1 Areas of interest—clinical psychiatry

Traditional/official areas of interest	
General adult psychiatry	Predominant field of psychiatry that covers all psychiatric disorders affecting people aged 18–65 years, in both hospital and outpatient settings
Addiction psychiatry	Focuses on the diagnosis and treatment of substance misuse and addictive behaviors, in both hospital inpatient units and community treatment units
Child and adolescent psychiatry	Focus on disorders occurring during the development of children and adolescents. Usually takes place in outpatient settings, although inpatient units, whenever available, are very useful
Old age psychiatry	Concerned with psychiatric disorders affecting the elderly, both hospital and community based
Forensic psychiatry	Traversing the interface between law and psychiatry, practiced in prisons, in hospitals, and in the community and dedicated to the mental health issues of offenders
Consultation/liaison psychiatry (psychosomatic medicine)	Based in the general hospital and dealing with mental illness among inpatients of all other medical specialties, including emergency rooms
Social and community psychiatry	Focus on assisting people in order to keep them in their own homes or in residential homes, usually applying a multidisciplinary approach and using social interventions
Psychotherapy	Enables psychiatrists to dedicate themselves to the specificities of several different types of psychotherapy treatments (further detailed below)
"*Super specialized*" *areas of interest*	
Neuropsychiatry	It is mainly concerned with psychiatric manifestations of neurological disorders and cognitive decline, such as Alzheimer's disease, traumatic brain injury, Parkinson's disease, epilepsy, and seizure disorders
Intellectual disability	Dedicates to acquired and inherited mental disorders that impair intellectual and social function, such as cerebral palsy and Down's syndrome. Traditionally an area of focus of child and adolescent psychiatrists, although some adult psychiatrists are increasingly involved as these conditions persist in adulthood
Eating disorders	It deals with forms of eating disorders, such as anorexia nervosa, bulimia nervosa, and binge eating disorder. Usually the domain of child and adolescent psychiatrists although there is growing acknowledgment of its prevalence in the adult population
Specific settings of care	
Early intervention psychiatry	Services focused on therapeutic interventions taking place during "at-risk" periods, usually during adolescence and the provision of care to specific "at-risk" populations
Emergency psychiatry	Area of psychiatry dedicated to addressing acute crisis situations, such as suicidal ideation, suicide attempts, homicide risk, and florid psychosis. Usually located in emergency rooms of hospitals with embedded mental health services

(continued)

Table 9.1 (continued)

Disaster psychiatry	Any onset of psychiatric symptoms after a disaster is the focus of disaster psychiatry. Psychiatrists dedicated to this area are trained for readiness in the advent of a major natural disaster or severe social disruption and usually deal with acute post-traumatic stress disorder, adjustment disorder, and dissociation
Military psychiatry	Specific area of interest of psychiatrists dedicated to dealing with mental health issues related to the military environment. Any psychiatric disorders can manifest in the military context, either as a result of warfare or not. Military psychiatrists usually treat military personnel but may also treat military family members

Table 9.2 Areas of interest—treatment

Biological/somatic treatments	
Psychopharmacology	Psychopharmacology training allows psychiatrists to effectively meliorate patients' symptoms. Despite the ongoing need for better drugs, the current medications are an important area of psychiatry sought by patients suffering from severe mental disorders
Electroconvulsive therapy (ECT)	ECT has been a treatment tool in psychiatry since the 1930s, and despite much controversy, it is still an effective and safe form of biological treatment. Usually applied for treatment-resistant depression, catatonia, severe mania, and other related situations where quick and effective response needs to be achieved. It is performed in hospitals, under anesthesia, and after informed consent has been acquired from the patient or his family. Psychiatrists working in ECT are part of a hospital team dedicated to this procedure, as it requires the assistance of other specialized medical professionals
Neurostimulation	Promising area of biological treatment that includes transcranial magnetic stimulation (noninvasively) and direct brain stimulation with the use of microelectrodes (deep brain stimulation). There is still much more work being done in research environment, but deep brain stimulation for obsessive-compulsive disorder has already been approved for clinical use. Future development of these techniques is much awaited by patients suffering from treatment-resistant psychiatric disorders
Psychotherapy	
Cognitive behavioral therapy (CBT)	Originally designed to treat depression, CBT nowadays has evolved as the most widely used evidence-based form of psychotherapy for a wide variety of psychiatric disorders. It combines a behavioral and a cognitive component, addressing the person's pattern of cognition (problematic beliefs, automatic distorted thoughts) and behaviors, as a very focused and practical type of psychotherapy
Interpersonal psychotherapy (IPT)	Conceptualized upon CBT and psychodynamic approaches, IPT is a brief and focused type of psychotherapy that links mood and social events, helping patients improve social skills in current interpersonal relationships
Parent management training (PMT)	Parent management training is a specific form of psychotherapy directed on changing behavior patterns of preschool and school-age children. The therapist teaches parents how to apply positive reinforcement methods to improve disruptive behavior of children (temper tantrums, difficulty following directions, positional behavior, and aggressive behavior). Usually the focus of child and adolescent psychiatrists

(continued)

Table 9.2 (continued)

Biological/somatic treatments	
Psychoanalysis	Psychoanalysis is an intensive individual psychotherapy usually done with frequent sessions over several years, focusing in the recollection and examination of past memories to reveal unconscious drives and thoughts, in order to help the patient understand present behavior and feelings
Psychodynamic therapy	Derived from the traditional concepts of psychoanalysis, this form of therapy also has the goal to explore unconscious content, but it has a shorter length, has less intensive frequency of sessions, and is more focused on a specific emotional problem than traditional psychoanalysis. Many times patients that start this psychotherapy might continue afterward in a classical psychoanalytic setting
Systemic therapy	Systemic therapy focuses on addressing the relationship between groups of people, dealing with its dynamics and patterns. It is the conceptual basis for family therapy and marriage counseling, although the therapist can also integrate other concepts from other types of psychotherapy into these types of psychotherapy

is plausible to assume that the picture in the United States has not changed and that outside the United States it may even be bleaker. Even more so than in other fields of medical research, e.g., in gastroenterology or ophthalmology, research in mental health is performed by professions other than psychiatrists, mainly psychologists and neuroscientists with a background in sciences. If nothing is done, the gap between basic neurosciences and clinical psychiatry will continue to widen [8]. In the long run this poses a challenge to psychiatry since the ability to generate its own knowledge base—or at least to make a significant contribution to it—is a core feature of an independent profession. In 2010, the future of psychiatric research was suggested to be "genomes and neural circuits" [9]. Yet, these and other research topics are hardly covered in current psychiatric training curricula. Moreover, most psychiatric training curricula do not include any kind of practical exposure to research. Consequently, many of today's psychiatrists—including recently graduated psychiatrists—do not understand current "hot topics" in psychiatric research, let alone contribute to it.

Not every psychiatrist has to become a researcher. Psychiatric training primarily serves the purpose to prepare medical graduates for their future role as clinicians. Due to the increasing complexity of mental health research, it can take years to acquire the specific skills and knowledge that are needed in clinical trials, animal research, neuroimaging, or other areas. Only few ECPs have the intrinsic motivation to follow that path. Of those, even fewer will find the required time, funding, and supervision [10]. Yet, every ECP should have some exposure to research. At the minimal level, this means having access to the current medical literature—which unfortunately is still not the case in many countries [11]. The ability to critically appraise the literature is not only a requirement for research but is also essential for high-quality clinical practice. If more resources are available in a training setting, protected time and funds should be provided for training in research methods, collecting and analyzing data, and publishing results.

Mentors play a key role at this stage. Indeed, research and career mentorship, individualized training plans, the integration of clinical and research experiences, protected research time, and research funding were the ingredients of a successful research resident training program in psychiatry at the University of California, San Francisco [12]. However, even with an ambitious program like this, only 48 residents enrolled over an 11-year period. Of these, only 17 published a peer-reviewed article during their residency or within 2 years after its completion. Thus, even "successful" programs do not appear to produce clinician-scientists in large numbers. After the first steps into a research career, when an ECP has gained methodological experience and been published, establishing oneself as an independent researcher is an even more difficult step [10]. It requires the identification of one's own niche and acquisition of research funds. Grant writing, peer-review, and editorial skills are usually picked up on the go during that period. Many promising researchers are lost at this stage [13]. Long-term support such as provided by the Career Development Institute for Psychiatry in the United States may help in easing that transition [14].

What are promising ways forward? Authors from the US National Institute of Mental Health recently proposed "stepping stones" toward a career as a clinical researcher [15]. According to this approach, research exposure should be inbuilt into medical training and efforts made to attract MD-PhDs to psychiatric residencies. Efforts to implement research should be made both on the level of the regulatory framework for psychiatric training as well as by residency programs themselves. While all these measures are certainly welcome and important, they have been proposed in the past, and their implementation across different countries and even across different training schemes has been far from complete. We therefore encourage early career psychiatrists not to wait indefinitely for research opportunities but to simply start their own research.

In the last couple of years, there have been several examples of successful research projects carried out entirely by ECPs [16–20]. Furthermore, a trainee-led academic journal has been established in psychiatry [21]. One thing that these examples have in common is that they are based on collaborative networks of ECPs working together across different cities or countries. Such collaboration is made possible by digital communication and cloud computing. In the future, such projects may also be facilitated by massive open online courses (MOOCs) on fundamental research skills such as statistics. These projects led by ECPs resemble participant-led research [22] since they look at ECPs as study subjects. While this may certainly be a limitation, the training effect for all stages of research is not to be underestimated. Notably, this includes the inception and design of a research project, phases that are usually not widely influenced by junior researchers in the classical mentoring model of research.

Researchers involved in ECP-led projects form lasting professional networks and learn to perform low-budget research. This skill may be particularly beneficial for future projects outside mainstream research, thus creating diversity. Finally, since these projects rely on peer-mentoring, mentoring skills are formed that may benefit future generations of researchers. Interestingly, peer-mentoring has recently been identified as a success factor of research training programs in psychiatry [23].

9.4 Early Career Psychiatrists in Medical Education

Perception and care of mental health disorders has changed significantly over the last centuries all over the world. For example, in contrast to historical paradigms, current approaches include the involvement of other mental health professionals and families in the care provided and predominantly community treatment [24]. Equally, the structure and organization of mental health services differs quite a lot across countries, with different models of care provided. Despite this flux, psychiatry should occupy a major part in the medical curriculum, as medical practice, at its core, relies on the unity of body and mind, mental health problems are common among patients seen by doctors in any specialty, and basic skills learned in psychiatry are imperative for all doctors.

Psychiatry education is inextricably linked with mental health services and should retain congruence. Services play an important role in the provision of education particularly as it is vital to take into account the specific circumstances of each country, when defining the basic prerequisites of knowledge that every medical student should acquire in psychiatry.

The World Psychiatric Association (WPA) together with the World Federation for Medical Education (WFME) has developed guidelines for the core curriculum in psychiatry for medical students. These include the acquirement of *attitude objectives*, concerned with medical practice in general and toward patients and their families; *knowledge objectives,* including psychiatric symptoms and syndromes, psychological aspects of medical disorders, and the psychosocial context; and *skills objectives* [25]. These skills expected of medical students range from those that they need to be *aware* that are practiced by others and skills which students are expected to *utilize* competently themselves. These imperative skills include communication skills, conducting an interview (opening, controlling, and closing), active listening, empathy and nonverbal communication, as well as formal history taking techniques.

Rather than in a classroom, teaching should take place predominantly in the settings in which students are likely to work when they qualify, thus honing skills like teamwork and collaboration with nonmedical staff. Likewise, education should be self-directed, include problem-based learning cases, and expose students to patients in different settings. Teaching staff should have an interest in teaching and be trained for their role as teachers. Research in mental health care should be promoted and supervised. Overall, medical students should acquire knowledge and skills that enable them to *diagnose* and *treat* common mental health problems and to *refer* complicated manifestations of psychiatric disorders to a specialist.

In this regard, it is undeniable that ECPs play an important role in the education and training process. Not only are ECPs recipients of training, but they come into close contact with both medical students and their junior colleagues. In the training process, residents learn mainly from their immediate senior colleagues whom they are supervised by. According to the UK General Medical Council (GMC), there are educational obligations on all doctors: to contribute to the education and training of other doctors, medical students, and other health-care professionals on the team, to

oversee the work of less experienced colleagues, and to make sure that students are adequately supervised [26].

With the growing emphasis on student autonomy, and training provision in settings that expose students to real-life clinical situations, the role of ECPs is increasingly indispensable. Apart from the lecturing role taken on by those who choose academic responsibilities, there are other important educational clinical roles. In particular, the passive diffusion from a good on-job role model is often underestimated. This is optimized by ensuring that ECPs are receiving the proper training themselves in not just clinical knowledge but also ethical practice and communication and leadership skills. This also serves to reflect a positive image of the specialty and attract more medical students to join the field. ECPs are also often instrumental in organizing training courses, developing curricula and teaching materials, and planning and coordinating examinations as part of their role in nurturing the next generation [26].

9.5 Early Career Psychiatrist Organizations

As Fiorillo et al. [27] noted, there are many ECP organizations in psychiatry [27] broadly divided into two categories as summarized in Table 9.3. ECP organizations are either formed through and supported by mother organizations on the national, regional, or international levels or established as independent associations. The aims of these ECP organizations are predominantly:

1. To facilitate communication and an exchange of experiences among ECPs
2. To identify areas of interest and problems to be addressed
3. To identify necessary training opportunities for ECPs to acquire skills in clinical practice, scientific research, medical education, and leadership
4. To evaluate training curriculum and improve its quality
5. To facilitate the professional development of ECPs
6. To conduct their own research utilizing ECP networks

The differing structures of ECP organizations have varying advantages and disadvantages. ECP organizations, which are part of a more senior umbrella organization, make way for ECPs to potentially be elected as board members of the senior organization and thus contribute directly to policy making together with their seniors. They could also participate in the activities of other sections or district branches in the umbrella organization. In contrast, the independent associations tend to prioritize their own activities and value their autonomy. One main advantage of the independent organizations is that their activities are not restricted by others. As they have to manage all operational matters including financial and legal ones related to the effective running of an organization on their own, involved ECPs are exposed to a plethora of learning experiences that clinical medicine may not otherwise provide. Such a diverse spread of experience is vital to future leaders in the field of psychiatry.

Table 9.3 Lists of organization for early career psychiatrists reviewed by Fiorillo et al. [27]

Country/region	Name	Started	Website
Argentina	Early Career Psychiatrists Section (Psiquiatras en Formación)	2010	http://psiquiatrasenformacion.blogspot.com.br/
Australia and New Zealand	Early Career Psychiatrists Section	2011	www.ranzcp.org/Membership/Faculties-sections/Early-Career-Psychiatrists.aspx
Brazil	Early Career Psychiatrists Section (Núcleo de Psiquiatras em Formação)	1988	https://www.facebook.com/Núcleo-de-Psiquiatras-em-Formação-da-APRS-1666674113565623/
Egypt	Early Career Psychiatrists Section	2010	https://www.facebook.com/Egypts-Early-Career-Psychiatrists-EECP-378603072201014/
Europe	Early Career Psychiatrists Committee	2010	www.europsy.net/committees/early-career-psychiatrists-committee/
Europe	European Federation of Psychiatric Trainees	1993	www.efpt.eu/
France	Association Française Fédérative des Etudiants en Psychiatrie	1998	www.affep.fr
Germany	German Young Psychiatrists' and Trainees' Association	2001	www.dgppn.de/english-version/aboutus.html
Italy	Early Career Psychiatrists Committee (Coordinamento Nazionale Giovani Psichiatri)	2000	https://giovanipsichiatrisip.wordpress.com
Japan	Japan Young Psychiatrists Organization	2002	www.jypo.org/en/
Portugal	Portuguese Association of Psychiatric Trainees (Associação Portuguesa de Internos de Psiquiatria)	2005	www.apipsiquiatria.pt
United Kingdom	The Psychiatric Trainees' Committee	2006	www.rcpsych.ac.uk/traininpsychiatry/trainees/ptc.aspx
United States	The Assembly Committee on Early Career Psychiatrists		https://www.psychiatry.org
Worldwide	Early Career Psychiatrists Scientific Section	2015	www.wpanet.org/detail.php?section_id=11&content_id=1703

Activities of ECP organizations vary greatly. Almost all organizations have their own website and/or newsletter and mailing list to share useful information and ECPs' opinions. Some organizations take the initiative to demonstrate and disseminate their opinions. For example, the European Federation of Psychiatric Trainees (EFPT) produces consensus statements to circulate the opinions of psychiatric trainees to the relevant bodies. Many ECP organizations hold symposiums,

workshops, and meet-the-expert sessions at psychiatric conferences. Of note, the World Psychiatric Association's (WPA) Early Career Psychiatrists Section now has an established conference structure bringing together ECPs and ECP organizations from around the world. The first International Congress of Early Career Psychiatrists "Towards Professionalism in Psychiatry" was held in Cairo, January 2013. Following this, ECPs contributed to the 23rd EFPT Forum in 2015 with "global mental health" as its focus. This forum received participants from different regions of the world, facilitating the opportunity for collaborative projects, nationally and internationally, and proved an excellent occasion for exchange of experiences and sharing of practices. A special issue on the Scientific Programme of the EFPT Porto Forum 2015 was published in the *International Journal of Clinical Neurosciences and Mental Health* describing the symposiums, courses, and workshops presentations by invited speakers as well as selected abstracts from the e-posters and oral presentations presented by participants [28]. Most recently, a collaboration between the Young Psychiatrists' Network, buoyed by the success of their national conference in Porto Heli, Greece, in 2015, the European Psychiatric Association (EPA)-ECP council, and the WPA ECP Section led to the 2nd Congress of Early Career Psychiatrists "Bridging science and culture" which took place in Athens, October 2016.

Some ECP organizations provide scholarships, mentorship, and international exchange programs for ECPs. ECP organizations also collaborate to conduct research for scientific publication. At times this can be directly beneficial in identifying an important issue for ECPs, conducting multicenter research, and successfully publishing their results leading to changes to working environments for ECPs [20].

Conclusion

Despite all possible difficulties facing an ECP, many opportunities for personal growth and career development have been presented. High-quality training in different areas of clinical interest, development of research skills, active engagement in the medical education process, and the increasing participation of current ECPs in psychiatric associations are central elements for the individual ECP but also for the future of psychiatry as a whole (see Fig. 9.1). As active players in the construction of the future of psychiatry, ECPs' needs should be a priority for all psychiatrists involved in training, research, and associations.

The search for better ways to treat our patients and the quest to improve accuracy and replication of psychiatric research, ultimately leading to better treatments and hopefully preventive approaches, should be the center of all our efforts. This mission also passes through the nurturing of a new generation of psychiatrists, capable of responding to such challenges in the next decades to come. It is our hope that these pages have sparked the interest for psychiatry in the undecided medical student, have empowered current ECPs, and have acknowledged the importance of ECPs for current senior psychiatrists.

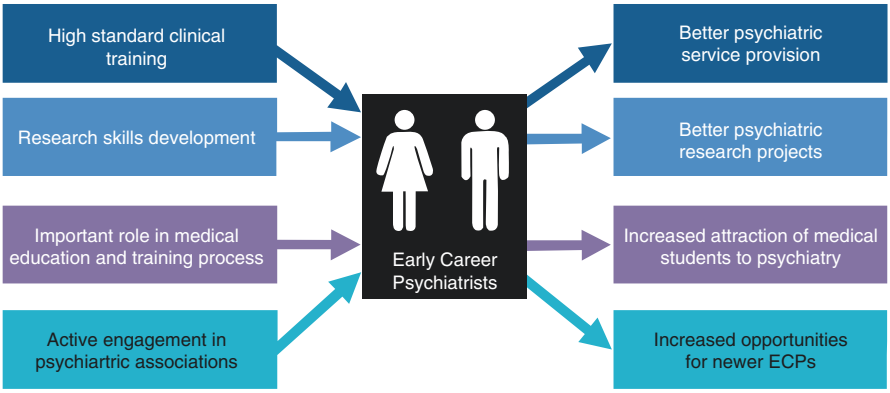

Fig. 9.1 ECPs' effective training outcomes

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Sport Psychiatry: Aspects of a Developing Field

10

David Baron and Thomas Wenzel

Abstract

Sport psychiatry can be seen as a new and rapidly developing global field, due not only to the growing popularity of sports in the general population but also to the highly challenging environments in a professional setting. Mental health problems like brain trauma, depression, suicide, doping, physical trauma and abuse, and also sport-specific problems like the female athletic triad or overtraining are risks endangering the physical and psychological benefits that can be expected from sport and exercise. Working with individual athletes or teams requires special knowledge and skills but also awareness of ethical challenges encountered especially in high-performance sports.

10.1 Introduction

Sport can be seen as one of the most common active and passive pastimes. For some athletes, whether elite or recreational, competition becomes the self-defined core of their emotional identity. Sport and exercise have been demonstrated to be key factors in maintaining a healthy lifestyle and are important components in the prevention and rehabilitation of numerous physical and psychological illnesses [1, 2].

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Sport has also become one of the most influential contributors to national pride and collective identity. Given this global, cultural identity-shaping impact on individuals, it is appropriate that studying the impact of sport and caring for athletes has developed into a recognized area of specialization for psychiatry [3, 4]. Sport has been demonstrated to be "Janus"-faced; it supports "healthy bodies and minds" when used with care but has the potential to be a risk factor for physical and emotional stress and disorders, especially if done in excess, an increasingly common problem encountered at all levels of competition worldwide.

Though basic research exploring the interface between activity, genetic background, neurobiology [5], health and performance has become an important component of the field and has demonstrated an epigenetic impact of sports [6], most practicing sport psychiatrists at present focus almost exclusively on the clinical aspects of sports [7]. A number of key issues have been identified and will be addressed in an upcoming training curriculum developed by the Sports Section of the World Psychiatric Association. The goal of this chapter is to provide a concise overview of the most important aspects of sport psychiatry and the challenges a health-care professional faces when working in this emerging field of study, with a focus on treating athletes. Due to space limitations, we will only briefly refer to the use of sport as a tool in treatment. Interested readers are encouraged to refer to the extant literature on the role of exercise in treating depression, anxiety, psychotic disorders and substance use disorders.

The frequently overlooked consequence of mild repetitive brain trauma (concussion) sustained by athletes in contact sports has become the signature sports injury dominating the field of sports medicine for the past 15 years. The most significant, long-lasting and complex symptoms of concussion are emerging as primarily neuropsychiatric [8–10]. This will be used to offer a deeper insight into the present state of research of one of the most important areas of study in sport psychiatry.

10.2 The High-Performing Career Athlete

High-performance sport must be seen as a special field, which can start shaping an athlete's life from early adulthood or even childhood, sometimes taking several hours of effort each day, especially when an athlete trains for national or international competitions. In successful athletes, this intensity can be a satisfying and stimulating experience, but more commonly it is characterised by severe strain on the mind and body, the experience of injuries and lost competitions. In many cases, being a professional athlete means being part of a special environment that is highly competitive and often partly replaces one's family or regular peer group. The special setting of high-performance sports varies depending on country and the background given by a specific discipline. Becoming an athlete could mean anything from becoming part of a team to participating in a lonely fight with a personal trainer or alone. In some countries like the former East German Republic, China or the Soviet Union, training was or is strictly controlled and supported by the government as part of an overall political and national effort to train children beginning at an early age. This is different from American sport culture, which is closely linked

to education and linked team sport and college or university sport activities. Athletes tend to participate in their preferred sports, especially team sports like football or baseball, with a possible later transition into professional sports. In any of these situations, when sport becomes a career and there is greater pressure for success as an individual or as part of a team you do not want to fail, risks increase. Physical injuries and reactive psychological and behavioural patterns that can lead to significant problems or increase the risk of developing a psychiatric condition must be anticipated as possible outcomes. Financial considerations arising from the commercialisation of some sport disciplines have become special adverse factors that lead to increased risk-taking or specific dangerous strategies such as doping. Especially in young adults, a lack of balance between focusing on career or personal psychological and physical health and development can lead to problems; either unspecific reactions to stressors or arising from a specific situation unique to a sport discipline. While mood disorders in situations of conflict, exhaustion or post-traumatic stress after accidents can be observed in nearly all high-performance settings, some disorders such as eating disorders are more commonly found in certain disciplines.

10.3 Clinical Aspects

10.3.1 Eating Disorders

Eating disorders have been observed to be common in a number of sport disciplines, like gymnastics, and are one of the best-documented problems in high-performance sports. They affect both female and male [11] athletes [12–15]. Extreme exercise or "exercise addiction" is a common symptom in eating disorders, especially anorexia [16], and cultural influences—including the "sub-culture" of performance sports—appear to impact the development of eating disorders [17, 18]. A complex model consisting of different contributing factors might best reflect the potentially involved factors, as the high overall prevalence in some groups cannot be explained by a predilection of adults with eating disorders to taking up those athletic disciplines. Early recognition of disordered eating can be important to prevent the development of full clinical disorders and the female athletic triad as discussed below [19]. Failure to do so carries a high risk for complications like impaired menstrual irregularity or amenorrhoea, bone density, fractures [20–22] and even lethal outcomes that can be observed in anorectic patients [23, 24]. This problem is addressed by the "Athletes Targeting Healthy Exercise and Nutrition Alternatives" (ATHENA) programme based on a short, scripted, coach-facilitated, peer-led model [25], for example.

10.3.2 Mood Disorders and Suicide

Suicide in athletes has been a public concern since the nineteenth century [15], probably due to the high media presence of athletes and the dramatic aspects and

lethal outcome. The problem still appears to be serious compared to other professions, as demonstrated recently in an epidemiological study by Meltzer in the UK that found the highest proportional mortality ratios (PMRs) for sport and fitness occupations, at least in women [26]. While mood disorders like depression certainly contribute to the problem and are an important predictor relevant for screening [27], other factors must be considered to understand each case. Adverse events might also occur after the career ends, including the break in careers and failing of expectations by the athlete [28] or his team, substance use and doping, brain trauma [29, 30] but also common factors for suicide in non-athletes [31] as while sport can be beneficial to mental health it still cannot protect against all mental health problems [32].

10.3.2.1 Post-Traumatic Stress

Sport can be dangerous and can result in severe or even lethal accidents. Bystanders and other athletes can develop psychological distress or even trauma spectrum disorders, in addition to the severely injured athlete [33].

10.3.2.2 Substance Abuse

Substance abuse in theory should be prevented by anti-doping policies, if not the simple fact that it is against the "spirit" of sport, but this is not true in practice [34–36], and it is a complex spectrum of specific problems. Differentiating between the medical usage of a legal substance with mental health impact versus intentional doping with it is a common challenge. Steroids can, for example, be used in some situations without violating doping rules, especially outside of competitive sports, but can have an adverse effect on physical and mental health including mood and affect control disorders and increase suicide risk [31, 37]. The problems are best studied in male weightlifters, who are at high risk to abuse other substances like human growth hormone [38]. Risk usually increases in cases when primary mental health problems are already present [39, 40]. The use of benzodiazepines in performance anxiety might lead to dependency, and alcohol abuse can be used as "self-medication" to cope with anxiety or frustrations and again develop into dependency [36]. Cannabis is also frequently abused in some groups to cope with anxiety [41, 42]. ADHD (attention deficit hyperactivity disorder) medication can also be seen as a well-known issue that requires special experience and skills [34].

10.3.2.3 Special Syndromes Specific for Professional and High-Performance Sport

Training athlete syndrome, i.e. underperforming in the competition after successful training, is a problem that might reflect underlying psychological problems or overtraining [43]. Overtraining syndrome "induced" by trainers or athletes not only does not improve results but can also lead to strain and injuries, especially on a developing body. Exercise addition can be part of the problem, manifesting not only from an eating disorder, but also from neurobiological, social and psychological factors [44–46].

10.3.2.4 Doping

Doping, as mentioned before, is rising to become probably the largest challenge in sport and sport psychiatry [47, 48], and the use of new substances is continuously increasing [49, 50]. Ambition by trainers or athletes, or group pressures or manipulation from doctors and trainers, might result in athletes not being aware of dangerous consequences. If uncovered, the experience can be traumatic and destroy the athletes' life plan and subsistence. As it has become a major field in itself, it will not be discussed in more detail here.

10.3.2.5 Injuries

Psychological factors can lead to increased risk of injury, though this can sometimes be prevented by psychological programmes [51–53]. Major injury can be distressful or even traumatic, again threatening the life plan of the athlete [54, 55]. Psychological and psychiatric care might be required especially when a difficult situation arises if pressure to start retraining too early comes from the athlete, coach or team [56]. A reconsideration of priorities in life can be a psychologically and physically painful part of the growth process.

10.3.2.6 Sexual Abuse

Sport primarily involving young adults must be seen as an especially high-risk situation for abuse and eating disorders [57]. The separate reality, physical closeness and transference phenomena when coaches and trainers take the place of parents [58] can be seen as contributing factors. A recent questionnaire study by Vertommen demonstrated self-reported experience of sexual violence in 14% of respondents but also indicated that exposure to interpersonal violence in general is high in sports [59]. Strict standards and preventions including guidelines and awareness programmes are of major importance to protect young athletes [60].

Female athlete triad—a combination of eating disorders, amenorrhoea or oligomenorrhoea and decreased bone mineral density in varying degrees—is also linked but not limited to eating disorder problems. The most recent review observes that it reflects a state where "energy intake does not adequately compensate for exercise-related energy expenditure, leading to adverse effects on reproductive, bone, and cardiovascular health" [19].

10.4 Concussion as an Emerging Field in Sport Science and Public Health

Sports-related concussions are common especially in athletes competing in contact and collision sports [61, 62]. These include boxing, hockey, lacrosse, rugby, football, American football and others where contact with the opponent is part of the game. Athletes competing in non-contact sports suffer concussions at a lower frequency. Given the high media profile of sports-related concussion over the past 25 years, significant effort has been given to better understand the aetiology, diagnosis and

management of athletes who have suffered a concussion. A growing appreciation of potential negative consequences from suffering repeated mild concussions [63] and a discussion on the "second-impact syndrome" [64] have led to rule changes intended to address brain safety and return-to-play protocols for athletes diagnosed with a concussion. The gladiator culture of certain sports is also gradually changing. Despite the significant increase in research focused on gaining a better understanding of all aspects of sports concussion, very little progress has been made in identifying effective treatment strategies [61]. Currently, the best treatment is prevention. No pharmacotherapeutic interventions have proven effective, but medications to avoid include aspirin and anticholinergics. Alcohol should be avoided, or used in very small amounts, during the initial and recovery phases. In general, a conservative approach to treatment, with ongoing symptom monitoring by a clinician well trained in concussion management, is the most effective treatment approach. Rest (but not too much), avoiding loud noises, avoiding direct exposure to sunlight without quality sunglasses, decreasing stress, maintaining adequate hydration and maintaining good sleep hygiene are helpful.

Current return-to-play protocols routinely require the athlete to be symptom-free after a gradual return to activity. Given the lack of reliable biomarkers, decisions to allow an athlete to return are subjective. A number of promising biomarkers are currently under investigation. Identifying reliable markers will greatly assist in the clinical management of concussed athletes but will not provide treatment. Educating the athlete about the importance of the above factors is important, especially as underreporting is a common problem [65, 66]. The athlete should be informed to listen to the body and brain, and not try to "work through" the pain. Post-concussive syndrome takes a long time to fully resolve in some athletes and is more common with repeated concussions. Brain safety should be a priority for all athletes, especially those who have a prior history of concussion of any type.

10.5 Taking Care of the Professional Athlete

The role of the sports psychiatrist is not limited to early recognition and prompt treatment of such developments but also in providing information, raising awareness [67] and offering support to individuals and teams [35, 68]. Of special importance is also the close and positive collaboration with key persons in the athlete's environment, especially for the young athlete [69] whose physical and psychological development is interacting with a sport career. This group includes trainers and coaches, parents, teachers and general team doctors, family physicians and councillors or psychologists employed by educational institutions like schools or universities. All of these people are important as they can support the healthcare professional in the identification of at-risk individuals' problems, supportive treatment or rehabilitation, by helping with considerations in the training plan, decrease of fear of a diagnosis and treatment [70] and compromise between sport- and health-related aims. They are also potential partners in the creation of a healthy sport environment. Just as with other close-knit groups, a psychiatrist, being a member of a stigmatised profession

and linked to subjects frequently avoided or "hushed up", has to build credibility. A personal background in at least one sport discipline is helpful both to better understand the special situation of athletes but also to support the process of building communication and trust with athletes and their caregivers.

In treating an athlete suffering from mental health problems, care should be taken in balancing psychopharmacological and other interventions. In prescribing medication, substances that can be seen as doping or interact with medication given for non-psychiatric complaints must be prescribed with special care and require special and up-to-date knowledge [71]. The special challenge of balancing success in competition with medical priorities like cancelling participation in an important event in case of health risks or of reducing training efforts can be a difficult part of the negotiation of the treatment contract with an athlete or coach. The same holds true for the responsible application of not yet extensively tested new treatment methods like transcranial direct current stimulation (tDCS) that has been demonstrated to improve depression and performance scores [72]. Medication should, if medically justified and possible, not interfere with factors relevant for training and performance like speed, concentration or reaction time, though athlete health is again the first priority.

In special situations, such as international competitive events like the Olympic Games, additional challenges for the sports psychiatrist might include working with athletes from different cultures and different sport cultural backgrounds. Crisis intervention in participants or helpers and functionaries as part of the healthcare services offered by the host and work on doping prevention are examples of other possible tasks.

10.6 Ethical Challenges

The psychiatrist consequently has an important role to promote healthy sports and should, by the guidelines given by professional ethics, prioritise his responsibility for the physical and psychological health of the athlete, especially for children and young adults, before any considerations like financial interests or the desire of teams and coaches for "success at any price". This can lead to conflict [73–76] especially when, for example, national pride or high economical outcomes are at risk and might coerce the health-care professional to tolerate, support or help hide significant problems, even participating in unethical and dangerous practices such as doping [77]. Being employed by a team can be a special risk [77].

Recognition and intervention against risks or illegal practices that might result in legal action can be highly unpopular tasks and require firm dedication to a code of moral ethics. This might come up even in everyday situations like the decision not to send a player back onto the field in case of suspected brain trauma, even if substantial pressure is put on the psychiatrist or other health-care professionals by the athlete, team, coach or parents, in the case of young adults. Confidentiality is another important challenge [78–80], as trainers, coaches or team functionaries might try to get privileged information from the therapeutic setting or even influence it in the name of team interests.

Conclusions

Healthy sport and exercise have become an important issue in popular and grassroots sports as well as in high-performing, competitive and professional sports. The new field of sport psychiatry can be seen as having a dual focus. The risks inherent in the special environment of high-performance sport, including, brain trauma, depression, suicide and eating disorders, as well as ethical challenges like doping and sexual abuse should not be avoided in public discussion. They must be addressed not only by early access to treatment but also by public awareness and prevention strategies developed in close collaboration with the athlete and stakeholders like trainers, coaches, school doctors and psychologists, family members and decision makers. Exercise and sport can contribute to important benefits for physical and mental health, for example in the prevention and treatment of depression [81–84], general rehabilitation [85, 86] and the resolution of post-traumatic stress [87] and social conflicts [88]. The integration of genetic-, neurobiological-, psychological- and social science-based research can contribute not only to better performance and safer sports but also to a better understanding of the human body-mind interaction.

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Family Inclusive Therapeutic Interventions

11

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11.1 Introduction

Given the significant surge in the literature in the field of family studies and interventions in recent years, this chapter will focus primarily on relevant data regarding common and severe mental disorders, namely, schizophrenia, bipolar disorder and depression.

Keeping the practising psychiatrists (specially the juniors) in mind, we view this chapter also as an attempt to promote "family-inclusive practices" within the bio-psycho-socio-cultural model in clinical practice.

Lastly, we chose to adopt an evidence-based approach rather than the discrete theoretical frameworks.

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This chapter comprises of three sections, one on bipolar disorder, the second on schizophrenia and the third on depressive illness. The three sections focus on the relationship between family functions and the psychopathology and a special emphasis on therapeutic approaches.

Despite of many publications in the last two decades or more, family-inclusive therapeutic approaches are still widely unused and misrepresented in the clinical practice in mental health. We hope this chapter will promote the concept and prove to clinicians the validity of those interventions in treating the mentally ill.

11.2 Bipolar Disorders (BD)

In the data gathering stage of family function in BD, Weinstock et al. [1] revealed that in contrast to a moderate degree of concordance in reporting family function between patients and their families in major depressive disorders (MDD), there was a weak link in BD. They highlighted the importance of collateral reports in the research and treatment of patients with BD.

For many patients with bipolar disorders (BD), despite optimal pharmacotherapy and treatment concordance, partial remission or relapse is almost inevitable.

Keitner et al. [2] summarised the evidence-based family interventions in BD. These are:

1- Integrated family and individual therapy.
2- Problem-Centred System Therapy of the Family (PCSTF). It is a type of short-term family intervention (based on McMaster model of *Normative Family Functioning*) which is problem-focused, behaviourally directed at empowering families (by focusing on their strengths) to work effectively to resolve their distressing situation.
3- Family-focused therapy.

Mansfield et al. [3], in a review of ten RCT of family-based interventions, found that family psychoeducation is effective in reducing relapse of manic symptoms, while other family-based interventions are more effective in reducing relapse of depressive features.

More recently Salcedo et al. [4] have critically reviewed the evidence for adjunctive psychotherapies. They found that family-focused therapy, psychoeducation, CBT, dialectical behavioural therapy and mindfulness-based therapy all appear effective in reducing depressive symptoms in BD. More specifically family psychoeducation (and CBT) led to increase time to relapse.

Consistently earlier Fiorillo et al. [5], after extensive review of literature in the last 20 years, reached the conclusion that supportive family interventions in BD can:

A. Improve the course of BD
B. Reduce the risk of relapse
C. Reduce hospitalisation
D. Improve patient's adherence to medications

Reinares et al. [6] highlighted in their review that not only family attitude/interactions affect the course of BD, but equally the illness itself has a strong impact on family functioning and caregivers' burden and health in both youth and adult population.

In *adolescent patients* with BD, family conflicts may be a useful predictor in the course of mood symptoms. Sullivan et al. [7] found that manic symptoms improved more rapidly in low-conflict families. Similarly a decrease in parent-reported conflict predicted a decrease in adolescent manic features over 2 years.

Similar findings were found in young adults with BD. Miklowitz [8] advocated that family-focused treatments (and dialectical behaviour therapy) are promising interventions, along with pharmacotherapy, to help young patients not only to manage their disorders but also to "become independent and healthy adults".

However, within the same young population group, Miklowitz et al. [9]—after a 2-year follow-up on bipolar 1 and 2 patients—found that intensive family-focused therapy (FFT for 21 sessions) did not confer advantages over brief psychoeducation for 3 weekly sessions (both along pharmacotherapy) in hastening recovery or delaying recurrence except that the FFT group had less manic symptoms in year 2 than the other group which is consistent with earlier finding of Sullivan [7].

Also within the adolescent group with BD and comorbid substance use disorders (SUD), Goldstein et al. [10] advocated to modify family-focused approach (for 21 sessions over 12-month period) to explicitly target substance use. In spite of the limitations of small sample, open treatment, no control and the modest reduction of cannabis use, there were significant reductions in both manic and depressive symptoms as well as improved global functioning after 6 months.

The relation of high expressed emotion (hEE) to relapse and course in BD is robust. However, historically the emphasis was mostly on the level of criticism. Fredman et al. [11] found that the level of emotional over-involvement (EOI intrusiveness, inappropriate self-sacrifice, distress about patient's well-being) affected mania trajectory (became less manic) and moderated the effects of family-based intervention. They advocated more studies to consider the prognostic value of family EOI.

Chronicity of BD was linked to adverse effects on the family. Koutra et al. [12], in a comparison of family with first episode vs chronic patients with bipolar disorder (and schizophrenia), found that the latter group has experienced poorer family function, higher EE, more family burden and poorer psychological well-being (reflected in higher score in GHQ-28).

Several recent studies linked history of suicide attempts (SA) to family functions in BD. Berutti et al. [13] found that bipolar patients with SA, compared to a sample without SA, showed worse family functions on family assessment device (FAD—an internationally recognised instrument). It included poorer problem-solving skills, impaired communication, blurred family roles, decreased affective responsiveness and poorer general functioning. They advocated these findings may help to identify environmental risk factors in suicidal behaviour among BD patients.

However, several challenges need to be addressed while implementing family-inclusive practice in BD (and possibly other) patients. Peters et al. [14] warned, after his work with relatives and care coordinators of 52 patients, that involving the families can sometimes increase the complexity of managing patients (and often

increase care coordinators' workload). This process can also be perceived by some patients as undermining the exclusivity of the therapeutic relationship with their care coordinators. One would wonder if the presence of a different therapist (if feasible) in such situation could offer the answer.

To address some of the above-mentioned difficulties in a cross-cultural perspective, Fiorillo et al. [15] examined the feasibility of psychoeducational family interventions (PFI) in bipolar 1 disorders and their relatives in "an Italian real-world" multicentre study. They concluded that "PFI are feasible in routine care and the main obstacles are related to the organization/structure of mental health centres and not to the characteristics of the intervention itself".

The family assessment device (FAD), originally developed by Epstein et al. [16] and translated into 27 different languages, is still used extensively as "gold standard" in both clinical and research context [17, 18]. However, the challenge is to complete the 60 items in busy clinical settings.

Recently, Keitner and Mansfield-Marcaccio (2017, Personal communication) developed a significantly shorter "Brief Assessment of Family Function Scale" (BAFFS). They found it as a valid measure of overall family functioning "that can be used quickly and easily in routine clinical practice and in situations when time and resources are limited".

Finally reassuringly to overcome one obstacle if the patient fails to engage or is absent, Perlick et al. [19, 20] concluded that family interventions may help families to manage stress and regulate their mood even if the patient is not available for treatment.

In summary, adjunctive family treatment, along with pharmacotherapy, has established itself as a robust tool to effectively manage patients with BD in different age group, with some comorbid conditions, and across different cultures. Many useful steps have been taken to make it feasible in routine clinical practice. In addition, many creative works were used to extend the training of family therapist via videoconference [21]. However, there are still unanswered areas for future work. A little has been mentioned in the follwoing aresa of research; namely: Is the effectiveness of family-focused interventions extend to other types of BD (mixed and rapid cyclers)? Does the shorter version of family assessment help in suicidal patients and in different cultural setting? How long treatment effects survive in routine clinical practice?

11.3 Family and Schizophrenia: Role and Therapy, with Focus on First Psychotic Episode During Adolescence

11.3.1 First Psychotic Episode and the Duration of Untreated Psychosis (DUP)

The first psychotic episode occurs approximately in 100,000 adolescents and young adults in the United States each year [22]. The peak of the onset occurs between 15 and 25 years of age. The burden of psychotic disorders such as schizophrenia affects the young person's social, academic and vocational development, as well as initiates a trajectory of accumulating disability. Schizophrenia has a very significant genetic component (see below).

Schizophrenia has a very significant genetic component. People who have a third-degree relative with schizophrenia are twice as likely to develop schizophrenia as those in the general population. Those with a second-degree relative have a several-fold higher incidence of schizophrenia than the general population, and first-degree relatives have an incidence of schizophrenia, an order of magnitude higher than the general populace [23]. Notwithstanding this evidence, the correlation of schizophrenia between identical twins is less than one-half, indicating that schizophrenia is not entirely a genetic disease.

The current belief is that there are several genes that contribute to susceptibility or pathology of schizophrenia, but none exhibit full responsibility for the disease. Dr. Weinberger, Director of the Genes, Cognition and Psychosis Program at the National Institute of Mental Health, stated that the current number of gene variations linked to schizophrenia is approximately 10. The gene variations that have been identified as being linked to schizophrenia are common in every population. The more of these gene variations that a person has, the greater the risk of developing schizophrenia. For example, in 2002 he linked a gene on chromosome 22 to a near-doubled risk of schizophrenia. When the gene, called COMT, is abnormal, it effectively depletes the frontal lobes of the neurochemical dopamine unleashing hallucinations and impairing the brain's reality check. The genetic predisposition interplays with schizophrenia-linked environmental factors and contributes to balance the possibility of psychotic onset.

Different researches highlight clear evidences of the association areas of particular chromosomes with schizophrenia. Chromosomes 11q, 3q, 18q and 6p have been examined, and the results have shown strong evidence for a schizophrenia susceptibility gene in 6p22-p24 and 11q21-22 [24, 25].

Moreover, two main genetic phenomena have been demonstrated in schizophrenia: *anticipation* and *CAG repetition.* Anticipation is defined by increasing severity or earlier age on onset of a disease across successive generations. It has been shown in families with history of schizophrenia. This phenomenon has been underlined in a recent study led in eight large families (186 patients) with a history of schizophrenia. The first generation showed no family members who met the diagnostic criteria for schizophrenia, while the second and the third generations recounted for, respectively, 8 and 30 members affected. Evidence of the role of CAG repetition has been highlighted by molecular biologists at UC Irvine. They isolated a gene, *hSKCa3*, located on 22q, which leads to an increased risk to schizophrenia confirming previous studies. *hSKCa3* codes for a potassium ion channel and acts to dampen the electrical activity and as an "off switch" to signals that are triggered by the NMDA receptors. This gene also contains a characteristic CAG repeat that leads to anticipation, in which subsequent generations accumulate CAG repeats; this increased poly-glutamine stretch is correlated with earlier onset and worsened states of the disease.

The discovery of these genes is considered the first step towards possible gene therapy. Even if that is not feasible, these findings can lead to a more detailed biochemical and mechanistic understanding of schizophrenia. Lastly, following the wake of genetic components, health experts started to recommend a tracking of own family's health history (for schizophrenia and other diseases that run in families) with a health family tree.

The Specialized Treatment Early in Psychosis (STEP) of Yale School of Medicine defines the first episode of psychosis simply as the first time someone experiences psychotic symptoms or a psychotic episode. The symptoms can be highly disturbing and unfamiliar, leaving the person confused and distressed. Unfortunately, negative myths and stereotypes about mental illness, psychosis in particular, are still common in the community and influence the public's attitude of seeking professional help.

The duration of untreated psychosis (DUP) is commonly defined as the time interval between onset of definite positive psychotic symptoms and first appropriate treatment. Often there is a long delay before treatment begins for the first episode. The longer the illness is left untreated, the greater the disruption to the person's family, friends, studies and work. Other problems may occur or intensify, such as unemployment, depression, substance misuse as well as law breaking and self-injury. Moreover, the longer the DUP, the greater is the global worsening of treatment response, symptom control and overall functional outcome [26]. Longer DUP is associated with:

- Psychosocial decline
- Prolonged morbidity
- Increased treatment costs
- Worse course and outcome
- Increased duration of the acute episode

Research has found that early intervention is beneficial for patients and loved ones for the following reasons:

- Less treatment resistance and lower risk of relapse
- Reduced risk for suicide
- Reduced disruptions to work or school attendance
- Retention of social skills and support
- Decreased need for hospitalisation
- More rapid recovery and better prognosis
- Reduced family disruption and distress

11.3.2 Environmental Contribution: The Family Role

Simultaneously to genetic aspects, the nurture has been esteemed as a great contributor to the onset of schizophrenia and its symptom relapse. The relationship between stress and schizophrenia is embodied in the stress-diathesis model, which provides a widely accepted and empirically supported description of the relationships among provoking agents (stressors), vulnerability (diathesis) and symptom formation and functional outcomes in schizophrenia [27, 28]. According to this model, McFarlane states that major psychotic disorders and their associated disabilities seem "the result of a continual interaction of specific biologic disorders of the brain with specific psychosocial and other environmental factors".

The mutual influence of biological and psychosocial leads to a process in which each element amplifies the other to yield a final illness outcome. Evidence suggests that expressed emotions (EE) represent an important form of psychosocial stressor,

which may contribute to precipitating relapse and, possibly, initial episodes of psychosis. The concept of expressed emotion (EE) has been introduced in 1962 by Brown and colleagues and is defined as emotion expressed by close relatives towards a family member with schizophrenia [29, 30].

Levels of parental expressed emotion (EE) may escalate in reaction to the functional deterioration of an offspring with emerging psychosis, thus contributing to increase the stress for the offspring [9, 27].

The other family interactional factor consistently associated with schizophrenic and bipolar disorders is communication deviance (CD), a measure of distracted or vague conversational style [31]. Both these factors have been found to predict the onset of schizophrenia [32, 33]. In support of the stress (or environmental risk) part of the stress-diathesis model, Goldstein demonstrated that onset of psychosis in disturbed adolescents seeking psychological treatment could be predicted by in vivo assessment of negative family affective style (AS, a directly observed form of EE, corresponding to the critical comments and hostility components of EE) and difficulties in clarity and structure of communication (CD).

A critical weakness moved to the research involving EE and AS is that these constructs reference only the attitudes and behaviours of family members towards the patient [34]. Such an orientation suggests a unidirectional causal process whereby the relatives cause the patient to become symptomatic. A more recent, stimulating and alternative line of research has focused on patient's behaviours that correlate with family members' EE. Leff, Miklowitz, Goldstein and Falloon questioned whether patient characteristics elicit EE in relatives. Leff and colleagues [35], in fact, compared high EE and low EE families on ratings of patients' symptom severity and found no differences. On the other hand, they found that a more likely elicitor of parental negativity towards the patient is the patient's negativity towards the parents, but not as a simple unidirectional causal agent, thus analysing the situation secularly. Cook, Kenny and Goldstein [36] studied the direction of effects for negativity, and their findings revealed that adolescents do elicit negativity from their parents (a partner effect) by virtue of being negative towards their parents (a reciprocity correlation). Moreover, the negativity elicited by the adolescents was a significant predictor of both mothers' and fathers' negative AS.

This is the strongest evidence to date that the dynamics of negative exchange in negative AS families (families with high levels of criticism) is reciprocally determined, and it emphasises that the patient plays a key role in the process.

11.3.3 Family-Focused Treatment

Clinical trials focused on high-risk period of psychosis have determined that the mean age of onset is in mid-adolescence, 16–18 years of age [37, 38]. Early intervention has to involve, by extension, adolescents' parents and other family members and supports [39].

Many partners and families find the onset of psychosis extremely distressing and feel helpless and confused. Their involvement is important in the overall plan towards recovery since family members can be an important part of the treatment team. However, it is also important that they take care or get help with their own concerns

and distress. Family members can learn about the nature of the illness and available treatment options for their family member by working with the treatment team.

They can provide information about the person's symptoms, how they developed and how the person functioned before the illness. Family members can also receive guidance on issues such as how to relate to, and support, a relative who is ill. It is also important for family members to be aware that their relatives need time to recover and may not be able to fully engage in all activities of daily living right away. A structured approach to gradually taking on tasks and activities usually works best.

Many families find that they need to develop coping strategies and effective communication skills to help them support the ill family member. Individual family counselling, psychoeducation workshops and support groups can help develop these strategies and skills. These groups and workshops can also provide the families themselves with ongoing emotional and practical support, as well as education about the illness. It is important that family members find a balance between supporting their recovering relative and finding time for themselves. This helps them prevent exhaustion and avoid becoming "burned out".

Family interventions and different approaches involving families (for an extensive description of the Italian situation, see references [40–57]) are designed to promote positive family environments and reduce levels of expressed emotions within families as well as provide insight into the signs and symptoms of mental illness, so family members can anticipate and help stop relapse.

Family intervention compared to standard care may decrease the frequency of relapses and may also reduce hospital admission and encourage compliance with medication, but it does not affect the tendency of individuals/families to leave care. It also seems to improve general social impairment and the levels of expressed emotion within the family [58].

11.3.4 Family Psychoeducation

The concept of psychoeducation is close to the concept of therapeutic education and refers to a kind of education intervention targeting people with a mental health condition. In the framework of psychosis, psychoeducation can be offered to patients, family members or both [59]. Psychoeducation was found to be consistently effective in improving family members' knowledge and coping. However, it was less successful in changing family members' psychological morbidities, burden or expressed emotion. Common ingredients across interventions included coverage of coping strategies and problem-solving strategies to enhance communication or coping. Particularly valued by family carers were a group format to share experiences with other carers, skilful facilitation by professionals and knowledge and skill development [60].

It is valuable to underline that family psychoeducation, even without patient psychoeducation, has proven effective in reducing relapse rate. This reduction is of the same order of magnitude as that obtained with an antipsychotic medication [59].

Miklowitz and colleagues [61] compared outcomes of family-focused therapy for individuals at clinical high risk (FFT-CHR) (adolescents and young adults with

attenuated positive psychotic symptoms, brief and intermittent psychosis or genetic risk with functional deterioration) in 6 months with three sessions of family psychoeducation (enhanced care or EC). FFT-CHR included psychoeducation about early signs of psychosis, stress management, communication training and problem-solving skills training, whereas EC focused on symptom prevention. Their results showed that psychosocial functioning improves depending on age: adolescents, in fact, had better improvement after EC, while young adults showed more improvement in FFT-CHR. As a consequence, the role of family psychoeducation appears crucial during the period of higher risk of psychotic onset.

Furthermore, a large comparative study of outcomes in community settings found that psychoeducational multifamily groups were more effective than single-family psychoeducation specifically in the first episode and in high-risk-for relapse cases [62, 63].

Family-aided assertive community treatment (FACT) combines psychosocial and pharmacologic interventions—family psychoeducation, supported employment, assertive community treatment and antipsychotic medication—as suggested by the Agency for Health Care Policy and Research survey as the most valuable treatment for schizophrenia and achieves very low rates of relapse, substantial reductions of symptoms and remarkable functional outcomes, particularly in the domain of competitive employment [35, 39, 64–66].

11.3.5 Brief Family Intervention

Brief family intervention is a form of family intervention where a mental health professional educates the person affected by schizophrenia and his/her family members about the illness over a limited number of sessions. The limitation of sessions contributes to increase participants' compliance and appears as an appealing factor in the evaluation of this therapy. Many researchers documented the efficacy of brief family interventions even if in different format. For example, Barber (1998, cited in [67]) reported results of a 6-h, 1-day workshop, while in Shinde's model (2005, cited in [67]) members were required to attend three (weekly) 1-h sessions within 4 weeks; the sessions were divided into education about schizophrenia, assessing and handling difficult problems and handling communication and emotions. Participants in the research of Smith and Birchwood [66] were required to attend four weekly sessions, in which a semi-structured seminar was delivered to family members. Family members also received a work booklet corresponding to the material covered in the brief education session. A patient-family teaching programme was employed in Youssef [68], in which participants attended three consecutive 1-h sessions of a discussion-based question and answer group, in order to explain the meaning of the illness, causes and treatments [67, 69].

Rewards of brief family intervention are represented by more hospitable family atmosphere for patients with schizophrenia and a much more reduced burden and stress for family members which, in turn, may improve patients' quality of life. Actual knowledge lack of patient-centred outcomes, thus the overall benefit a person may expect to achieve after receiving brief family intervention, is still unclear.

11.4 Family and Depressive Disorders

Depression is a major public health problem associated with increased functional disability and mortality. The annual economic consequences of depression were estimated at 83 billion dollars in the United States in 2000 [70] and 118 billion euros in Europe in 2004 [71]. Depression is highly prevalent throughout the world, and the prevalence appears to be increasing [72]. Nationally or regionally representative community surveys in 14 countries found that the estimated lifetime prevalence of unipolar major depression and persistent depressive disorder (dysthymia) is 12% [73]. Depression is also known to be highly recurrent, adding to the disease burden, and reaching chronicity [74].

The impact on the families is enormous, and the family atmosphere can play a causative factor to herald relapse of major depression [75]. Families of depressed bipolar patients have been described in literature as sharing the burden and themselves being at risk of physical and mental distress [20]. The comorbidity with substance use complicates the picture and has a negative impact on the psychopathology and response to clinical interventions. This, together with other factors, leads to more frequent hospital admissions and prolonged inpatient stays [76].

11.4.1 Family of the Depressed Patients and Aetiopathogenesis of the Psychopathology

The aetiology of depressive illness is still unknown, but many theories and hypotheses are widely accepted. Besides the biological hypothesis of the aetiology and the known bio-neurochemical changes, the argument is whether these are primary or secondary to the clinical symptomatology. The psychosocial factors were described in the literature since Freud's time and remain a matter of fertile research and near certainty.

Since the early twentieth century, the dynamics of the genesis of depression included family dynamics. The feeling of exquisite narcissistic vulnerability from a variety of sources, including the experience of early loss of parents, is perceived as traumatic, unempathetic, frustrating and rejecting [77].

Attachment theory, in relation to experiences associated with childbirth, has also been invoked, mainly in relation to the impact on the mother's interaction with the newborn. But research into attachment style in relation to adult psychopathology vulnerability has proven that poor support and adverse childhood experience are instrumental in the formation of psychopathological depressive symptomatology [78].

Moreover, depressed patients affect family functioning, as in quality of life and relationships [79]. Wang and Zhao [80] have eloquently discussed the family functioning of the depressed patients using the self-report family assessment device (FAD) and the observed rated McMaster clinical rating scale (MRCS). He concluded that both instruments are valid to provide a comprehensive understanding of family functioning of couples with a depressed partner.

11.4.2 Treatment of Depression

Treatment of depression runs into three phases:

- Acute phase: aims at symptom control, full remission and function restoration
- Continuation phase: as to sustain the achieved gains
- Maintenance phase: designed to prevent recurrence of the debilitating illness of depression [81]

Psychotherapeutic interventions have been the core of the short- and long-term interventions. Despite of the many modalities in applying psychotherapy, and the many names given by different authors, psychoeducation, involving the family, is rated as the most effective in managing major psychiatric disorders [82].

Lewinsohn and Clarke [83] and his group designed couple intervention courses, where they incorporated skills of assertiveness, providing support and increasing reward interaction between partners, and for each partner, in couple therapy.

In his study, Shimazu et al. [84] randomised a group of patients with major depression, receiving four sessions of family psychoeducation or "treatment as usual". They reported a significant reduction in relapse rate with 9 months follow-up, and this was not moderated by baseline EE (expressed emotions) status nor was statistically significant with EE reduction as measured with FMSS (5-min speech samples) or FAS (family attitude scale) after the family psychoeducation.

Similarly, Shimodera et al. [85] measured relapse-free days for patients with major depression, who received treatment as usual and family psychoeducation, compared to the group of patients who received treatment as usual only. The family psychoeducational sessions comprised of four 2-h family sessions, consisting of didactic lectures about depression for half an hour, followed by 60–90 min of open discussion about depression, treatment, prognosis and problem-solving techniques. He found the group with family psychoeducation to have totalled 272 relapse-free days, compared to 214 relapse-free days for the other group. He correlated the findings to cost-effectiveness and concluded that family psychoeducation for major depression is effective in the relapse prevention of major depression.

Keitner and Miller [86] reviewed the role of the family in the development and the course of major depression. They found that family pathology was evident before and during the episode of acute depression. They stressed that the course of the illness, the relapse rates and the suicidal behaviour are all affected by the family functioning. They concluded "there is evidence to support family and marital interventions, particularly in the treatment of depressed women".

In an innovative approach to assess efficacy of pharmacotherapeutic agents on depression and family function, Francois and his group [87] published an interesting study to assess the impact of either agomelatine or vortioxetine on family functioning, with patients suffering depression. Patients were switched from an existing antidepressant which was proven ineffective and randomised to take either of the two antidepressants mentioned above. They used "Depression and Family Functioning Scale" (DFFS), which comprises of 15 items to be rated from 0 to 4.

The scale was used to provide baseline and remeasured on week 8 and week 12. Descriptive statistics characterizing depressive symptoms (Montgomery-Åsberg Depression Rating Scale (MADRS)), functioning (Sheehan Disability Scale (SDS)) and quality of life (Qol) EQ-5) were stratified according to DFFS total score quartiles at baseline. Their findings supported the superiority of vortioxetine over agomelatine on DFFS score. They concluded that depressed patients with impaired family functioning showed worse overall functioning and quality of life scores, suggesting that attention should be given to family functioning of depressed patients.

In general, family-inclusive therapeutic approaches have proven effective in acute and maintenance treatment (and prophylaxis) of depressive illness. Miller et al. [88] published a study of 76 depressed inpatients who were randomly assigned for treatment with a combination of pharmacotherapy and cognitive behavioural therapy and family therapy and followed up for 6 months after discharge from a hospital admission. A significantly greater proportion of patients whose treatment included family therapy experienced either remission or improvement in their depression than those patients who did not receive family therapy.

Conclusions

Treatment of depressive disorders varies greatly depending on the specific disorder and the training of the clinician offering the management of the disorder.

Educational family therapy has been, and continues to be, an integrated psychoeducational intervention and has expanded to include family problems, mainly disease focused, like attention deficit disorder, cancer and terminal illness, family in crisis and trauma [89].

Although much of the work addressed schizophrenia and its effect on family, Anderson and different researchers [90] expanded the family psychoeducational model to include home visits, to provide intensive workshops and seminars for families. This helped both in understanding the psychopathology and creating a supportive environment for the patient.

Mc Farlane [82] delineated a list of guidelines for family members and friends to accept the slow recovery process and set realistic targets. These helped to reduce the harsh confrontation and arguments and helped with the adherence of the given medical advice.

Treatment of depression remains a fertile area of research. The usage of pharmacotherapy and different modalities of psychotherapy is supported by many studies and publications [91].

Behavioural marital therapy (BMT) was also supported by studies by Neil Jacobson and colleagues [92]. They demonstrated that when individuals are depressed in the context of distressed marriage, BMT is as effective as CBT (cognitive behavioural therapy) in reducing depression. In situations where depression and marital discord coexist, marital therapy is an important intervention to consider.

Since Miklowitz's family-focused therapy approach [93], the involvement of the families in the therapeutic interventions to treat major depression (and bipolar depression) has been accepted and adopted by many researchers and treat-

ment centres around the world. This intervention tool in the armamentarium of treating major depression has gained momentum by the successful results in treating depression and by the consumer's affirmative acceptance of such a treatment option.

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Institutionalization, Deinstitutionalization, and the Penrose Hypothesis

12

Adrian P. Mundt and Norbert Konrad

Abstract

Psychiatry began to emerge as a medical specialty and science after the French revolution with the transinstitutionalization of mentally ill from imprisonment to psychiatric hospitals. Psychiatric hospitals grew in size, many of them housing thousands of people by the end of the nineteenth century. The twentieth century was characterized by psychiatric reforms shifting services from institutions to outpatient care settings and removing large numbers of psychiatric beds. In the year 1939, the British psychiatrist Penrose pointed to a possible inverse relationship between psychiatric bed numbers and prison population rates. Prison populations were on the rise throughout the twentieth century in most countries. By the end of the twentieth century, worries about a transinstitutionalization of people from psychiatric institutions to penal justice institutions came up again. In the beginning of the twenty-first century, the Penrose hypothesis was in the focus of scientific interest again. Studies from Western Europe and South America point to a significant inverse relationship of psychiatric bed numbers and prison population rates in longitudinal data.

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12.1 Enlightenment Split

Prior to the enlightenment, people with deviating or disturbing behaviors were mostly imprisoned or restrained. The enlightenment brought changes on how societies usually dealt with deviant behaviors. Medical doctors started to conceptualize certain types of rather deviant behaviors as mentally ill. They proposed new recovery-oriented psychological treatments for mentally ill based on humanistic principals [1]. Those interventions intended to replace restraint and harsh methods of treatment. Psychiatry emerged as a medical specialty to treat those deviant behaviors considered illnesses. Other types of deviant behaviors were considered criminal or moral failures that were continued to be treated with restraint or imprisonment. This distinction has been called "enlightenment split" [2]. Following the enlightenment split, the psychiatric hospital became the preferred place to treat mental illness. The transinstitutionalization from prison to psychiatric hospitals constitutes the foundation of psychiatry.

Up to date the distinction between criminal and mentally ill behaviors is complicated and at times vague or fragile. With all the advances of research regarding biological, psychological, and social determinants or correlates of deviant behaviors, we still have difficulties to draw a clear line between illness and moral failure. There is important overlap in current classifications. For example, pedophilia and illicit drug abuse are considered mental disorders in the tenth version of the international classification of diseases, and they are criminal offenses at the same time. Evaluations to determine the degree of illneess possibly causing a criminal behavior belong to the most difficult tasks in psychiatry.

12.2 The Psychiatric Hospital of the Nineteenth Century

Mentally ill people were increasingly treated in psychiatric hospitals or mental asylums during the nineteenth century. Psychiatric hospitals were built outside of the important cities in most European countries. In colonial times, this type of service provision was implemented worldwide [3–5]. The psychiatric hospitals intended to provide therapeutic environments during retreat [6] or long-term hospitalization [5]. The erosion of the distinction between insanity and immorality by medical scientism and the inclusion of immorality in the systems of disease have been given as possible explanations for the increase of numbers of people in those institutions [7]. The line between criminal and mentally ill behaviors was pushed into the territory of criminality. By the end of the nineteenth century, many of the institutions were housing thousands of people [8]. Increasingly custodial structures, crowding and growing criticism gave rise to a call for new approaches [9, 10].

12.3 A Century of Psychiatric Bed Removals

In the beginning of the twentieth century, large numbers of people were living in mental health institutions. Carceral narratives dominate the histography of psychiatry and its institutions [11]. First ideas of psychiatric reforms came up questioning

the sizes of those institutions and the numbers of people being institutionalized in psychiatric hospitals. In 1939, the British psychiatrist Lionel Sharples Penrose pointed for the first time to a possible inverse relationship between the number of people in psychiatric hospitals and prisons, a notion that later was referred to as Penrose hypothesis [12].

In the 1950s and 1960s, Anglo-Saxon countries systematically implemented psychiatric reforms that implied reduction of the numbers of people living in mental asylums. Growing recognition of the detrimental effects of long-term hospitalization, the availability of new pharmacological agents in the 1950s, and new models of outpatient treatments in psychiatry lead to a paradigm shift on how to best treat people with mental illness. Reforms included the creation of community housing facilities and intensified outpatient services to care for people with chronic mental illnesses. Long-term hospitalization was replaced by short-term and if necessary intermittent hospitalization. In the 1970s and 1980s, psychiatric reforms were implemented in many other European countries. The ideas of psychiatric reforms gained political momentum in the second half of the twentieth century. They had a philosophical or ideological correlate in antipsychiatric movements. The most radical implementation of psychiatric reforms took place in Italy based on the idea to reject every form of institutionalization in mental health care. The protagonists of this movement in Italy was Franco Basaglia [13] with the intention to focus on human rights of mentally ill and dismiss all custodial structures in mental health care [14]. There were ideas to dismiss circuits of social control and give a different meaning to madness [15]. The consequences of the famous Law 180 in Italy removing nearly all psychiatric beds were critically discussed not only in Italy but across Europe starting in the 1980s [16]. There were concern especially about severely chronically ill, the acutely ill, and homeless with mental illnesses. Whereas North American countries had a more pragmatic approach to deinstitutionalization driven by ideas of necessities, cost savings, and efficiency [15], the South American approach was strongly influenced by Basaglia, more radical, political, and emotional [17]. In the 1990s psychiatric reforms and the corresponding service developments became the worldwide model also for low- and middle-income countries. Psychiatric bed removals were such a fundamental and strong principal of psychiatric reforms that they were recommended and conducted irrespectively of the number of beds per population and irrespectively of minimal standards in community and social care systems.

12.4 The Role of Forensic Psychiatry

Usually forensic psychiatrists are concerned with the assessment of complex cases, including risk assessment, and act as expert witnesses in court, commenting, e.g., on issues of competency to stand trial and criminal responsibility. While the ethical issues facing forensic psychiatrists may be similar across cultures, they do also depend on the specific legal system and service provision within each country. Therefore a forensic psychiatrist should not only look on technical guidelines to structure the report but should also respect the ethical frame as well as to be

conscious of the cultural and societal context. The concepts of "criminal responsibility" or "guilt" in legal thinking do not exist as an empirical entity in psychiatry. Even if a psychiatric expert does not comment directly on criminal responsibility—and he should not do as a matter of fact—his expert opinion aims at enabling this finding. The forensic psychiatrist acting as expert witness is confronted with a double dilemma: either he is legitimating punishment by labeling only a fraction of the accused as disordered and in need of treatment; in this case he might be called a servant of justice. Alternatively, if he is offering treatment for a large number of offenders, he might be accused of brain washing and treatment tyranny. Forensic psychiatrists as well as forensic psychologists should not, as a matter of principle, and in order to avoid a conflict of roles, assess their own patients. Their task is the psychopathological evaluation of the mental condition of a perpetrator and his personality performed on the basis of empirical knowledge and competent specialist examination. Regarding risk assessment future behavior cannot be predicted with any certainty, no matter how sophisticated risk assessment instruments are, giving rise to particular challenges in balancing the civil liberties of the patient and the protection of the public from (potential) future harm by that patient. In an increasingly risk-aversive society, public pressure demands to reduce false-negative predictions with the expectation to eliminate risk [18].

12.5 The Penrose Hypothesis in the Twenty-First Century

After decades of latency, the Penrose hypothesis was reconsidered in the twenty-first century in different countries and contexts. Decades after the psychiatric reforms in Europe, concern was expressed about the increase of numbers of people in forensic psychiatric institutions and prisons co-occurring with continuous removal of psychiatric beds. The question arose whether an era of transinstitutionalization or re-institutionalization had started [19]. Had institutionalization in the twentieth century been characterized by trends of transinstitutionalization from psychiatric hospitals to prisons? Do we need to decarcerate mentally ill from prisons and jails [20] as in the time of Pinel when psychiatry was founded as a medical science? Had general psychiatry turned away from severe behavioral problems and turned toward the treatment of mild to moderate emotional problems that mostly do not result in deviant behaviors [21, 22]?

12.5.1 Cross-Sectional Evidence

In a recent systematic review on the Penrose hypothesis, studies were sorted according to the type of design sampling cross-sectional data, time point data, or longitudinal data [23]. Cross-sectional studies have the advantage that they can easily include large numbers of countries [24]. However, they do not acknowledge trends within countries or regions. Similarly to the original study by Penrose, a study assessing different regions in Australia found that areas with more psychiatric beds

had less prisoners and vice versa [25]. The largest and most systematic cross-sectional study including all countries worldwide did not detect any inverse relationship between psychiatric bed numbers and prison population rates [24]. It even found a direct positive association between psychiatric bed numbers and prison population rates in low- and middle-income countries. This indicated that when development was still poor, both institutions were developed in parallel at first.

12.5.2 Time Point Data

A paper assessing two time points is one of the few studies from the USA addressing the Penrose hypothesis for six US states [26]. The first time point was 1968 and the second 1978. Between the two time points, there was a massive increase of the prison population and decrease of psychiatric bed numbers. The authors concluded that there was not likely any relationship between the two phenomena. However, the argument was weak and based on the history of criminal justice involvement of psychiatric inpatients and the history of hospital treatment in prisoners. Longitudinal studies were first presented with data from single countries such as Hungary and Norway [27, 28]. Hartvig, Kjelsberg [28] reported a 74% decrease of psychiatric bed rates between 1960 and 2004 in Norway, whereas prison populations increased 52%, and violent crime increased 900% in the same time span.

12.5.3 Longitudinal Studies

There have been more recent studies testing the Penrose hypothesis using statistical models of longitudinal data from several countries with contrasting results. The first evidence for a significant inverse relationship between the number of psychiatric hospital beds and prison population rates in a longitudinal data set is from South America [29]. In the year 1990, South American countries committed themselves to psychiatric reforms [30]. The study evaluated trends of psychiatric bed numbers and prison population rates in the two decades following this initiation of reforms. A massive increase of prison population rates associated with the reduction of the numbers of psychiatric beds. When and where more psychiatric beds were removed, the prison population rate rose more. There are risks to find spurious correlations between longitudinal trends over time; nevertheless, this seems the most robust way to assess this possible relationship so far [31, 32]. A study applying similar models to Western European datasets also reported a significant relationship between the decrease of psychiatric bed numbers and the increase of prison population rates over the last two decades [33]. However, this relationship was less robust than the one observed in South America. The relationship was not significant any more when year-fixed effects were added and when economic indicators were introduced to a multivariate model [33]. Since this study covered a time period that started when most countries had concluded psychiatric reforms, the decrease of bed numbers had been modest and not as strong as in South America. A further recent study that

reported longitudinal time trends of prison population rates and psychiatric bed numbers for Eastern and Western Europe argued against the Penrose hypothesis [34]. Including time trends from Eastern Europe, the trends between the countries are very heterogeneous, especially with respect to the prison population rates. A previous study had described the parallel trends of prison population rates and psychiatric bed numbers for the post-communist context [35]. Eastern European and Post-Soviet countries underwent penal justice reforms after the political change, which implied mass amnesties of political prisoners. Against the worldwide trend, prison populations decreased after the political change in most of Eastern Europe departing from very high numbers. There has been surprisingly little empirical research on this from the USA. But radical viewpoints such as "Bring back the asylum" have been published [36]. They acknowledge the problem that there is insufficient psychiatric long-term care and show the desperateness how to face this. The critical decline in public psychiatric hospital beds in the public sector in the USA has even been related to the increase of suicide rates [37].

12.5.4 Mental Disorders in Prisoners

Further research points to the interdependence of the psychiatric care systems and penal justice systems: There has been consistent evidence of high rates of severe mental disorders in prison populations [38, 39]. Substance use disorders are very common in prisoners [40]. The severe mental disorders frequently co-occur with substance use disorders [41] and with personality disorders [42] in prisoners.

12.5.5 Hospitalization and Imprisonment as Revolving Doors for the Same People?

People with penal justice involvement have high rates of psychiatric hospitalization prior to [43, 44] and after [45] imprisonment in countries where short-stay hospitalization is the preferred mean of service provision and psychiatric hospital beds are still provided in a relevant number to the public sector. The revolving-door phenomenon has been described for the prison system [46] and for the psychiatric hospitalizations [47]. Especially people with dual disorders may even enter in a ping-pong situation between the two institutions as the difficult to manage and "unwanted" people.

A systematic review of longitudinal studies following up people discharged from long-term hospitalization did not reveal elevated rates of homelessness or imprisonment as compared to the general population [48]. However, people included in the original studies were elderly and had spent on average continuously several decades in psychiatric hospitals, which is not the case for current or future generations of severely mentally ill. The criminogenic energy decreases with age [49], and severe mental illness requiring repeat hospitalization in systems with short stay may stabilize over the lifespan with respect to the need of hospitalizations [50].

Linkage studies of registries also pointed to a relationship between mental illness and violent crime. This relationship has been understudied and even rejected in some countries for a long time to reduce stigma of people with mental illnesses. The risk to be convicted of violent crime is more than sixfold increased in men, and more than 14-fold increased in women with schizophrenia in the 5 years following the diagnosis [51]. Linkage studies of a national crime register up to the year 2006 and a systematic whole population mental examination in the late adolescence in the year 1969–1970 before obligatory military service in Swedish men showed the relationship of mental disorders and violent crime. For the late adolescents with mental disorders, there was an increased risk to be convicted of a violent crime in the 35 years following the examination. Risks were severalfold elevated for people with mental retardation, substance use disorders, and personality disorders. Even for anxiety disorders and depression, there was a modest but significant increased risk to commit violent crimes, whereas there was no difference for people with neurological disease [52].

The question whether or not mentally ill people "should be" in prison is primarily jurisprudential and political. Countries, which apply the construct of psychological incompetence or incompetence to stand trial, can prevent mentally ill people from being imprisoned. Secure confinement in a forensic psychiatric institution can then be imposed if necessary. This could be in one of three separate institutions, which each have a completely different legal framework (a general psychiatric ward, a forensic psychiatric ward, or a forensic psychiatric ward in a prison). This differentiation gives rise to ongoing debate about the misplacement of mentally ill offenders [53]. The high prevalence of mentally ill being detained in prisons found in most countries can have many driving factors which include the criminalization of mentally ill individuals by pressing charges instead of tolerating socially deviant behavior, cost savings in the treatment of mentally ill by closing institutions for long-term care, and a reduction of the duration of inpatient treatment together with inadequate preparation for discharge and inadequate structures in community care for long-term stabilization, especially with respect to their availability and suitability to young adult severely ill patients with dual disorders. Changes in the legal frameworks could play a role, with the trend to apply stricter criteria for confinement in psychiatry that are in accordance with public or civil law and in line with international human rights declarations. This can lead to a gap that, for the lack of other social control mechanisms for individuals with abnormal and legally deviant behavior who require therapy but are unwilling to adhere, seems to be closed by the penal systems. Other factors include the reluctance of general psychiatric facilities to accept mentally disordered prisoners on the assumption that they pose a danger that the institution is not equipped to handle (e.g., inadequate security conditions, the staff has no practical forensic psychiatric experience) or a lack of beds, rejection of "difficult" patients with chronic psychoses due to doubts about their suitability for treatment. The "death of liberalism" may imply a political climate that keeps the resources for mentally disordered offenders at a low level. The problems and interactions are complex. Their relevance for mentally ill in correctional systems should be discussed for each specific country and legal context [54].

The Penrose hypothesis is still unresolved, especially, to what degree it is generalizable or whether it applies for specific regions and time spans. It is also still open how politics, service planners, and stakeholders act upon recent findings. Fact is that most societies function with intermittent institutionalization. Among the different types of institutionalization, a psychiatric hospital bed seems to be one of the best-resourced, most therapeutic, and least custodial options.

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Biobanking for 'Omics' in Psychiatry: Logistical and Ethical Aspects

13

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Abstract

Biobanks are highly specialized repositories for both biospecimens and associated demographic or clinical data. They have become a crucial component of big data research in all fields of medicine, in particular as regards genomic approaches. However, biobanking faces several non-trivial logistical and ethical questions, with the majority of logistical and conceptual issues arising from the ethical challenges.

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13.1 Background

Chronic diseases, including psychiatric diseases, contribute to the main causes of death and suffering and thus constitute a major burden for health systems globally. Due to demographic changes (e.g. higher life expectancy), this burden is projected to increase [1]. Medical research focuses on improving patients' well-being and maximizing clinical benefits. Therefore, in addition to approaches of curative therapy, prevention has become more important than ever. Prevention is based on a better understanding of chronic diseases. Against this background, 'omic' approaches (e.g. genomics, genetics, proteomics, transcriptomics) have become integral parts of medical research and have already proven successful in some fields during the last couple of decades [2, 3]. It is hoped that a gain of knowledge of 'omic' aspects will contribute to better diagnosis and improved approaches to personalized medicine such as risk calculation and individual treatment strategies. Still, our knowledge of long-term clinical course and chronicity is sparse, which is why genetic approaches should be complemented by longitudinal studies. In general, this type of research delivers ever-increasing numbers of biospecimens, as participants are followed up. To handle this quantity of data, complex databases and biobanks are crucial. Thus far, all over the world, in particular in highly industrialized countries, numerous such resources have been established over the last 5–10 years, with new efforts already underway. Biobanks collect and store massive volumes of diverse and highly sensitive material and data. They also transfer raw data into potentially useful clinical information. The ability to compile diverse panels of data and biomaterial for an individual carries huge potential: it may eventually enable us to create a unique biological signature of a patient that can help guide diagnostic and therapeutic procedures.

However, this novel and rapidly developing field does not come without potential risks and thus faces ethical challenges that need to be addressed and will impact the overall design and infrastructure of a biobank.

The success of biobanking critically hinges on the participation of research volunteers. Researchers have to ensure that the biomaterial and the associated data donated by a study participant are maximally protected and preserved. Many participants furthermore wish to receive detailed information about the measures set in place to prevent sensitive information from being compromised or misused [4]. Biobanking projects involving the study of psychiatrically ill individuals are subject to even more scrutiny than usual regarding the protection of sensitive data and biomaterial and adherence to ethical standards.

With an increasing amount and variety of data and biomaterial being collected for an individual, an ever more coherent signature of a study participant (and potentially also of her or his family members) arises. This calls for the utmost stringency when setting up safeguards to ensure the highest levels of privacy and autonomy of participants. Researchers, study participants, policymakers and the general public alike have to come to accept that in today's world there always remains a potential risk of de-identification (especially through genomic information) even in the presence of sophisticated precautions like anonymization or pseudonymization [5].

The best safeguard against such an undesirable event is thorough planning before a biobank is set up. The issues surrounding the protection of sensitive data should be discussed and addressed ahead of embarking on a biobanking project [6]. The complexity of issues requires the collaboration of many disciplines and institutions. It is widely agreed that successful contemporary research can only be achieved via data sharing, irrespective of national borders. Thus, regulations regarding data collection, data storage, ownership and access, e.g. by third parties, have to be clarified transparently in advance [7, 8]. Trends towards internationalization, privatization and commercialization of research and its results have to be taken into account.

In the following section, we outline principles of how to set up a biobank, as illustrated by our own experiences within the framework of German-wide multicentre longitudinal research projects (www.kfo241.de; www.PsyCourse.de). We delineate a comprehensive biobanking framework for biological psychiatric research addressing the issues discussed above.

13.2 Ethical Aspects

Recommendations and national law regulate access and data sharing options to protect an individual research volunteer's rights and point researchers in the right direction. At the international level, the latest ethical guidelines for biobanks are described in the 'Declaration of Taipei' (2016) [9]. The Declaration of Taipei extends the 'Declaration of Helsinki' and considers the relevant ethical challenges that arise from health databases and biobanks. The declaration underlines the importance of individuals' dignity, autonomy, privacy and confidentiality by protecting their data (par. 1 and 9). Individuals have to give their consent voluntarily (par. 11) and be allowed to exercise control over the secondary use of their individual data and the biological material they have given (par. 14). The right to withdraw personal data for future use is mandatory (par. 15). Furthermore, an ethics committee should approve the establishment of the biobank and should have the right to monitor ongoing activities (par. 19). The WMA (World Medical Association) proposes that a potential research participant be given a comprehensive document detailing, among other things, the storage and use of data and material and the potential risks and burdens associated with the collection. Only when these pieces of information have been shared with and sufficiently explained to a prospective donor can an informed consent procedure be considered adequate for a biobanking project, which is characterized by its multiple and indefinite uses of data and samples (par. 12).

The overall goal of biobanks is to facilitate large-scale 'omic' research approaches. Such research includes the potential to reveal so-called incidental or additional findings. Wolf et al. describe additional or incidental findings in the research context as 'a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research, but is beyond the aims of the study' (p. 219) [10]. If an incidental finding implies the possibility of medical prevention or treatment, disclosure to the individual is highly recommended [11]. In case of a non-actionable finding (e.g. genetic information

about a risk of developing dementia), the individual's right to informational self-determination can only be assured if he or she can decide how to deal with such findings (prior to the involvement in the study). Here the right not to know (also known as 'opt-out', right to an open future, right of ignorance), the right to reject information about findings that are not actionable, has to be a realistic option for the participant.

During the informed consent procedure, the individual should receive enough information about potential consequences to make a truly informed decision. A study conducted by Ormond et al. showed that many participants find informed consent processes complicated and have a tendency to misunderstand essential information [12]. Thus, it is crucial to align the informed consent procedure with the participants' needs.

In the context of psychiatry, specific ethical issues for patients who are temporarily unable to consent (e.g. during a psychotic episode) need to be taken into account. These patients are often excluded from studies because they might not be able to make an informed decision. According to Article 6 of the Convention of the Council of Europe (2005), interventions on individuals without a full capacity of consent may be carried out, however, only if they have a direct benefit [13]. As this is obviously not the case in biobank-related research protocols addressing basic science questions, acutely ill patients are typically excluded from participation. Such blanket denial of patients' right to participate in research, however, may to some degree amount to discrimination or even stigmatization as it infringes on a patient's right to be part of research that may prove to be beneficial, even though it may not be of immediate relevance to the study participant [14]. To illustrate, a severely depressed patient with delusions of worthlessness and questionable suicidality may require involuntary admission at one point but may nevertheless be capable of understanding the overall usefulness of research. Furthermore, as far as additional or incidental findings are concerned, the decision to disclose such findings to vulnerable individuals (e.g. individuals with depression or anxiety disorders) should not be taken lightly as this could lead to feelings of anxiety, grief or loss of control and unpredictable long-term consequences. Psychiatric disorders often come with cognitive biases (e.g. black and white thinking, catastrophic thinking [15], negative style of attribution [16]) that could affect the way patients cope with disclosed findings. If disclosure of critical incidental information to a psychiatric patient is deemed necessary from a medical perspective, it should only be done in conjunction with the provision of psychological counselling.

13.3 Data Protection Principles

As we collect and work with masses of sensitive phenotypic and biological data, the development of data protection principles is one of the most essential aspects of biobanking. In most countries, in particular the Western world, the protection of an individual's privacy and sensitive data has become a major focus of the political debate across their societies and of actions taken by their respective legislatures.

Several state and federal laws govern data protection in Germany. Similar scenarios exist in other countries. While a more unified global approach may be desirable, it is unlikely to be feasible at this point in time. While this may not be achievable at the political level, it may be possible at the global psychiatric level by working towards consensus through bodies like the WPA.

The most important objectives of data protection principles are to avoid unauthorized access to data and unauthorized reidentification [17]. Organizational and technical measures have to be taken: identifying data are to be stored separately from phenotypic data and biospecimens [17–21]. Furthermore, personal data are to be replaced by an anonymous or pseudoanonymous code. Third, technical security measures such as cryptographic algorithms have to be installed [17, 19, 20, 22]. Only authorized researchers may obtain access to this data in specific cases such as follow-up studies on a subset of participants or communication of incidental findings.

The measures set in place to achieve these aforementioned goals should be transparent to the participants, as this is likely to increase the acceptance and willingness to participate in a study. On the other hand, the data protection principles should be flexible, feasible, cost-efficient and sustainable.

13.4 Information Technology (IT) Structure

To ensure confidentiality and the utmost protection of sensitive data, four different IT components are required: an identity tool, an administrative tool, a phenotypic database and the biomaterial repository, i.e. the biobank proper (Fig. 13.1) [22]. The identity tool is responsible for storing the identifying data and for generating two different pseudonyms, one for the phenotypic and one for the biomaterial data. The administrative tool manages the study organization, the informed consents and the communication with the study participants and is linked to the identity tool in order to exchange the identifying data and pseudonyms. Clinical information is stored in the phenotypic database using the special phenotypic pseudonyms. These phenotype pseudonyms are created by the identity tool. In an analogous manner,

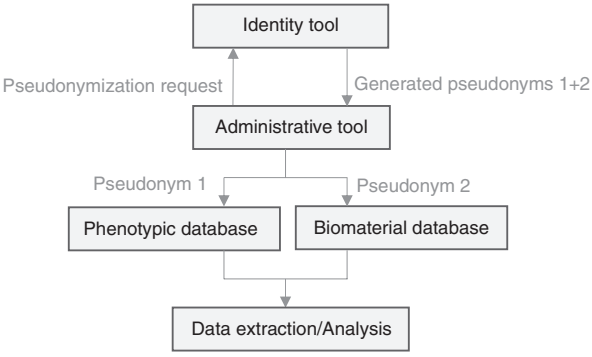

Fig. 13.1 The schematic structure of the IT components responsible for identifying, managing, storing and evaluating the phenotypic and biological data collected in the CRG241/PsyCourse Project [22, 24]

the biomaterials are managed through the biomaterial database using the special biomaterial pseudonyms. Nussbeck et al. provide a guideline on designing biospecimen identifiers [23]. Both databases are detached from the other IT tools. A data backup is performed daily. For the purpose of targeted recontacting of patients, biospecimen retrieval and analyses, phenotypes, biomaterial and sometimes identifying data need to be linked. In our view, this is only possible through an honest broker system, aimed at adding an additional safeguard against illegitimate access. The honest broker system is an independent computing facility. It means that the ID management (random ID generation and linking of all data sources) is done via a third party. The honest broker has access to key identifiers to enable him/her to facilitate such processes. Of necessity, the honest broker has to be a person of integrity who has sufficient expertise and can be held accountable for breaches in confidentiality.

At this point, there exists no one-stop-shop generic IT solution. Custom-made approaches are required to create the kind of system we have described [24]. Further developments in the Medical Informatics World, however, will facilitate the handling of comprehensive data, and these could lead to more easily implemented approaches in future research projects.

13.5 Broad Informed Consent

The basic tenet underlying biobanking is that biomaterial and data are collected without a specific or well-defined research project at the time of collection. Research objectives are rather broad, and both phenotypic data and biospecimens are stored for an undefined period [25]. Therefore, participants cannot be informed in detail about analyses and storage. This is crucial to the communication with patients and the process of informed consent. The 'Declaration of Taipei' provides recommendations as to how to deal with these uncertainties [5]. One approach is to use a broad informed consent which covers the essential parts. The participant has to be informed about (a) the data protection principles; (b) the purpose of the study; (c) the description of the relevant biomaterials and data; (d) information on the risks that arise from the donation of biomaterials and data; (e) the description of personal benefits, incidental findings and financial advantages; (f) the consent to be contacted again for follow-up studies; (g) the right to withdraw the consent; and (h) the insurance coverage. Participating individuals have to agree to these measures explicitly. As regards the issue of incidental findings pointing to an illness or the risk of developing an illness, participants have to decide whether they want to receive such information or not. Here, the informed consent procedure should also specify two scenarios: one for illnesses for which curative actions can be taken and one for which no treatments exist. If the patient withdraws the consent, an standardized algorithm is applied. In the Appendix, we provide an English-language version of our informed consent procedure addressing the aforementioned aspects.

13.6 Future Challenges

As we move towards collecting more detailed data and a large quantity of biomaterials, the risk of reidentification increases; the information gathered can no longer be considered 'loosely associated' with the individual it is derived from, rather in its entirety it truly constitutes an individual signature. As measures to bypass technical solutions to data security and encryption are likely to develop faster than such solutions, the protection of personal rights will remain a challenge to the field of biobanking. Furthermore, the issue of data protection needs also to be discussed in the context of increasing privatization and commercialization of biobanks. Despite multidisciplinary efforts to protect personal rights, a residual risk of reidentification of participants in biobanking projects cannot be eliminated. At the same time, networking and international collaborations have become indispensable for successful research. Against this background, the medical field and policymakers should strive to monitor these developments closely and offer the necessary legal frameworks.

Appendix 1: Patient/Proband Information

Dear Sir/Madam,

The study of human biomaterials and the analysis of data obtained, or to be obtained, thereof have become an important tool in medical research. We therefore ask our patients/test persons, including you, whether they would be willing to provide us with certain body materials and data for research purposes. Your participation is entirely voluntary. If you decide not to participate, or if you wish to revoke your consent at a later time-point, you will incur no form of disadvantage.

In the information below, we inform you of the objectives of our study, the study procedures, and the measures applied to protect your personal data. This information is intended to enable you to form your own opinion concerning participation and reach an informed decision.

If anything is unclear, please ask your physician or clinical investigator before agreeing to provide your consent. You will also be able to contact the physician who informs you about the study at a later date should you have any questions or require any form of clarification.

Aims of the Study

The study involves the investigation of the biological and environmental basis of diseases of the central nervous system, e.g. major depression, manic-depressive (bipolar) disorder, schizophrenic disorders, personality disorders, anxiety disorders, posttraumatic stress disorder, pain disorders, neuropathic and somatic pain disorders, drug and alcohol dependence, and dementia.

These are all common disorders and they are responsible for a high degree of suffering in patients, in their relatives as well as in their social environment. Advances in modern medicine are continuously improving diagnostic and therapeutic methods but currently available therapies are often not effective enough and medications cause side-effects.

We now know that both genetic factors and environmental influences are important in the development of these disorders. Through the medical-genetic investigation of these factors, we attempt to gain insights into the development and course of such diseases and thereby contribute to the development of more effective treatment options and prevention strategies.

It is assumed that the development of neuropsychiatric disorders is determined by genetic factors, i.e. by individual variations in DNA (the material containing your genes).The combinations of DNA-variations that are present in a given individual can be determined through analyses of the DNA.

We aim to elucidate the means by which DNA variations as well as variations in metabolic patterns contribute to the development of neuropsychiatric disorders. We know that the development and course of psychiatric and other common disorders (e.g., hypertension, diabetes, and asthma) are not determined by one genetic variant, but that genetic information interacts through multiple pathways on the development and course of the disorders. In order to understand these complex processes we would like to investigate as many factors associated with the disease as possible. These include changes in hormone metabolism, lipid metabolism, and stress tolerance.

Which Types of Biomaterials and Data are Involved?

The required biomaterial is blood/tissue. The biomaterials and data will be obtained from you during your period of participation in the present study. The collected data will concern information about you personally, including medical data. Therefore, we would like to conduct a structured clinical interview concerning your psychiatric symptoms. In addition, some neuropsychological tests will be performed to evaluate your cognitive abilities. By means of various questionnaires we would also like to gather information about important life events, personality characteristics, and medical treatment history. We would therefore like to ask your permission for us to access your medical records.

Many psychiatric diseases present in an episodic form, e.g. the depressive and manic episodes seen in bipolar disorder. The transformation of genetic information into proteins (the chemicals made by genes, i.e. gene expression) alters depending on the nature of the presenting episode. We would therefore like to re-contact you if you should later present with a different episode to that seen at the baseline examination. As it is possible that you may be treated in the clinic and be unable to give consent for the taking of another blood sample for our research, we would like to ask you for your consent to this procedure in advance. You can of course withdraw your consent at any time once your psychological condition has improved, and we will bring this to your attention at that time.

How Will the Biomaterials and Data be Used?

The biomaterials and data provided by you will only be used for medical research purposes. However, at the present time we are unable to specify the exact research objectives. You should be aware that in consenting to participate in this study, you are granting us very wide-ranging authorization. Therefore, we request explicit consent to this wide-ranging authorization, which you can indicate by ticking the respective boxes on the informed consent document.

Using your biomaterials, genetic studies, i.e. investigations into the genetic material, will be carried out. Under certain circumstances, this may include the investigation of your entire genome. Your biomaterials and data will be stored and made available for medical research purposes for an indefinite period.

What Risks Arise from the Donation of Your Biomaterials and Data?

(a) *Health Risks*
We would like to collect 40 ml of your blood (equivalent to ca. four tablespoons).The only risk associated with the donation of your blood to the biobank is the low risk involved in any normal blood taking procedure. In rare cases, stronger secondary bleeding may occur from the puncture site, or in very rare cases, persistent damage to nerves or blood vessels may occur.

(b) *Other Risks*
The collection, storage, and transmission of data obtained from your biomaterials for research projects carry the risk of a breach of confidentiality (i.e., the possibility exists that you may be identified). This applies in particular to information concerning your genetic material. These risks cannot be completely ruled out, and they increase as possibilities for linking data together increase, e.g. if you yourself publish your genetic data on the Internet (i.e., for genealogical research). The personnel in the XXX assure you that they will do everything possible to protect your privacy in accordance with the latest technology, and that your samples and data will only be transferred to researchers who can demonstrate an appropriate data protection strategy (see point 8: "Who has access to your biomaterials and data?").

What are the Benefits for you Personally?

You personally can expect no immediate advantage or benefit to your health from the donation of your samples and data. The results are intended solely for research purposes. We would like to point out that all investigations within the context of the study are conducted for scientific purposes only and that no comprehensive diagnostic procedure for the detection of physical or neuropsychiatric diseases is involved. In individual cases, this means that potential pathological changes may not be recognized.

Feedback can be provided if, in our view, certain information is of significant importance to your health. This is the case if the development of a (possibly life-threatening) disease can be avoided or a previously unrecognized disease can be treated. However, you may then need to disclose this information to other bodies (i.e., to an insurer). If you do not wish to be informed, please delete the re-contact option (see point 10 below).

Which Conditions Apply to the Use of Your Data and Biomaterials?

(a) Your written consent is a prerequisite for the obtaining and use of your biomaterials and associated personal data for research purposes. Your consent is voluntary and may be revoked at any time (see also clause 11 "What does your right to revoke your consent mean?").
(b) Your biomaterials and data will be stored at the bio-bank of XXX under standardized quality and safety conditions (for an unlimited time period) and will be made available to researchers for research purposes upon request. They will be protected against unauthorized access using the latest technology.
(c) The review of a research project by an ethics committee is a prerequisite for the use of biomaterials and data for a specific medical research project. The ethics committee examines the ethical and legal aspects of the proposed research project.

Who has Access to Your Biomaterials and Data, and How are they Protected?

(a) All of the personal data that can directly identify you (name, date of birth, address, etc.) will be replaced by a code immediately after they are obtained (i.e., rendered pseudonymous, encrypted). Afterwards, the data will be newly encoded and stored. According to current knowhow, such double coding is the best way to exclude your identification by unauthorized persons. The biomaterials and data will be provided in this form only for research purposes.
(b) Data which identify you directly will remain at the institution at which they were collected under the responsibility of the head of the study. They will be stored separately from the biomaterials and medical data. Access to such data will only be granted in order to add further or missing medical data from your hospital records if necessary, or to contact you again if you have consented to this (please see clause 10 below). No transfer of personal data to researchers or other unauthorized third parties, such as insurance companies or employers, will occur.
(c) Following an appropriate application, the double encrypted biomaterials and medical data can be passed on to other universities, research institutes, or research companies—if necessary abroad—under pre-established criteria for medical research. Under certain circumstances, the data may be linked with medical data sets in other databases, provided that the necessary legal require-

ments are met. Under certain circumstances, the data may be disclosed to research projects abroad with potentially lower standards of data protection.

(d) Biomaterials and data which have been passed on to third parties may only be used for the proposed research purpose and will not be transferred by the recipient for other purposes.

(e) Scientific results will be published in an anonymous form only, i.e. in a form that does not allow any conclusions to be drawn about your person.

Will You Obtain Any Financial Advantage from the Use of Your Biomaterials and Data?

You will receive no remuneration for the use of your biomaterials and data. If any commercial benefit is gained from the research, you will not partake in this.

Upon donation of your biomaterials, they become the property of the XXX. Furthermore, in providing your consent, you are authorizing the use of your data by the XXX. You have the right to amend wrongly stored or processed data at any time.

Will We Contact you Again?

It may be useful to contact you again at a later date to request additional information, such as additional historical data, and/or biomaterials. In addition, when re-contacting you we may request your consent, for example, to compare your data with those in other databases or to provide you/your physician/medical investigator/GP with feedback on results of relevance to your health (please see clause 5 above), or results of relevance to the study. Contact will be made by the head of the study—or by a person delegated by the head of the study—via telephone, letter, or e-mail.

If you do not wish to be contacted again, please tick the appropriate box on the consent form.

What Does Your Right to Withdraw Your Consent Mean?

You may withdraw your consent to the use of your biomaterials and data at any time without stating any reason and without incurring any adverse personal consequences. If you revoke your consent, you will be asked to decide whether your biomaterials should be destroyed and the associated data deleted, or whether they may be used in an anonymous form for further research projects. However, once all reference between you personally and the biomaterials and the remaining data have been deleted, their destruction is no longer possible. In addition, data from previously performed analyses can no longer be removed. Despite revocation, a later attribution of the genetic material to you personally via other sources can never be excluded.

To revoke your consent, please contact: XXX

Insurance Cover

For harm arising as part of the investigation, which may be caused by the principal investigator or other personnel at the XXX during the course of their professional duties, we have arranged appropriate insurance cover through our public liability insurance policy with the company XXX.

For any damage occurring en route to a study investigation, an accident insurance policy is also available.

Thank you very much for your interest in our research!

Declaration of consent
Patient/test person: _____
(Name, first name)
Date of birth: _____

I agree to donate my biomaterials and data, as described in the information document, to the XXX, and to their use for medical research purposes. Under certain circumstances, this also applies to their transfer for the purposes of research projects abroad where potentially lower levels of data protection are in place. I transfer the ownership of my biomaterials to the XXX.

I have read the information sheet and have had the opportunity to ask questions.

I am aware that my participation is voluntary and that I can withdraw my consent at any time and for any reason, and that such withdrawal will have no disadvantageous consequences for me.

I agree that I may be contacted again at a later date (if you do not wish to be contacted again, please tick "no" as appropriate):

- For the purpose of obtaining further information/biomaterials; ☐ **no**
- For the purpose of obtaining consent for comparisons with other databases; ☐ **no**
- For the purpose of feedback regarding results of possible relevance to my health ☐ **no**
- For the purpose of feedback concerning results of relevance for the study ☐ **no**
- For the purpose of feedback concerning secondary findings of relevance to my health as follows:
  (a) I agree that I will be informed about medically-significant findings not related to the aim of the present study for which a targeted therapy or preventive strategy is currently available. ☐ **no**
  (b) I agree that I will be informed about medically-significant findings not related to the aim of the present study for which there is no treatment or preventive strategy currently available, but they may be important for my life planning. ☐ **no**

This feedback should be provided by the establishment, in which my biomaterials/data were obtained, or by the following specialist (please specify if applicable)
.....
Name and address of the responsible study leader:
XXX

Privacy statement:
I hereby agree that the XXX—as described in the information documentation

- May collect and store my personal data;
- May gather further details about my health from my medical records;
- May pseudoanonymize (i.e., encrypt) my data and biomaterials

The biomaterials and data may be used for an unlimited time period for medical research projects.

They may be provided in a pseudonymized form to universities, research institutes, and research companies—if necessary abroad—for the purpose of medical research.

I have been informed that I may revoke the consent I have given to the XXX at any time and for any reason. In the event that I revoke my consent, the remaining biomaterials and the data collected from me will be destroyed, erased, or made anonymous if I so request. Data from already completed analyses cannot be removed.

I have received a copy of both the consent form and the patient/test person information. The original will remain at the XXX.

_____
Patient's/test person's name in capital letters

_____
Place, date (to be completed by patient/test person), patient's/test person's signature
I have conducted the informed consent briefing and obtained the patient's/test person's consent.

_____
Name of specialist in capital letters

_____
Place, date, signature of specialist

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HIV as the Great Magnifier of Maladies: Challenges for Prevention and Compassionate Care

14

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Abstract

Many persons in the world do not believe that there is still a human immunodeficiency virus (HIV) pandemic and that epidemics of acquired immune deficiency syndrome (AIDS), HIV stigma, and AIDSism still exist. However, throughout the world there is evidence of an HIV pandemic: 36.9 million persons are living with HIV despite the fact that HIV and AIDS are entirely preventable. Although HIV is easy to diagnose with rapid HIV testing, 19 million or 54% of persons with HIV are unaware that they are infected. Once diagnosed, persons who were previously unaware of the HIV infection can be referred for medical care and treatment with antiretroviral medication that will enable persons with HIV to live relatively healthy lives. Psychiatric factors play an important role in the transmission of HIV. Psychiatric illnesses are vectors of HIV, and psychiatrists can prevent transmission and decrease suffering, morbidity, and mortality in persons with HIV. If lupus, multiple sclerosis, malaria, Lyme disease, and syphilis can be thought of as "The Great Masqueraders of Maladies" because

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many of their symptoms are similar to those of other illnesses, HIV/AIDS is "The Great Magnifier of Maladies" of both illness and aspects of health care. HIV magnifies disparities, stigma, and discrimination in health care and leads to both transmission and lack of access to care. An integrated approach to medical and mental health is needed to prevent transmission of HIV and improve care for persons affected by and infected with HIV.

14.1 Introduction

Psychiatric factors play a significant role in the perpetuation of the human immunodeficiency virus (HIV) pandemic. In just under four decades, great progress in HIV medical care and research has transformed acquired immune deficiency syndrome (AIDS) from a rapidly fatal illness of unknown cause into a chronic, manageable illness.

These vast strides have yet to be matched in prevention of HIV transmission, in achieving full viral suppression through adherence to medical care, or in the psychiatric care of persons with HIV/AIDS. Although AIDS is an entirely preventable infectious illness, HIV transmission continues throughout the world. Psychiatrists are in a unique position to prevent transmission of HIV, encourage early testing and access to care, and provide compassionate comprehensive care. Transmission of HIV is fueled by the triple stigma of mental illness, HIV, and its modes of transmission, as well as by discrimination, criminalization, and risky behaviors. "Globally, new infections among key populations and their sexual partners accounted for 36% of all new HIV infections in 2015. Criminalization and stigmatization of same-sex relationships, cross-dressing, sex work and drug possession and use block access to HIV prevention services and increases risky behaviours. Homophobia drives gay men and other men who have sex with men away from HIV testing and HIV prevention activities and is associated with lower adherence to treatment. Women in key populations face specific challenges and barriers, including violence and violations of their human rights" [1].

A comprehensive biopsychosocial approach to sexual health and mental health and diminution of stigma are essential to both HIV prevention and HIV care [2–5]. Integration of psychiatric care into the prevention and treatment of HIV entails the use of a biopsychosocial approach to care that maintains a view of each individual living with HIV as a member of a family, community, and society who deserves to be treated with dignity and compassion [2, 4]. This chapter provides an update on HIV psychiatry, introduces the concept of HIV/AIDS as "The Great Magnifier of Maladies" [3], and sets the stage for an understanding of how integrated care can prevent transmission of HIV and decrease morbidity and mortality in persons with HIV.

Persons with HIV are living longer and healthier lives as a result of medical care and advances in research and antiretroviral therapy. Some of the medical advances

as well as concomitant changes in society have catalyzed research and led to vast improvements in care. The advocacy and activism of gay men and their clinicians from the outset of the epidemic resulted in many of these changes. In some areas of the world, advocates' voices have been heard and have led to diminution of HIV stigma and discrimination. However, HIV stigma, discrimination, and criminalization still exist throughout the world. Much work is still needed with a greater emphasis on sexual health [5], harm reduction, competent and compassionate care for persons with HIV, and for persons with the psychiatric disorders that may serve as vectors for HIV transmission. Similarly, more work is needed to diminish stigma and discrimination against persons with psychiatric disorders [6], including substance use disorders [7]. Another area that needs further attention is that of health education for illness prevention. Education about sexual health and prevention of illnesses including HIV can begin in elementary school and continue through high school, college, medical school, residency, and fellowship training. Despite advances in medical care and advocacy for persons with HIV in the United States and throughout the world, some men, women, and children with HIV and acquired immune deficiency syndrome (AIDS) are unable to benefit from medical progress. Inadequate access to HIV care is multifactorial and multidimensional and includes economic, social, cultural, political, societal, and psychiatric obstacles.

UNAIDS [8] data from 160 countries report 36.7 million people living with HIV in the world as of 2015. Of these, 17 million persons, or fewer than half, are on antiretroviral therapy. Regional disparities are startling and reflect multiple determinants. Treatment coverage in the Asia and Pacific region is 41%, in Eastern Europe and Central Asia is 21%, in Western and Central Africa is 28%, and in North Africa is 17%. Of concern is that the number of new infections in persons aged 15 years and over in the underserved areas of Eastern Europe and Central Asia disproportionally increased by 57% from 2010 to 2015, while it remained stable or decreased elsewhere in the world [8].

Psychiatric disorders and distress play a significant role in the exposure to and transmission of HIV [9–13]. They are relevant to prevention, clinical care, and adherence throughout every aspect of illness from the initial risk behavior to death. They result in considerable suffering from diagnosis to end-stage illness [14]. The prevalence of HIV in persons with untreated psychiatric illness may be 10–20 times that of the general population [11]. Furthermore, many of the changes in the prevention and treatment of HIV have significant psychological implications. Below is a list of facts, changes, and advances in the prevention of HIV and in the care of persons with HIV that have salience to HIV psychiatry. These facts are of significance in substantiating the need for an integrated approach to the care of persons with HIV and AIDS. Stigma, discrimination, and fear in conjunction with denial, omnipotence, and lack of awareness complicate and perpetuate the HIV pandemic. The creation of a supportive, nurturing, nonjudgmental healthcare environment can help to diminish the stigma of HIV and mental illness and can provide comprehensive and compassionate care for persons with HIV.

In this chapter, we try to eliminate words that stigmatize and dehumanize both medical illness and medical care and present an evidence-based approach to the prevention of HIV transmission and the care of persons with HIV and AIDS.

14.2 HIV/AIDS: The Great Magnifier of Maladies: Is Entirely Preventable

If lupus, multiple sclerosis, malaria, Lyme disease, and syphilis are "The Great Masqueraders" because many of their symptoms are similar to those of other illnesses, HIV/AIDS can be thought of as "The Great Magnifier of Maladies"—of symptoms, illnesses, and aspects of health care. HIV magnifies disparities, stigma, and discrimination in health care and leads to both transmission and lack of access to care. As long as HIV is stigmatized, persons who have risk behaviors or suspect that they have HIV will fear discrimination or ostracism and may delay or avoid getting tested, being diagnosed, disclosing HIV to potential partners, or accessing care. Hence there are extremely negative aspects of HIV as "the Great Magnifier of Maladies." Ironically, there are positive aspects of HIV as the Great Magnifier of Maladies. The HIV pandemic and its advocates forced topics of addiction, sexuality, gender identity, and death to "come out of the closet," and led to the need for integration of medical and mental health care and contributed to the development and application of bioethical principles such as patient self-determination, advance directives, and care planning.

14.2.1 Negative Aspects of HIV as Magnifier

Healthcare disparities in HIV occur across many dimensions including gender, age, race/ethnicity, sexual orientation, socioeconomic status, geographic location, immigration status, and disability status. The negative aspects of HIV as a magnifier are:

- Stigma and discrimination
  - Ageism
  - Misogyny
  - Racism
  - Addictophobia
  - Homophobia
  - Mental illness stigma
  - AIDSism
- Avoidance of getting tested
- Avoidance of access to care
- Treatment refusal
- Medical and psychiatric multimorbidities in persons with HIV

- The much higher frequency of HIV infection in people with psychiatric illness
- Nondisclosure of HIV infection for fear of rejection or ostracism
- Criminalization of HIV, of risk behaviors, and of persons at potential risk

14.2.2 Positive Aspects of HIV as Magnifier

Great strides have been made in moving persons living with HIV along the HIV care continuum and provision of integrated mental health, and psychosocial outreach services have met the critical need for care delivery to individuals with multiple diagnoses [15]. HIV has magnified:

- Need for a biopsychosociocultural approach to care to:
  - Prevent transmission
  - Ensure comprehensive assessment and diagnosis
  - Access treatment
  - Improve and enhance doctor-patient communication and care
  - Improve doctor and patient satisfaction
- Need for integration of mental health care into HIV medical care
- Need for compassionate, empathic care
- Need for routine HIV testing as part of health care and prevention of HIV
- Need for a comprehensive approach to multiorgan and multisystem involvement of HIV
- Need for the skills of every health discipline and medical subspecialty
- Need for awareness of bioethical issues
- Need for an understanding that HIV transmission is entirely preventable through risk reduction, harm reduction, pre-exposure and postexposure prophylaxis, behavior change, and integrated medical and psychiatric care and antiretroviral medication

14.2.3 Facts, Changes, and Advances in HIV Prevention and Care

1. An estimated 36.7 million people are living worldwide with HIV [16].
2. An estimated 1.2 million persons in the United States are living with HIV including 156,300 (1 in 8 persons or 12.8%) who are unaware of their infection [17], thus indicating that routine opt-out testing is critically important for HIV prevention and early intervention and treatment.
3. HIV continues to magnify healthcare disparities in the United States and throughout the world. The global pandemic is characterized by a compilation of distinct regional epidemics, with varying geographic impact across age groups, among men, women, men who have sex with men, and persons who inject drugs. Strathdee and Beyrer documented ways to address the recent outbreak of HIV in rural Indiana catalyzed by the heroin epidemic [7].

4. While there are now far fewer perinatal transmissions in areas of the world with access to perinatal care and antiretroviral therapy (ART), there are many more problems for children with perinatally acquired HIV transitioning to adolescence and adulthood. These include the attendant problems of nonadherence and early demise or the issues surrounding pregnancy, labor, and delivery for newborn girls who were infected perinatally and are now emerging into womanhood and motherhood [18].
5. Severe multimorbid medical illnesses are prevalent in persons with access to appropriate HIV medical care, and these include severe illnesses requiring complex treatments such as hepatitis C, cancers related and unrelated to HIV, renal disease, diabetes mellitus, and cardiovascular illness including coronary artery disease.
6. There is evidence that early intervention can prevent the central nervous system (CNS) from becoming an independent reservoir for HIV and ultimately prevent HIV-associated neurocognitive disorders such as HIV-associated dementia. Starting treatment as soon as HIV is diagnosed, regardless of clinical stage, can prevent the development of independent HIV reservoirs in the brain and thus protect against HIV-associated dementia [19, 20].
7. At present, one of the leading causes of death for persons with HIV is hepatitis C virus (HCV)-related liver disease. Thus, the treatment of persons with HIV/HCV coinfection has become a major concern [21]. This of course involves understanding how to motivate people with HIV infection to get tested for HCV and to accept treatment. Issues of depression and cognitive impairment are magnified by the affinity of both viruses for the brain. Adherence to two regimens is even harder than to one. The availability of better tolerated and less complex treatments for HCV has markedly and dramatically improved the care of persons co-infected with HIV and HCV. The elimination of interferon alpha has led to far better adherence and acceptance of care. Until 2011, there were only two drugs approved for treatment of HCV, and these were interferon alpha (parenterally administered) and ribavirin. To effectively cure HCV, they were taken for 48–52 weeks and caused severe side effects of extreme fatigue, depression, and, in some individuals, suicidal ideation. Subsequently several medicines have been developed and have replaced these treatments. Current treatments are now once-daily, all-oral, interferon-, and ribavirin-free treatment for adults with genotype 1 HCV infection. Within 12 weeks, individuals with HIV/HCV coinfection can be cured of hepatitis C. The side effects are far less complex than those with the earlier regimen. The need for integrated medical and psychiatric care is intensified in co-infected individuals.
8. One of the most salient advances in the United States has been the recommendation for routine HIV screening of all adolescents, adults, and pregnant women. The recommendation is for routine HIV testing in medical settings available to everyone from age 13 to 64 and to all persons at substantial risk at even younger or older ages [22–24].
9. Biomedical advances in prevention include pre-exposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) in combination with other prevention

measures. PrEP and PEP can prevent HIV transmission from an HIV-positive to an HIV-negative individual [25, 26]. In 2012, the FDA approved the first drug treatment for PrEP. Occupational exposure is no longer the only indication for postexposure prophylaxis. PEP can be used for sexual exposures such as coerced sexual encounters, unanticipated unprotected sexual encounters, or parenteral exposures such as intravenous drug injection with contaminated needles and drug paraphernalia [26, 27].

10. Following an unanticipated, unplanned, or forced unsafe sexual encounter, any person can be encouraged to take tenofovir and emtricitabine for non-occupational postexposure prophylaxis or nPEP [27]. One of the authors (MAC) had a patient who was HIV-negative and unable to access nPEP after unsafe sex until 74 h after his exposure to HIV and developed an acute antiretroviral syndrome within 10 days after exposure. His infection could have been prevented with nPEP. Occupational exposure can be addressed through the use of occupational postexposure prophylaxis or oPEP [28].
11. Treatment as prevention (TasP) is a proven approach to prevent new infections by suppression of viral load among persons living with HIV such that they become virtually "noninfectious." In contrast to primary prevention among persons who are HIV-uninfected, via condoms, microbicides, PrEP, and PEP, secondary prevention among persons living with HIV infection via TasP is a complementary approach. Widespread scale-up of ART allowing for population-level reductions in circulating HIV is largely responsible for the 35 percent reduction in annual new global HIV cases since 2000 [26, 29].
12. Simple, rapid HIV testing is widely available around the world [1].
13. Aging with HIV has become more complex, and research is underway to explore aspects of successful aging with HIV [30, 31].
14. The introduction of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5)* in 2013 introduced alternative categorizations and definitions of diagnoses frequently used in HIV psychiatry. These alternative categorizations include the reclassification of neurocognitive disorders and bereavement [32].
15. The area of adherence research continues to advance, with new evidence about expanding adherence beyond ART to also include adherence to clinical care [33].
16. AIDSism [34], stigma, and discrimination [35–39], as well as criminalization of drug abuse, sex work, and behaviors that may unintentionally expose individuals to HIV, all serve to complicate and perpetuate the HIV pandemic [40, 41].
17. At the 21st International AIDS Conference in Durban, South Africa, in July 2016, there was also "good news and bad news" as reported in the *Journal of the American Medical Association* [42]. Steinbrook states "Overshadowed by the Zika epidemic, concerns about terrorism and security, and the US presidential election, the global HIV/AIDS pandemic persists, with 1.9 million new HIV infections and 1.1 million deaths worldwide in 2015" [16, 42]. This article also substantiated that early and ongoing treatment was necessary to attain the goals set by the World Health Organization: "Recently updated World Health

Organization guidelines recommend the provision of "lifelong [antiretroviral therapy] to all children, adolescents and adults, including all pregnant and breastfeeding women living with HIV, regardless of CD4 cell count" [43]. "Many nations, however, have yet to adopt these guidelines or fully implement them. In 2016, an estimated 18.2 million people living with HIV were receiving antiretroviral therapy [16], yet only an estimated 60% of all persons infected with HIV knew their HIV status, 46% of people living with HIV were receiving antiretroviral treatment, and 38% of people with HIV were virally suppressed, and thus less infectious to others [1]. These percentages lag far behind the Joint United National Programme on HIV/AIDS (UNAIDS) 90-90-90 targets to be reached by 2020: that 90% of all people living with HIV know their HIV status, 90% of those who know their status receive sustained antiretroviral therapy, and 90% of those receiving treatment be virally suppressed. The recommended initial regimens in the United States and other Western nations remain expensive and are not the regimens that many people in low- and middle-income nations typically receive" [42].

18. Education about medical, mental health, sexual health, and illness prevention along with parenting education to prevent child abuse and sexual abuse as well as intimate partner violence can be instrumental in primary prevention of HIV throughout the world. Initiation or continuation of education in primary or elementary school, high school, college, medical school, and psychiatric residency and fellowship training is a key to developing a generation of clinicians who are prepared to meet the challenges of HIV prevention until a vaccine and cure are available. Education has been identified as one of the prevention gaps: "Two-thirds of young people do not have correct and comprehensive knowledge of HIV. Condom use is much too low across all population groups at higher risk of infection. 43% of countries with documented injecting drug use do not have needle-syringe programmes in place" [1]. Programs have been developed for comprehensive HIV education for psychiatric trainees and clinicians [44, 45].
19. Unique opportunities for HIV prevention exist in many settings not usually thought of as in need of significant attention. These include psychiatric facilities such as outreach, day treatment, drug treatment, and rehabilitation facilities; geriatric facilities including chronic care facilities and assisted living; adolescent psychiatry facilities as well as adolescent pediatric practices; and programs for homeless and marginally housed individuals. One of the most important and unique opportunities is that of correctional facilities [46].
20. An integrated approach to care can improve adherence to medical treatment.

14.2.4 The Syndemic of Psychiatric Disorders, Violence, PTSD, Trauma, Suicide, and HIV

Understanding the interplay between HIV and psychiatric illness leads to improved insight into how integration of care allows persons with HIV and AIDS to better cope with their illness, live their lives to the fullest extent, and minimize pain and

suffering for them and their loved ones. The personal and societal costs to health, productivity, fitness, careers, partners, spouses, parents, and children take an enormous toll in suffering. Related to this is the suffering of the loved ones and orphans left behind by AIDS. The tragedy of preventable death in young and productive individuals is heightened by the multiplicity of infections, severity of illness, and the multisystem and multiorgan involvement of this devastating illness. The illness is complicated by the psychological reactions to and psychiatric manifestations of HIV infection. Psychiatric disorders can accelerate the spread of the virus by creating barriers to risk reduction including risky sexual behaviors and sharing of needles in persons who inject drugs.

Some persons with HIV may have no psychiatric disorder while others may have one or more of the psychiatric disorder described in the DSM 5 [32]. A brief overview of the psychiatric disorders that have most relevance to transmission of HIV and adherence to care will serve to clarify the need for the integration of psychiatric and medical care for persons with HIV. The relevant diagnoses include addictive disorders, trauma-related disorders, depressive disorders, psychotic disorders, and neurocognitive disorders.

14.2.4.1 Substance Use Disorders

Substance use disorders, including nicotine, alcohol, and cannabis use are prevalent among people living with HIV [47, 48]. Such disorders often result in multidimensional obstacles to risk reduction and adherence to care. These include obvious barriers to prevention of transmission such as sharing of drug paraphernalia and subtle barriers such as, for example, inability to adhere to perinatal antiretroviral therapy because of intoxication, withdrawal, and drug-seeking behaviors. Furthermore, intoxication and disinhibition associated with alcohol and drug use and exchange of sex for drugs result in risky sexual behaviors and difficulty with adherence to complex medical regimens. Cognitive disorders associated with alcohol and other drugs can also impair judgment and ability to adhere to care. Active substance use may interfere with adherence to prevention strategies, to medical care, and to the care of children infected with or affected by the virus. Mortality trends indicate an increase in death from end-stage liver disease as a result of comorbid infection with HIV and HCV in persons who inject drugs.

The relationship between HIV disease progression, ART adherence, substance use, and physical comorbidities is complex and multidirectional. Suboptimal ART, for example, has been shown to increase the risk of tobacco, alcohol, cannabis, methamphetamine, opiate, and polysubstance use [47, 48]. Other risk factors for these conditions include younger age, male gender, criminal justice involvement, unstable housing, and unprotected sex. On the other hand, high levels of alcohol use have significant negative effects on CD4 counts, ART adherence, viral load, combined index of 5-year mortality risk, and liver fibrosis [49]. Independent of their ART adherence, people with concurrent HIV and alcohol dependence are nine times more likely to have CD4 cell count $\leq 200/mm^3$ [50]. Both heavy drinking and frequent binge drinking are associated with worse retention in HIV care [51]. Cocaine use, a common comorbidity among some people living with HIV, is associated with

a nearly twofold increase in odds of depression, and a dose-response relationship between increasing duration of cocaine use and depression has been observed [52]. On the other hand, anxiety disorders are associated with needle-sharing behaviors among cocaine users [53]. Substance use has also been shown to decrease adherence to psychiatric treatment. For instance, adherence among cognitive behavioral therapy (CBT) participants has been shown to be significantly lower among those who use cocaine (45.0%) compared to those who do not (72.3%) [54]. Concurrent HIV infection and substance use can also exacerbate patients' other medical and psychiatric illnesses. Comorbid HIV and methamphetamine use, for example, increase the likelihood of neural injury in the brain [55].

14.2.4.2 Post-traumatic Stress Disorder

A trauma-related disorder, post-traumatic stress disorder (PTSD), is highly prevalent in persons with HIV infection and increases morbidity risk [56–59]. It is often overlooked in persons with HIV/AIDS because it may be overshadowed by other psychiatric diagnoses [59]. HIV infection and PTSD share common risk factors. For example, intimate partner violence and a history of childhood physical trauma or childhood sexual trauma all increase the risk of HIV infection as well as for PTSD. Gender-based violence significantly increases the risk of HIV and other sexually transmitted illnesses among women and girls who use drugs [60]. Violence and victimization are intertwined with poor decision-making, increased risk-taking, and negative health consequences, particularly in the context of substance abuse among women with HIV [61]. The severity of HIV-related PTSD symptoms is associated with a greater number of HIV-related physical symptoms, extensive history of pre-HIV trauma, decreased social support, increased perception of stigma, and negative life events. Moreover, PTSD is often multimorbid with other psychiatric and medical disorders, pain, and depressive symptoms. PTSD can lead to risky behaviors and decrease harm avoidance as a result of dissociative phenomena, isolation of affect, and a sense of a foreshortened future. Persons with PTSD as a result of early childhood trauma may have difficulty protecting themselves from harm or may unconsciously seek to reenact their early trauma in later life.

PTSD is associated with nonadherence to risk reduction and medical care [56, 57]. The diagnosis of PTSD is further complicated by repression or retrograde amnesia for traumatic events and difficulties in forming trusting relationships and disclosing trauma if it is recalled [59]. In persons with HIV infection, there is a high incidence of early childhood and other trauma with consequent PTSD, substance use disorders, and other psychiatric disorders [57, 59]. Violence may include perpetuation of early trauma in persons with PTSD who may unconsciously seek to master early childhood trauma in adult relationships.

Synergistic epidemics, or syndemics, were first described by Singer [62] and subsequently associated with nonadherence to HIV care and poorer outcomes [56, 63]. Syndemics of triple diagnoses include co-occurring substance use disorder, other psychiatric disorders, and HIV [61]. The number of syndemic conditions is incrementally associated with more types of sexually risky behaviors among persons with or at risk for HIV. Women with five syndemic conditions (childhood sexual abuse, depression, substance use, violence, and financial hardship) have reported

72% more types of risk behaviors over 6 months, as compared to women without any syndemic conditions [64]. Similarly, the association of nonadherence with the syndemic of substance use, violence, and AIDS (the SAVA syndemic) has been documented [63, 65].

Mental health problems among women with HIV and a history of gender-based violence include depressive, anxiety, traumatic stress symptoms, and suicidal thoughts [66]. Stressful/traumatic life events have been shown to be associated with increased suicidal ideation among adults with comorbid HIV and depression [67]. State anger (the intensity of anger as an emotional state, as compared to trait anger) is significantly associated with suicidal ideation [68]. Physical, sexual, and emotional violence against women living with HIV is widely prevalent and perpetrated to a large degree by untested husbands accusing their wives of marital infidelity following a positive HIV test result. Among women, a high likelihood of potentially traumatic events has been associated with depression and inconsistent condom use [69].

14.2.4.3 Psychotic Disorders, Depressive Disorders, and Neurocognitive Disorders

Other psychiatric disorders such as psychotic disorders, depressive disorders, and neurocognitive disorders may be associated with HIV transmission and nonadherence to care. Risky behavior and nonadherence may result from poor judgment with regard to sexual partner choice, lack of attention to barrier contraception, and, at times, hypersexuality, disinhibition, and multiple sexual partners. When persons are psychotic, they may seek sexual contact or may become victims of sexual predators as a result of efforts to obtain love, affection, and attention or in attempting to relieve the anguish of psychosis.

14.2.4.4 Depressive Disorders and Bipolar Disorder

On the other hand, depressive disorders can lead to apathy and a negative self-image that can lead to vulnerability, self-neglect, and unsafe sex practices. High anxiety or depression scores are associated with lower levels of condom use and sexual concurrency [70]. High rates of depressive symptoms are reported in women living with HIV compared to men [71, 72]. Factors that are associated with depression in the HIV-positive population include disability, unemployment, increased age, discrimination at hospital, physical pain, having fewer years of schooling, being bullied for taking medications, and CD4 <300 cells/mm^3 [72, 73]. Racial/ethnic minorities have been shown to be less likely to initiate antidepressants and receive evidence-based treatment [72].

Numerous studies have shown the negative impact of stigma and discrimination on health-related outcomes among people living with HIV. HIV-related stigma and discrimination are associated with higher rates of depression, lower social support, lower levels of adherence to antiretroviral medications, and lower access to and usage of health and social services [74]. Major depressive disorder makes individuals more vulnerable to HIV because of its impact on behavior and adherence to care. It is associated with more rapid illness progression and higher morbidity and mortality rates [75]. A considerable proportion of people with concurrent HIV and

major depressive disorder experience suicidal ideation and attempts [68]. Some of the risk factors for suicidal ideation include female sex, depression, lower CD4 levels, being single, and presence of opportunistic infections [76].

Youth with perinatal HIV who had depression or disruptive behavior symptoms had greater odds of nonadherence with antiretroviral treatment at later visits. Youth with concomitant HIV and attention deficit hyperactivity disorder (ADHD) have had greater odds of unsuppressed viral load than peers without ADHD symptoms at later visits but not at entry. Similarly, youth with anxiety have had lower odds of unsuppressed viral load compared to youth without anxiety [77]. Lifestyle significantly mediates the relationship between depression and antiretroviral therapy adherence behavior [78]. Mania, due either to bipolar disorder, HIV-related infections, or prescribed or illicit drugs, can result in hypersexuality, poor impulse control, and impaired judgment, all of which increase the risk for HIV infection.

14.2.4.5 HIV-Associated Neurocognitive Disorder (HAND)

A further complication is the occurrence of HIV-associated neurocognitive disorders (HAND), including asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and HIV-associated dementia (HAD). The prevalence of HIV-associated dementia has considerably diminished in prevalence in persons who have access and adherence to antiretroviral therapy. However, the prevalence of ANI and MND remains the same, although receiving treatment has been shown to postpone its development [79]. The significant predictors of HAND include duration of illness, detectable viral load, CD4 count, education, stopping medication, and severity of illness [80].

Risk factors for HAND include female sex, higher age, higher HIV viral titers, lower socioeconomic group, substance abuse, and iron-deficiency anemia. HAD is generally observed in seropositive individuals who have a high viral load and CD4 cells at an all-time level below 200/mm^3 and may be a contributing factor to suicide in AIDS patients [75]. Cognitive impairment can lead to poor judgment in sexual partner choice, unsafe sex, and disinhibition.

14.2.4.6 Delirium

Hospitalized patients with AIDS have been shown to have higher rates of delirium compared to those without AIDS [75]. This can contribute to longer hospital stays, more complicated course of treatment, and worse outcomes among this population.

14.2.4.7 Suicide and HIV

Living with HIV and AIDS is arduous and can become intolerable. Even after more effective antiretroviral treatments were developed and the mortality of HIV was significantly reduced in countries and regions with access to competent HIV medical care and antiretroviral therapy, psychological and medical multimorbidities continue to create great distress [81, 82]. Psychosocial issues such as stigma and discrimination compound the distress experienced by persons with HIV and contribute to not getting HIV tested, not disclosing serostatus, and reluctance to adhere to medical care leading to inadequacy of viral suppression even with access to care. Suicide is always multifactorial in causation and requires a multidimensional approach for its

prevention. Suicide is preventable even when hopelessness is tangible and overwhelming. By identifying the treatable predisposing psychosocial factors and reducing distress, clinicians will be able to anchor the ambivalent suicidal patient and prevent deliberate self-harm. Suicidality is treatable with crisis intervention, networking, and psychiatric care. The recognition and treatment of suicidality can prevent suicide [83].

HIV seropositivity and AIDS continue to be independent risk factors for suicide. HIV-positive persons with multimorbid psychiatric and medical illnesses are at an even higher risk of dying by suicide than are those without these complications. Aging with HIV is another risk factor for suicide [84, 85]. Although completed suicides in the general population are statistically relatively rare events, the majority of persons with HIV frequently experience thoughts of suicide and commonly engage in suicidal behavior, and a substantial number end their lives by suicide [82].

Predisposing factors for suicide in persons with HIV include gender (female), course of illness with a bimodal distribution (at the time of diagnosis with HIV and at end-stage illness), symptomatic medical and psychiatric multimorbidities, physical incapacity causing distress, history of childhood trauma, past suicide attempts, hopelessness, family history of suicide, bereavement, anniversary reactions, poor social support, decreased social integration, poor family relations, unemployment, unstable housing, a detectable viral load, stressful life events, and access to means. Protective factors include positive reappraisal coping skills, treatment adherence, increasing social support, feelings of responsibility toward family, reporting reasons for living, religious considerations, higher emotional expression and depth processing, experiential involvement, self-esteem enhancement, and secure attachments. With support, networking, establishing a therapeutic alliance, opportunities for reparative emotional experiences and earned secure attachments, conflict resolution, palliative care, adequate medical treatment, and alleviation of psychological distress, persons with HIV may be open to resolution of a suicidal crisis and reconstruction of new relational and coping strategies. By identifying protective and risk factors for suicide, clinicians will be better equipped and cognizant of those who are at risk. Timely application of psychotherapeutic, pharmacologic, and psychosocial interventions in person with HIV can treat suicidality and may prevent death by suicide [83].

14.2.5 Stigma

HIV-related stigma has significant effects on health-related outcomes in persons with HIV including higher rates of depression [86, 87] and suicide, lower social support, lower levels of adherence to antiretroviral therapy, lower CD4 cell counts, and lower access to and utilization of health and social services [74]. Due to widespread stigmatization and internalization of negative social signals, persons living with HIV are exposed to social isolation and psychosocial traumas [88]. Social stigma affects disclosure, linkage, and continuity in care in the HIV treatment cascade. Stereotypes and prejudicial attitudes among inmates about HIV/AIDS affect decisions about disclosure to one another in correctional facilities [46, 89]. In order

to effectively link persons who inject drugs to HIV care, the role of stigma and different clinician and patient perspectives need to be acknowledged and addressed [90]. In the caregiver context, lack of social support has been the strongest predictor of poor patient mental health and is largely determined by caregivers' stigma toward HIV/AIDS [91]. Stigma against persons living with HIV poses a major barrier to both PrEP access and uptake among adolescents and young adults [92].

14.2.6 The Role of Psychiatrists in the Prevention and Care of Persons with HIV/AIDS

Psychiatrists and other mental health clinicians can have a major impact on the prevention of HIV transmission and the compassionate and comprehensive care of persons with HIV. Psychiatrists can play direct and indirect roles in every level of prevention and in any psychiatric setting.

14.2.6.1 HIV Prevention: Unique Role of the Psychiatrist

The psychiatrist can ensure that every patient from the age of 13 (or at any age if there is evidence of substantial HIV risk) has HIV testing as part of routine initial evaluation. This is especially important on inpatient psychiatric units, drug treatment programs, outreach programs, and programs for homeless or marginally housed individuals. Routine testing for hepatitis C is also recommended since this is now relatively easily curable and worsens HIV outcomes.

Since all psychiatrists routinely take sexual histories as well as histories of substance use and addiction, psychiatrists are in a unique position to recommend prevention measures where indicated. For persons who are in ongoing monogamous relationships that are serodiscordant, the psychiatrist can refer the HIV-positive individual to an HIV specialist for care and treatment with antiretroviral therapy and can provide a referral for the HIV-negative partner to be evaluated for the ongoing use of PrEP as part of a comprehensive program of prevention including barrier contraception.

HIV prevention measures for psychiatrists include:

- Routine testing for HIV and HCV
- Taking sexual and substance use histories
- Assessing current risk behaviors
- Recommendations for treatment of alcohol and other drug use
- Recommendations and help for behavior change including psychotherapy, medications, motivational interviewing, and harm reduction
- Provision of visible bowls or boxes of condoms in clinic and office waiting rooms or hospital units
- Provision of educational materials for prevention

Recognition and treatment of psychiatric disorders that can be vectors of HIV:

- Substance use disorder (including alcohol, not just other drug or injection drug use)
- Post-traumatic stress disorder, recognition of intimate partner violence and other trauma and referral for appropriate care and crisis intervention
- Major depressive disorder
- Bipolar disorder
- HIV-associated neurocognitive disorder
- Psychotic disorder

Recommendations for special psychiatric settings and encounters with unknown or known HIV-negative individuals

- Emergency room encounters following coerced sex or rape should include careful history, testing for HIV and HCV, and referral for treatment with postexposure prophylaxis within 72 hours after exposure.
- Emergency room or other encounters following inadvertent or accidental sexual encounters (while intoxicated or with unknown partner) should include careful history, testing for HIV and HCV, and referral for PrEP within 72 hours after exposure.
- Rape kits should be equipped with starting doses of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) and referral for follow-up care and testing.

Linkage to ongoing psychiatric care and engagement in care are both important measures of HIV prevention. In addition, psychosomatic medicine psychiatrists and other psychiatrist can take the lead in organizing comprehensive and integrated approaches to care of persons with risk behaviors, mental illness, and HIV.

Psychiatric facilities such as methadone maintenance programs or drug treatment rehabilitation programs are ideal settings for both prevention and treatment. A methadone maintenance program where a patient visits every day to obtain a dose of methadone can also obtain antiretroviral therapy or HCV therapy under direct observation.

Recommendations for unique antiretroviral or antiviral treatment opportunities for HIV and or HCV:

- Drug treatment programs
- Day treatment programs
- Safe injection sites
- Inpatient psychiatry units
- Adolescent units
- Geriatric units
- Correctional facilities

Psychiatrists can prevent HIV and provide referrals to care and decrease suffering, morbidity, and mortality in persons with HIV/AIDS.

14.2.6.2 Integrated Care and Treatment

The high prevalence of psychiatric conditions in persons with HIV infection has resulted in closer clinical collaboration among primary care physicians, infectious disease specialists, and psychiatrists. While psychiatric disorders may be linked directly and indirectly to risk behaviors, HIV infection, or AIDS, persons with HIV may have no psychiatric disorder or any disorder described in the DSM 5. Alternatively, psychiatric disorders may be the first and, at times, the only manifestation of HIV infection. Early diagnosis of HIV can lead to the timely introduction of treatment with appropriate HIV medical care and ART and prevent the establishment of independent central nervous system reservoirs for HIV. The immediate introduction of postexposure prophylaxis in the non-occupational setting (nPEP) within 72 hours after HIV exposure may entirely prevent HIV infection as well as the establishment of independent reservoirs for HIV in the central nervous system. Psychiatric disorders may be a manifestation of an initial reaction to awareness of a diagnosis of HIV infection. Alternatively, psychopathology can be related to intrinsic involvement of the brain with HIV or opportunistic infections such as toxoplasmosis and cryptococcosis in persons who lack access to care or are nonadherent with care. In addition, antiretroviral therapies, treatments for opportunistic infections, and treatment for multimorbid illnesses, such as with chemotherapy for cancer, can have central nervous system side effects, including psychiatric symptoms.

In addition to the role of psychiatric disorders in the transmission of HIV, psychiatric factors also play a major role in the suffering endured by patients, their partners, families, and caregivers. If psychiatric disorders go untreated, persons with HIV may have difficulty adhering to medical care, attending appointments, and adhering to the complex medical treatments involved with care. Physicians and clinicians in every specialty may find themselves frustrated that patients are not adhering to appointments and are getting ill in the same ways that they did in the beginning of the pandemic, when few or no treatments were available and mortality was high. Now that perinatal HIV transmission can be prevented by antiretroviral protocols, even obstetricians may find themselves stymied when pregnant women do not adhere to prenatal care and to antiretroviral treatment. There is an ample body of evidence that psychiatric treatment can decrease transmission, diminish suffering, improve adherence, and decrease morbidity and mortality.

Persons with HIV have a high prevalence of multimorbid complex and severe medical and psychiatric illnesses with psychosocial and public health implications and consequences. Despite remarkable advances in the care of persons with HIV that have transformed AIDS from a rapidly fatal illness to a chronic manageable illness, the incidence of HIV in the United States has remained stable at about 50,000 new cases annually [25]. Missed HIV clinic visits are independently associated with all-cause mortality in persons with HIV [33]. Thus, communication, integration, and coordination of care are of special significance in order to improve adherence to risk reduction as well as medical care. Since HIV is associated with discrimination and stigma and also disproportionately affects vulnerable populations and magnifies healthcare disparities, providing compassionate, comprehensive, and coordinated care becomes even more significant.

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The Future of Psychoneuroimmunology: Promises and Challenges

15

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Abstract

This chapter aims to provide an overview of the burgeoning field of psychoneuroimmunology as it relates to psychiatric and neuropsychiatric disorders. It is a relatively young field, having come of age only recently, but the progress that has been made just in the past three decades has exceeded all expectations. It is fair to say that the field has opened up new horizons in our understanding of the complex interrelationships between the immune and nervous systems or as is otherwise referred to as the brain-immune interaction. Hitherto unknown biochemical pathways have been identified, and their complex interactions with

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neurotransmitters and immune mediators present opportunities for innovative research and identification of new targets for drug development. Biomarkers are being established that hold great promise for more precise diagnostic classification of psychiatric disorders but also understanding of the high comorbidity between specific psychiatric disease entities and a host of medical and neurological diseases. At the same time, immune biomarkers, neurotrophins, and antibodies enable prediction of response and understanding of treatment resistance. Imaging techniques of increasing sophistication hold great promise for visualization of aberrant connectivity and dysfunctional brain circuitry. The goal of practicing personalized psychiatry is now closer to becoming reality than ever before in the history of our specialty. The coauthors of this chapter have each contributed subsections commensurate with their individual expertise.

15.1 Introduction

Psychoneuroimmunology, or, as it has been more recently called, *immunopsychiatry*, has come of age. It has moved from a niche area of biological psychiatry and psychosomatics to an established mainstream research and translational area in mental health and clinical neuroscience [1]. Understanding the complex interactions between the nervous and immune systems with cognition, mood, and behavior has vastly increased our knowledge and understanding of mental disorders. We can now achieve a better translation of this knowledge into targeted therapeutic interventions aimed at improving the lives of many patients afflicted with psychiatric and neuropsychiatric disorders. At the same time, the complex comorbidity between psychiatric disorders, notably depressive and anxiety disorders, and cardiovascular, cerebrovascular, and neurological disorders can now be better understood, thanks to breakthroughs in psychoneuroimmunology [2–4]. It is appropriate to make the claim that psychoneuroimmunology represents the new frontier in psychiatry.

15.2 Scientific Advances, Promises, and Challenges

15.2.1 Stress and the Immune System

Activation of the immune system and associated inflammatory factors have been consistently identified in patients with cardiac pathology and in patients diagnosed with an affective disorder. Mental stress can act as a common instigator initiating the cascade of complex central and peripheral events that lead to sustained activation of the immune system resulting in a chronic pro-inflammatory status with its associated sequelae. The homeostatic challenge is recognized by the innate immune system that surveys the organism for threats by invaders. The inflammatory response aims to restore homeostasis and health, as long as inflammation is commensurate

with the threat and limited by anti-inflammatory responses. However, inflammation can persist and expand, both centrally and peripherally, especially in instances of chronic physical or mental illnesses that perpetuate the stressful condition. The relationship between stressful events and the onset of inflammation-related diseases, notably cardiovascular, neurologic, and immunologic, has been adequately documented in the literature.

The role of the immune system and interactions between the endocrine, neurotransmitter, and immune systems in affective disorders have opened up new avenues to pursue in psychiatric research. Exploration of a potential causal relationship between inflammation and depression has lent support to the contention that a bidirectional relationship is at play. Exogenously administered cytokines can induce a syndrome mimicking many symptoms of the spontaneously occurring syndrome of depression. The majority of clinical studies of depression, in which pro-inflammatory biomarkers were measured, confirmed that a chronic inflammatory status is present, as measured mostly in blood but also in cerebrospinal fluid and postmortem brain of suicide victims with a history of depression. However, it is unclear as to what happens to the pro-inflammatory status following symptom resolution and remission of the depressive episode. In this context, the precise role antidepressant agents play in the resolution of inflammation and return of the immune system to homeostasis has been the object of numerous studies.

15.2.1.1 Early Life Stress and the Immune System

Life stress and traumatic events in early life are being increasingly recognized as pivotal factors that may have profound influences from a neurobiological and psychological standpoint throughout life. Young adults with a history of childhood trauma show increased inflammation, as demonstrated by increased C-reactive protein (CRP), increased white blood cell counts, and increased fibrinogen levels [5]. Importantly, this increased inflammation is present in subjects who are depressed and have a history of childhood maltreatment and also in those who have experienced maltreatment but are not depressed [6]. These observations suggest that the increased inflammation is a "biological scar" of the early exposure to high levels of stress, which originates in childhood and is characterized by abnormalities in both mental and physical health [7]. Interestingly, the association between trauma and increased inflammation in young adults has also been linked to in utero exposure to stress [8], in the offspring of the South London Child Development Cohort, a longitudinal sample of depressed women who were recruited and assessed during pregnancy in 1986. Exposure to maternal depression during pregnancy (but not in the postpartum period) doubled the risk of the offspring developing depression and other mental disorders in adolescence [9], an association in part mediated by an increased risk of the offspring being exposed to maltreatment and other stressful events in childhood [10, 11]. These same offspring exposed to maternal depression in utero have increased inflammation as young adults, as shown by raised CRP levels [8]. Exposure to medically related inflammation in childhood (e.g., through infections and autoimmune disorders) appears to increase the risk of depression in adulthood [12].

Besides drugs, there is converging evidence on several levels that stress-relieving methods, including physical exercise, psychotherapy, and BMTs, benefit brain function throughout the lifespan and across various neuropsychiatric disorders. Most of these methods are cost-effective and relatively free of adverse effects, and therefore they could also be used as adjunctive therapeutic tools to arrest neuroprogression.

15.2.2 Immune System Dysregulation and Affective Disorders

The role of a dysregulated inflammatory response has been widely studied as a correlate as well as a possible cause of several mental health disorders. Focusing on depression, associations with altered serum and plasma cytokine levels have been confirmed by a series of meta-analyses [13–15]. We have now descriptions of how cytokines can influence pathophysiological domains, such as neurotransmitter metabolism, neuroendocrine function and regional brain activity, all of which are relevant to depression [16, 17]. Additionally, studies have shown that antidepressant treatments can normalize levels of cytokines, and anti-inflammatory treatment can decrease depressive symptoms. While a wide range of evidence supports the role of an immune dysfunction in depression, not all depressed patients have increased inflammation. So, what information is available and what is missing?

Our knowledge has been greatly enriched by results from a combination of peripheral human studies and in vitro models utilizing human blood cells and neuronal precursors. For example, measurements of mRNA expression of candidate genes in the peripheral blood of patients with major depression and healthy controls from the Genome-Based Therapeutic Drugs for Depression (GENDEP) sample, a large European study funded by the European Commission, showed increased inflammation in depression, with patients having increased mRNA expression of the pro-inflammatory cytokines IL-1, IL-6, TNF-alpha, and macrophage migration inhibiting factor (MIF), together with a reduced expression of the anti-inflammatory cytokine IL-4. These same patients also have molecular evidence of glucocorticoid receptor (GR) resistance, as shown by a reduced expression of GR mRNA together with an increased expression of the GR chaperone protein, FKBP5 [18]. Both these findings indicate the possible molecular signature underlying GR resistance and increased inflammation in depression: a reduced GR expression (i.e., less receptor available) together with a decreased GR responsivity (as FKBP5 binds to the GR and maintains it in an unresponsive state). The role of glucocorticoid resistance and its relation to inflammation was further observed in a group of severely depressed inpatients with treatment-resistant depression who had increased plasma cortisol levels and increased plasma IL-6, whose peripheral blood mononuclear cells displayed a reduced in vitro ability to respond to dexamethasone and cortisol during an immune stimulus [19, 20]. Patients with the highest IL-6 levels were also the least likely to respond to antidepressants [21]. These findings confirmed the notion that glucocorticoid resistance, cortisol hypersecretion, and increased inflammation are indeed coexistent in some

patients. Interestingly, increased inflammation in depression can also coexist with HPA axis hypoactivity rather than hyperactivity, as shown in a group of older depressed patients with coronary heart disease. Depressed patients with coronary heart disease had higher levels of IL-6 mRNA and higher levels of CRP together with a reduced expression of GR mRNA and lower levels of cortisol [22].

A clear characterization of different populations would be of benefit toward a better personalized medicine approach, as this can inform treatment. The study based on the GENDEP sample mentioned above showed that depressed patients who respond to the prescribed antidepressants, escitalopram or desipramine, have higher baseline mRNA levels of IL-1, MIF, and TNF-alpha [18]. A recent study of a cohort of depressed patients used a novel "absolute mRNA values" measurement approach to identify cutoff values for the absolute mRNA measures of IL-1 and MIF that predict response probability on an individual basis [23]. The measurement of blood mRNA immune genes can complement and at times possibly surpass the routine measurement of serum/plasma cytokines [24]. Indeed, patients taking IFN-alpha who develop depression during the immune challenge present a hyperactive immune response that is evident by measuring mRNA but not plasma cytokines [25].

15.2.3 Inflammation's Impact on Serotonergic Transmission: The Tryptophan/Kynurenine Pathway

It is now recognized that depression involves a complex and bidirectional interaction between the brain and the immune system. As the immune system responds to stress with increased production of pro-inflammatory biomarkers, notably cytokines, these inflammatory responses exert a powerful influence on the HPA axis and neurotransmitters critical to mood regulation and cognition. HPA activation contributes to reduced serotonergic activity centrally and peripherally. This is why serotonergic transmission has emerged as a possible "common denominator" between cardiovascular disease (CVD), depressive illness, and the immune system. This is not meant to ignore the role of other neurotransmitters, notably acetylcholine, norepinephrine, or dopamine, but due to space limitations, the discussion will focus on serotonin. Abnormalities of serotonergic mechanisms in depression have been described extensively, and Leonard [26] and Mendelson [27] have written useful reviews. One such example is serotonin 2A receptor upregulation in depression [28, 29]. Studies have reported decreased platelet aggregation in response to serotonin, but platelet reactivity to serotonin is significantly increased in depressed patients [30]. Of relevance here is the work of Whyte et al. who demonstrated that depressed patients with the serotonin-transporter-linked promoter region l/l genotype had increased platelet activation compared to depressed patients without this genotype or non-depressed control subjects. These authors hypothesized that persons with this polymorphism are likely to experience higher mortality rates. If this finding is replicated, "genotyping could be used to help identify the patients with ischemic heart disease at greater risk of depression associated cardiovascular mortality" [31].

Another possible mechanism linking serotonergic transmission, depression, and CVD is the cytokine connection. Palazzolo and Quadri [32] had shown that IL-1 inhibits the release of serotonin, and Zhu et al. [33] have reported that two pro-inflammatory cytokines, IL-1beta and TNFα, activate serotonin transporters. Both of these mechanisms may act synergistically to reduce serotonin availability at the postsynaptic neuronal membrane. The resulting serotonergic deficiency has been linked pathophysiologically to depression and can be overcome by administration of serotonin reuptake-inhibiting antidepressants (SSRIs).

In addition to the effects described above, a more compelling case for the interaction between inflammation and serotonergic transmissions can be made on the basis of data involving the tryptophan/kynurenine pathway. Serotonin is synthesized from about 1% of the available tryptophan in the body, and its synthesis occurs predominantly in the gut with only 10–20% occurring in the brain. Under physiological conditions, about 99% of tryptophan is metabolized to kynurenine in the liver by the enzyme, tryptophan 2,3-dioxygenase (TDO). In inflammatory conditions, infections, or oxidative stress, the first rate-limiting enzymatic step involving the enzyme, indoleamine 2,3-dioxygenase (IDO), is activated. The IDO enzymatic activity is enhanced by pro-inflammatory cytokines, such as IFN-γ [34, 35], IL-1, IL-2, IL-6, and TNFα, and inhibited by the anti-inflammatory cytokine IL-4 [36]. (For a comprehensive review, see [37].) Overstimulation of IDO leads to tryptophan depletion and resulting serotonin deficiency in the brain [38]. Additionally, during inflammatory states, peripheral kynurenine formation is increased and is transported through the blood-brain barrier, thereby increasing the brain concentration of kynurenine. A metabolic product of the kynurenine pathway is quinolinate that is neurotoxic. An increase in tryptophan breakdown and kynurenine formation has been demonstrated in depression [39], and the kynurenine metabolism has been implicated in the pathophysiology of depression, especially the chronicity of the disorder [40]. The upregulation of the initiating step of the kynurenine pathway has been demonstrated in postmortem anterior cingulate cortex from individuals with schizophrenia and affective disorders [41]. This group of investigators [39, 42] has observed a lower plasma tryptophan index and neuroprotective kynurenic acid and higher tryptophan breakdown also in bipolar patients compared to controls.

15.2.3.1 Pro-inflammatory Cytokines, Glucocorticoids, and Tryptophan-Kynurenine Pathway in Major Depression and Alzheimer's Disease

Over 40 years ago, Lapin and colleagues [43] published a series of experimental studies demonstrating that depressive-like behavior in rodents could be caused by the metabolic end products of the tryptophan-kynurenine pathway. The authors demonstrated that quinolinic acid and 3-hydroxykynurenine, formed from kynurenine as a component of the neurodegenerative arm of the pathway, caused anxiety and stress-like changes in the animals.

Approximately 60% of brain kynurenine arises from the blood [44] where it is further metabolized to either the excitotoxic metabolite, quinolinic acid, which acts as an agonist at NMDA-glutamate receptors, or to the neuroprotective metabolite,

kynurenic acid, that acts as an antagonist at the NMDA receptor [45]. Under non-inflammatory/non-stress conditions, there is a balance between the end products of the neurodegenerative and neuroprotective pathways [40].

The regions of the brain involved in the metabolism of kynurenine may differ according to the pathophysiology of the psychiatric disorder [46]. In major depression, Steiner and colleagues [47] have shown that the quinolinic acid concentration in microglia from subregions of the anterior cingulate gyrus is increased. This evidence that the excitotoxic pathway is increased in depression is further supported by the increase in plasma 3-hydroxykynurenine [44].

Thus, as a consequence of immune activation, the changes in the tryptophan-kynurenine pathway play a major role in the dysfunctional neurotransmitter systems in the brain and, in addition, contribute to the changes in brain structure and function which characterize depression.

In recent years, attention has centered on the neurotoxic consequences of the increase in quinolinic acid and the intermediates formed from kynurenine in the tryptophan-kynurenine pathway. While such neurotoxins undoubtedly play a critical role in the neurodegenerative changes associated with chronic psychiatric disorders, such as depression and schizophrenia, it is often overlooked that quinolinic acid is also an important substrate for the formation of nicotinamide adenine dinucleotide (NAD+). As NAD+ is a key component of the respiratory chain, chronic pathological changes that reduce its formation are liable to have adverse consequences for intermediary metabolism particularly in neurons that are critically dependent on high-energy sources.

It is estimated that approximately 99% of tryptophan that is not used for protein and serotonin synthesis is metabolized to NAD+ via the tryptophan-kynurenine pathway, and therefore this pathway is important for the synthesis of this vital cofactor [46]. This situation would be compounded by a reduction in the availability of insulin, a key factor in the transport of glucose into neurons [48]. As there is evidence that insulin receptor resistance is a frequent feature of depression and other major psychiatric disorders and with age-related pathology associated with the dementias [49], it is reasonable to conclude that a chronic decrease in high-energy substrates resulting from a deficit in glucose and essential cofactors may be of crucial importance in understanding the causes of increased neuronal apoptosis [49].

This situation is further complicated by mitochondrial dysfunction in depression which results in a decrease in the synthesis of adenosine triphosphate (ATP) and related high-energy molecules, combined with an increase in oxidative damage. In addition, the synthesis of superoxide radicals results from a decrease in the respiratory chain and causes increases in the damage to mitochondrial membranes by opening the permeability transition pores [50]. The oxygen free radical synthesis is further enhanced by xanthurenic acid and 3-hydroxykynurenine which are formed in the brain as a result of the inflammation-enhanced tryptophan-kynurenine pathway.

The combination of chronic inflammation, endogenous neurotoxins, and oxidative stress leads to adverse changes in brain energy metabolism. This may provide the pathological link between the degenerative changes in the brain of the elderly depressed patient and the onset of dementia, particularly Alzheimer's disease.

Recently much attention has been directed toward the tryptophan-kynurenine pathway, and as already discussed above, the diabetogenic kynurenine metabolites, xanthurenic acid, and 3-hydroxykynurenine exert an antagonistic effect on the availability of insulin and glucose metabolism [49]. In addition to these changes, the reduction in the synthesis of NAD+ and the dysfunctional changes in the mitochondria of depressed patients combine to impair brain glucose metabolism and neuronal function. Thus, it may be concluded that a combination of the neurotoxicity of the pro-inflammatory cytokines, coupled with hypercortisolemia and depression-induced brain glucose dysfunction, predisposes the brain to neuroprogressive changes and ultimately dementia. Clearly further research is needed to determine how such changes may be prevented and possibly reversed.

15.2.3.2 Genetic and Epigenetic Factors

Gene-environment interactions should be considered as well. We know that some genetic variants that increase immune responses are more frequent in patients with depression or characterize a group of individuals who are at risk of developing a depressive phenotype in the context of an immune challenge [51]. For example, the functional G-174C polymorphism (rs1800795) in the promoter region of the IL-6 gene predicts depressive symptoms in patients taking interferon alpha for chronic viral hepatitis [52]. Two polymorphisms in genes regulating prostaglandin synthesis, the BanI polymorphism of the cytosolic phospholipase A2 (cPLA2) and the COX2 rs4648308 polymorphism in the cyclooxygenase 2 (COX-2) genes, also regulate the risk of developing interferon-alpha-induced depression. Interestingly, carriers of the two "at-risk" PLA2 and COX2 genotypes also have lower levels of the omega-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), before and during IFN-α treatment [53].

15.2.3.3 Clinical Evidence Linking Depression with Dementia

Epidemiological studies implicate chronic depression as a predisposing factor for dementia in later life. Nevertheless, the link is incompletely understood and controversial. However, epidemiological studies do indicate that chronic depression is an important predisposing factor for dementia in later life. Depression has been shown to be a frequent antecedent of late onset Alzheimer's disease, and there is now evidence that minor cognitive and memory deficits may be an early manifestation of dementia before the full cognitive symptoms become apparent [54, 55]. In support of these observations, patients with depression who later develop dementia often have a poorer baseline performance in cognitive tasks [56]. Depression increases the risk of developing dementia by at least twofold [56]. This suggests that depression might be a prodrome for dementia [57].

Depression and Alzheimer's disease are associated with neuroinflammatory changes in the brain [57]. Clinical studies have demonstrated that pro-inflammatory cytokines are elevated in the blood of depressed patients [58, 59], while the increase in oxidative and nitrosative stress pathways by inflammation plays a significant part in the consequent neurodegeneration [60]. The diagnostic features of Alzheimer's disease include the accumulation of hyperphosphorylated tau protein, which destroys

the microfilamentous structure of neurons, and extracellular beta-amyloid plaques [61]. The deposition of beta-amyloid in the brain activates microglia which release pro-inflammatory cytokines and chemokines [62]. Thus, current evidence suggests that brain inflammation is a pathological feature of Alzheimer's disease that results from the interaction between activated microglia, neurons, and beta-amyloid plaques [63, 64]. In addition, elevated concentrations of cortisol in both depression and Alzheimer's disease not only cause direct damage to neurons but also potentiate the neurotoxic effects of beta-amyloid [65, 66]. Such effects contribute to the impairment of cognitive function in both these disorders [67]. Furthermore, there is evidence that neuronal apoptosis is increased in both disorders, resulting in structural changes in the hippocampus, frontal cortex, amygdala, and in other brain regions [65, 66, 68].

15.2.3.4 The Immune System and Inflammation in Major Depression and Alzheimer's Disease

Neuroinflammation in chronic depression and Alzheimer's disease, which is mediated by pro-inflammatory cytokines, occurs as a result of the interaction between stress and/or beta-amyloid, activating microglia and astrocytes [61]. In addition to the pro-inflammatory cytokines, such as interleukin (IL)-6, tumor necrosis factor (TNF)-alpha, interferon (INF)-gamma, activated neuroglia also produce chemokines, prostaglandins, leukotrienes, thromboxanes, nitric oxide, and oxygen free radicals [69].

Microglia are the principal cells in the brain which are involved in innate immunity and are mediators of neuroinflammation. The structure of microglia changes according to their functional role. Thus in the healthy normal brain, their structure is round with numerous branching processes. This form supports and partially protects neuronal growth and synaptic remodeling in the brain and spinal cord. In addition, in this state (termed the M2 phenotype), microglia exhibit a scavenger expression and by phagocytosis remove cell debris, release neurotrophic factors, and thereby preserve neuronal function [70]. When microglia are activated by bacterial or viral infection, traumatic injury, ischemia or, in the case of depression, stress, they are transformed into an amyloid state which facilitates their movement.

In Alzheimer's disease, these inflammatory mediators enhance the synthesis of beta-amyloid, thereby increasing the amyloidogenic cascade which is considered to be the pathological hallmark of the disease [69]. As there is evidence that amyloid plaques also accumulate in geriatric patients with chronic depression [71, 72], it is reasonable to postulate that Alzheimer's disease could be an outcome in these patients [73].

Pro-inflammatory cytokines, such as IFN-gamma, activate IDO, and more recently, it has been proposed that IL-18 also plays a significant role in Alzheimer's disease and possibly also in major depression [74]. This cytokine is induced by stress and, following its cleavage by caspase-1, mediates the increase in IFN-gamma [75]. This could be an important mechanism in the pathology of both depression and Alzheimer's disease. IL-18 is increased in the brain of patients with Alzheimer's disease and in the CSF of those with cognitive impairment, and also shows a

synergic interaction with the Apo-E4 allele associated with the increased susceptibility of patients with Alzheimer's disease [76, 77]. This mediator provides another link between the pathological changes initiated by inflammation and dementia.

In chronic depression, bipolar disorder, and Alzheimer's disease, the concentration of BDNF is reduced [78–80], an event associated with the activation of the central glucocorticoid receptors by glucocorticoids. This, combined with the neurotoxic effects of the elevated pro-inflammatory cytokines and the activation of N-methyl-D-aspartate (NMDA) receptors by nitric oxide and quinolinic acid (discussed elsewhere in the review), together with oxidative stress, provides a toxic environment for neurons in the brain of patients with depression or Alzheimer's disease. This has been discussed in detail elsewhere [81].

15.2.4 Neuroinflammation at the Core of CNS Pathology

The term "neuroinflammation" is used to describe the changes in the central nervous system caused by injury, physiological and psychological stress, or infection. Neuroinflammatory processes underlie psychiatric and neurological disorders, and many excellent reviews are available [82, 83]. Inflammation is the response of the innate immune system in an attempt to protect and defend the organism against any threat to its integrity and homeostasis. Such threats can range from invasion by microorganisms to environmental stressors and emotional stresses leading to allostasis [84]. The inflammatory response is implemented by orchestrated mobilization and complex interactions of various cell types and signaling molecules. The composite response can be localized or systemic or both. The ultimate goal is to control and eliminate the initial noxious stimulus by means of phagocytosis and activation of the inflammasome, an intracellular multiprotein oligomer that is a component of the innate immune system. The inflammasome activates inflammatory processes to enable tissue repair and regeneration. Neurons express inflammasomes which are involved in the maturation of the pro-inflammatory cytokines, interleukin-1β (IL-1β), and interleukin-18 (IL-18). Trauma increases inflammasome expression in rat neurons, and programmed cell death, known as pyroptosis, is induced by the inflammasome [85, 86]. The inflammatory response is intended to be beneficial and protective; however, if it is excessive and/or prolonged, it can cause tissue damage and induce pathological changes. It is also noteworthy that once activated and deployed, participating cells (leucocytes, monocytes, endothelial cells) target not only the initial site of inflammation but also remote sites including penetration into the brain parenchyma. Thus, peripheral inflammation can trigger a neuroinflammatory response that involves the blood-brain barrier (BBB), neurons, astrocytes, and microglia. Contrary to previously held beliefs, the BBB is permeable, not only at the site of circumventricular organs, to pro-inflammatory mediators that originate in the periphery and can allow leucocyte migration. Additionally, the BBB can itself, upon stimulation, release pro-inflammatory mediators. Consequently, neuroinflammation

is a term used to connote the broad range of CNS immune responses that may result in synaptic impairment, neurotransmitter dysregulation or deficiency, neuronal cell death, and exacerbation of brain pathology.

In the periphery, macrophages are the key elements responsible for the first-line immune response. Upon stimulation by interferon-gamma (IFN-γ) and tumor necrosis factor-α (TNFα), they produce and release pro-inflammatory mediators, known as cytokines. Centrally this function is carried out predominantly by microglia, the resident immune cells in the brain, and their activation is believed to be related to neuroinflammation. Activated microglia produce cytotoxic factors, such as TNFα, IL-1β, eicosanoids, nitric oxide, and reactive oxygen species. Astrocytes can also release, when stimulated, pro-inflammatory mediators, such as TNFα, in the cortex and midbrain. It is believed that the combined glial response is, at least in part, related to the neurodegeneration seen in dementia [87].

15.2.5 Neuroinflammation and Severe Mental Disorders

15.2.5.1 Autoimmune Encephalitis and Mild Encephalitis: New Challenges in Psychiatry

The etiology of severe mental disorders (SMI), including schizophrenic and affective spectrum disorders, remained a puzzle to be solved, best exemplified in schizophrenia research [88]. A major problem for research has been the apparent lack of specificity of psychiatric syndromes due to various etiologies. Striking examples are organic psychosyndromes resulting from infections or any type of encephalitis [89]. The development of psychosyndromes in infectious or autoimmune encephalitis, previously termed limbic encephalitis, often manifests itself slowly, is accompanied early on by neurological soft signs and only later by neurological hard signs. In SMI on the other hand, especially in schizophrenia, neurological soft signs are often but not always present [90]. The high prevalence of neurological soft signs has hampered the early detection of emerging encephalitis in SMI patient cohorts. Thanks to more detailed knowledge from experimental research and research on Borna disease virus infection, caused by a highly neurotropic virus, the recently updated mild encephalitis (ME) hypothesis proposes that an underdiagnosed subgroup of SMI cases actually suffers from ME [91]. Mild neuroinflammation should causally underlie brain dysfunction and the observed psychiatric syndrome, the latter presenting with variable psychiatric symptoms. Additionally, brain dysfunction is not just a secondary consequence of systemic inflammatory signaling to the brain, i.e., the term ME indicates a special though mild type of neuroinflammation. The ME hypothesis, although initially not well accepted, has gained more support recently from various pieces of evidence, not the least of which is new insight into the overall probably low prevalence rate of autoimmune encephalitis (AE). The surprisingly remarkable prevalence of CNS autoantibodies without proven AE in SMI cohorts has added to this evidence but has at the same time raised new key questions, as will be discussed in this section.

15.2.5.2 Autoimmune Encephalitis

With the discovery of *N*-methyl-D-aspartate receptor (NMDAR) autoantibodies, Dalmau and his group have named a new neurological disease entity as "anti-NMDAR encephalitis" which can now be diagnosed with clearly defined clinical and laboratory markers [92]. Some of these cases had been previously diagnosed as limbic encephalitis. Interestingly, researchers in this intriguing new neurological field continue to discover new CNS autoantibodies and in associated neurological disorders, previously not thought to be of the autoimmune type, e.g., cases of epilepsy, and not attributed to encephalitis. In addition, when SMI patient cohorts were systematically tested for CNS autoantibodies, many of them were rediagnosed as AE patients. Great interest was therefore generated in ways of detecting encephalitis in SMI patients, because early detection and early immune modulatory treatment can often dramatically change the disease outcome of patients diagnosed with encephalitis, often achieving full remission with immune suppressive treatment. Based on emerging experiences, "red" and "yellow" flags were developed, and these recommendations appeared to be extremely helpful in sorting out AE or other types of encephalitis in patient cohorts of new onset SMI, including schizophrenia, bipolar disorder, or other severe affective disorders [93, 94]. The recommendation to transfer SMI patients, when diagnosed with encephalitis, to neurological wards as soon as possible came as a shock to clinicians, but also it signaled the emergence of an intriguing new opportunity to diagnose and manage these patients. The challenge now is how psychiatric wards will become ready to perform the required and rather aggressive immune-modulating treatments [95], and physicians will need to acquire specialized training about diagnosing AE.

The potential consequence of underdiagnosing NMDAR encephalitis in SMI cohorts became evident with the retrospective reexamination of collected CSF samples in a schizophrenic cohort from the University Clinic in Magdeburg, Germany. Within a cohort of 300 schizophrenic patients, 2 patients had to be rediagnosed as NMDAR encephalitis according to the results of retrospective antibody testing [96]. Just as interesting was the result that about 10% of these schizophrenic patients demonstrated NMDAR antibodies without fulfilling criteria for NMDAR encephalitis. An explanation of the pathological relevance of these CNS autoantibodies was not available. However, in the meantime more data have been published, and it appears that circulating anti-NMDA autoantibodies might not in principle be pathogenic, but rather they may have pathogenic relevance only with disturbed blood-brain barrier integrity [97–99].

In addition, findings about cases of encephalitis proven by biopsy but without circulating CNS autoantibodies were similarly intriguing. Souhel Najjar and his group demonstrated a number of cases of encephalitis presenting without detectable CNS autoantibodies, while each case was confirmed by brain biopsy. According to these authors, 10% of cases presenting with acute psychosis may fall in this category (Najjar et al.) [100], updated with a presentation at the yearly Congress of the German Association for Psychiatry and Psychotherapy, DGPPN (Berlin, November 2016). These findings lend clear support to the ME hypothesis. Another recent

finding should be considered in this context. CSF cells isolated from patients with defined NMDAR encephalitis produced a variety of CNS autoantibodies: only 6% of these cells produced NMDAR antibodies, while the other CSF cells produced other CNS autoantibodies [101]. Nevertheless, the NMDAR autoantibodies fully explained the psychiatric syndrome.

The remarkable number of cases of previously unsuspected encephalitis in the SMI samples investigated so far, presenting with or without CNS autoantibodies, and finally diagnosed as encephalitis (or with ME), is compatible with a scenario predicted with the ME hypothesis. An even larger subgroup of SMI cases presented with various overall minor CSF abnormalities. CSF examination represents the most sensitive clinical approach to neuroinflammation available today. Therefore, these CSF abnormalities are very intriguing and support the ME hypothesis although a conclusive interpretation is still outstanding.

15.2.5.3 Mild Encephalitis

Taken together, an increasing number of findings from various approaches to SMI are compatible with the assumption that immune inflammatory mechanisms are involved in the pathogenesis of a large subgroup of SMI cases. Such a psychoimmunology scenario is supported by robust findings often matching the ME hypothesis and is discussed here in more detail.

Subgroups of schizophrenic patients demonstrate changes in either immune or growth factors and hormonal pathways [102]. The tryptophan pathway is apparently involved in mood disorders and other SMI syndromes [103]. Human endogenous retrovirus may be involved in the gene environment interface [104]. In rare instances, specific infectious agents may be involved [105]. Inflammatory metabolites can modulate glutamate and NMDA receptors, a phenomenon relevant in depression and suicidality [106]. C-reactive protein concentrations are increased across the mood spectrum in bipolar disorder [107]. Cognitive disturbances are related, at least in part, to brain structure in schizophrenia [108]. When studied in the context of viral antibodies in serum, associations with hippocampal volume are reported [109]. Cytokine abnormalities (IL-23/IL-17) and the immune axis seem to be involved in schizophrenia [110]. There is broad evidence that immune inflammatory toxicity, nitrosative stress, and neuroprogressive changes are involved in the pathogenesis of schizophrenia [111]. Microglial activation (or mild neuroinflammation) has been shown in schizophrenia-related psychosis by PET imaging [112]. Schizophrenia risk genes include variation of complement component, and interestingly, the gene is active in the brain as well [113]. The mild brain atrophy prevailing in a subgroup of schizophrenic patients is explained by neuroprogression, a newly introduced term involving immune-neuroinflammatory conditions as described by Davis et al. [114]. In new onset cases, the progressive reduction in cortical thickness, as psychosis develops, has been associated with peripheral inflammatory markers [115]. Microglial activation and the onset of psychosis seem to be associated [116].

Causality in such a psychoimmunological perspective concerning the pathogenesis of SMI is an important question. Large, conclusive studies from Denmark have

demonstrated autoimmune diseases and infections are important and additive risk factors for SMI [117, 118]. Taken together, these studies suggest that at least 20% of SMI cases could be explained by these two risk factors, namely, infections and autoimmune disorders requiring hospital treatment. A potential additional pathogenic role of less severe courses (not requiring hospital treatment) of infections and autoimmune disorders in the general population remains open. Interestingly, in the data from Denmark, no risk increase was observed from infections during pregnancy but clearly from infections during the lifetime. Overall, these findings are compatible with the ME hypothesis [119] and point to cumulative epidemiologic aspects versus single contributory factors in the etiopathology of SMI. In this context, another finding is interesting: a comprehensive transcriptional map of primary brain development shows spatiotemporal enrichment within the developing neocortex of candidate risk genes for neurodevelopmental disorders, including schizophrenia, with shared etiology to other neurodevelopmental disorders. These genes were not enriched in neurons until infancy, suggesting a larger role for dysfunction in circuit refinement rather than prenatal processes such as neurogenesis [120].

Subsequent studies have clearly demonstrated CSF abnormalities, minor or mild, in nearly 50% of SMI patients with routine CSF analysis. These analyses have detected mild but definite albumin or protein increases, oligoclonal bands (indicating immune-inflammatory responses within the CSF spaces and therefore mild neuroinflammation), or rare slight CSF cell number increases or rare agent-specific antibody increases (increased antibody index CSF to blood). These findings indicate agent-specific immune responses within the CSF spaces and agent-specific mild neuroinflammation [121–126]. When including new CSF markers, like activation markers of CSF cells, neopterin, and/or cytokines into the summary findings (methods newly used in research approaches may be less valid as compared to findings with routine methods), we found that 70–100% of treatment-resistant SMI patients presented some CSF abnormalities, classifying them into a minimum of three pathogenic subtypes [127]. In addition, using new laboratory methods with fresh CSF from patients with schizophrenia or affective disorders, there were microscopic particles demonstrated, the molecular analysis of which demonstrated a neuroinflammatory signature [128, 129]. The potential source of such neuroinflammatory signals remained difficult to identify, with extracellular vesicles apparently involved in this volume transmission in the brain neural-glial networks [130].

The role of CSF cells in such a psychoimmunological or neuroimmunological scenario in humans is not yet fully understood. Convincing experimental evidence has demonstrated that CSF cells play an important role in health and disease to support brain function [131]. In addition, meningeal immunity can directly influence spatial learning and memory and is also critical for social behavior via cytokine signaling from meninges to neurons in the brain. These findings suggest a coevolutionary link between social behavior and an anti-pathogen immune response [132]. Immune cells were enriched in the postmortem brains of SMI cases, especially when the subject had died by suicide associated with acute disease, lending direct support to the ME hypothesis [133].

15.2.5.4 Recommendations and Challenges

The recent insights into the prevalence of AE, with or without CNS autoantibodies, strongly suggest this entity should be included in the differential diagnosis of SMI patients, especially in new onset and therapy-resistant cases. Thus, previously undiagnosed cases of AE, i.e., SMI cases presenting with CNS autoantibodies with various (and emerging newly detected) antigen specificities, can be accurately diagnosed and treated appropriately. This objective represents a major challenge and necessity not only for psychiatric research but ultimately for psychiatric practice in general. Psychiatry needs to accept this challenge urgently because early diagnosis is important, and appropriate treatment of AE may lead to rapid remission. More extensive and focused studies are required. CSF examination is the most sensitive clinical approach to the differential diagnosis of encephalitis and neuroinflammation in general and should be recommended to SMI patients more frequently than is presently the case [93, 94, 127]. This recommendation is based on experiences with neurological or neuropsychiatric patient samples in which CSF abnormalities, MRI abnormalities, focal neurological symptoms, EEG abnormalities, and high disease acuity represented "red flags." Less suggestive "yellow flags" have included autonomic disturbances, motor abnormalities, disturbances of consciousness, hyponatremia, rapid disease progression, catatonic symptoms, comorbid autoimmunity (e.g., Hashimoto thyreoiditis), and focal neurological deficits [93, 94]. Apparently, the "red flag CSF abnormalities" can only be detected when CSF examination is performed especially in new onset cases of SMI or treatment-resistant cases.

We understand that this perspective of including AE in the differential diagnosis of SMI presented here and supported by clinical and experimental evidence will require a much broader general discussion and debate in psychiatry. Clear recommendations and guidelines will have to be developed, and the acquisition by psychiatrists of new expertise in CSF diagnostics will become necessary. Similarly, psychiatric research will have to focus more on neuroinflammation in general and more specifically mild neuroinflammation as well as the role of mild systemic inflammation. To make progress in understanding the psychoimmunology of potentially large subgroups of SMI cases, there is a need to establish sensitive methods to detect mild neuroinflammation in the individual patient in vivo. This effort will require the adoption of the most advanced methods and experience available from other fields, especially in neurology, but also the development of refined methods designed for specific psychiatric needs. Studies will need to be designed to investigate the immuno-inflammatory pathways and respective functional and structural consequences, over the long-and the short-term, in blood, CSF, and the brain by available and newly developed methods, including neuroimaging, biopsy, and postmortem approaches.

15.2.6 Neuroprogression

15.2.6.1 Definition and Neuropathological Considerations

The concept of neuroprogression describes the progressive, recurrent, and chronic course of the disease entity under consideration. It subsumes clinical manifestations of the disease process and may also entail, if known, morphological, biochemical,

neurochemical, immunological, physiological, and genetic aspects that contribute to the progressive and relapsing course of the disease in question. It also describes a constellation of progressively deteriorating clinical and neuropathological outcomes including increasing chronicity, declining cognition, and treatment nonresponsiveness [134, 135].

An activated inflammatory system is of particular relevance to the etiology and progression of neuropsychiatric disorders characterized by neuroprogression, including depression and schizophrenia [111]. In psychotic disorders, inflammatory dysfunctions have been associated with physical health, brain structure, clinical outcome, and the action of antipsychotic drugs [136–141]. Of all the sources of inflammation and risk factors for the development of neuropsychiatric diseases, early-life insults, such as stress or infection, are common to both depression and schizophrenia [142]. Such early-life insults appear to lead to a pro-inflammatory phenotype that persists into adulthood [143, 144]. Critically, such insults may sensitize peripheral and central nervous system innate immune responses to subsequent immunostimulatory insults, resulting in neuroinflammation and the exaggerated release of neurotoxic molecules [145]. This is one mechanism by which an immunostimulatory insult in early life might render an individual more vulnerable to the development of neuropsychiatric illness in adulthood following a second immunostimulatory insult, a concept known in general as the "double hit" model [145].

This sensitization also appears to occur in adulthood, with prior episodes of depression sensitizing immune responses to subsequent depressive episodes, resulting in levels of peripheral pro-inflammatory cytokines and chemokines increasing with sequential depressive episodes [146]. Indeed, evidence demonstrates that certain immune challenges are capable of reprogramming the function of peripheral innate immune cells over the long-term, such that upon a secondary, distant, stimulation the production of pro-inflammatory cytokines is enhanced. This is known as "innate immune memory" or "trained innate immunity" and is mechanistically characterized by stable epigenetic changes in immune and metabolic pathways [147]. Microglia, the resident innate immune cells of the CNS, are also susceptible to long-term reprogramming. In response to inflammation, microglia can develop an activated pro-inflammatory phenotype, characterized by morphological changes, upregulation of cell surface receptors, and the release of various inflammatory and neurotoxic mediators, including cytokines (e.g., IL-1β, IL-6, IFN-γ, and TNF-α), reactive oxygen species, and reactive nitrogen species. Such cytokines and neurotoxins can cause disruptions in neuroplasticity and neurogenesis, including growth, differentiation, myelination, apoptosis, synaptic branching, and neurotrophin regulation, ultimately contributing to and driving neuroprogression [148].

The neuropathological changes seen in neuroprogression range from volumetric/morphometric changes in gray matter regions such as putamen and hippocampus, diffusivity changes in white matter fiber bundles, and functional connectivity changes between large-scale functional networks. Corticostriatal network dysfunction and pathologies are among the most commonly reported neuroprogressive features and can lead to a variety of hard-to-treat clinical symptoms including anhedonia, psychomotor slowing, and fatigue. The central hubs of the corticostriatal network including

basal ganglia, anterior cingulate cortex (ACC), and ventral medial prefrontal cortex (vmPFC) integrate key cognitive, affective, and motor functions [149]. These regions are uniquely vulnerable to the effects of neuroprogressive pathologies including inflammatory activation and glutamate dysregulation [149, 150]. In the following paragraphs, we advance the hypothesis that the key hubs of the corticostriatal networks contribute to neuroprogression through their unique vulnerability to inflammatory and glutamate dysregulation.

15.2.6.2 The Hypothalamic-Pituitary-Adrenal (HPA) Axis and Its Importance in Neuroprogression

The impact of stress-induced activation of the HPA axis is well established in most cases of major depression [151, 152]. The chronic elevation of the glucocorticoids, as distinct from the transitory changes which occur following acute stress, is linked to neuronal damage [153]. As mentioned previously, the reduction in hippocampal volume is associated with hypercortisolemia and the suppression of neurogenesis [154, 155]. In Alzheimer's disease, raised plasma and CSF cortisol commonly occur and, like depression, are resistant to dexamethasone suppression, thereby suggesting that, like depression, the glucocorticoid receptors are resistant to feedback inhibition [67]. However, there is a difference in the circadian regulation of cortisol between these two disorders. Unlike depression, the circadian rhythm in Alzheimer's disease is relatively normal despite the rise in the concentration of the glucocorticoid whereas in depression is partly accentuated and fairly flat [156]. However, in both conditions, cognitive dysfunction is associated with the raised cortisol levels and also with normal aging.

The Apo E4 genotype is considered to be a major risk factor for late onset Alzheimer's disease, but it is also associated with raised CSF cortisol in non-depressed geriatric individuals [157]. The link between elevated glucocorticoids and the pathophysiology of Alzheimer's disease is provided by the increase in the synthesis of beta-amyloid and phosphorylated tau protein shown to occur in a genetically expressed mouse model of the disease; stress has been shown to increase the deposition of these neurotoxic proteins [158]. Similarly, there is evidence that amyloid plaques also occur in the brains of elderly patients with chronic depression, thereby providing further evidence that major depression and subsequent dementia.

15.2.7 Glutamate Mediates Inflammation-Induced Dysfunction of Corticostriatal Pathways

15.2.7.1 Inflammatory and Glutamate Pathologies in Mood Disorders

At least four independent meta-analytic studies have confirmed that plasma concentrations of inflammatory molecules, such as cytokines (tumor necrosis factor (TNF)-alpha and interleukin (IL)-6) and acute phase proteins (such as C-reactive protein or CRP) are increased among patients with depression [13–15, 159]. In addition, depression and related mood symptoms can be reliably precipitated by induction of

inflammation by experimental agents (such as endotoxin and typhoid vaccine) or therapeutic interventions (such as interferon (IFN)-alpha treatment) [160]. Depressive symptoms may also be relieved by administration of anti-inflammatory treatments including cytokine antagonists and nonsteroidal anti-inflammatory medications (NSAIDs) [161, 162]. Chronic inflammatory activation is known to be associated with several neuroprogressive pathologies including oxidative/nitrosative stress, mitochondrial dysfunction, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, epigenetic changes, and neurotrophic disturbance [135, 163, 164].

Glutamate is the major neurotransmitter and a neurometabolite that is present in large quantities in the human brain [165]. Glutamate is very toxic in its free form and hence is cleared from the synaptic space by highly efficient excitatory amino acid transporters (EAATs) located on the synaptic surface of astroglial cells [166]. Experimental or pharmacological ablation of astroglial cells or their surface EAATs can lead to increases in intrasynaptic glutamate and anhedonia in experimental animals [167, 168]. Glial cell pathology and glutamate gene dysregulation resulting from chronic immune stimulation has been one of the most replicated histopathological findings in postmortem studies using brain specimens from individuals diagnosed with major depression [167, 168]. Taken together, these data strongly connect inflammatory activation to glutamate dysregulation in depression. However, researches on these areas have progressed along independent lines with minimal overlap.

15.2.7.2 Immune Activation, Brain Glutamate, and Behavioral Changes

Our preliminary experiments in this area were conducted examining behavioral toxicity resulting from the therapeutic administration of IFN-alpha to patients with hepatitis C as a model of inflammation-induced depressive symptoms [169, 170]. IFN-alpha is an antiviral, inflammatory cytokine used in the treatment of medical disorders such as hepatitis C and is known to reliably induce inflammation and lead to severe depressive symptoms in up to half of the patients treated with this agent [160]. Multiple earlier studies had shown that IFN-alpha can lead to symptoms of depression by selectively targeting nodes of the corticostriatal brain systems [150].

15.2.7.3 Impact of IFN-Alpha on Brain Glutamate

We used proton magnetic resonance spectroscopy (MRS) to measure changes in glutamate concentrations over the 4-week study period in dorsal anterior cingulate cortex (dACC) and bilateral basal ganglia [171]. Four-week treatment with IFN-alpha led to significant increases in glutamate normalized to creatine in both dACC and left basal ganglia, which was associated with increases in plasma inflammatory activity (indexed by tumor necrosis factor receptor (TNFR)-type 2), severity of behavioral impairments including depressed mood and reduced motivation. These findings helped confirm our hypothesis that IFN-alpha might precipitate depressive symptoms by increasing brain glutamate concentrations in regions that serve as hubs that connect key regions of the corticostriatal circuitry [171].

15.2.7.4 Impact of Aging Upon Inflammation and CNS Glutamate

In a subsequent study, we tested the hypothesis that advancing age may interact with inflammation to exaggerate the effects of inflammatory stimulation on CNS glutamate and behavior. We hypothesized that older individuals compared to younger individuals would demonstrate greater increases in inflammatory activity, corticostriatal glutamate increases and motivational/anhedonic symptoms, psychomotor slowing, and fatigue during IFN-alpha treatment. Our results demonstrated that older patients treated with IFN-alpha exhibited a significantly greater increase in glutamate in the left basal ganglia over the 4-week study period compared to older controls and younger IFN-alpha-treated and untreated subjects [172]. In addition, increased glutamate in older but not younger IFN-alpha-treated and untreated patients was associated with increased tumor necrosis factor (TNF), reduced motivation, and prolonged reaction time. Effects of senescence upon microglia and other immune cells can lead to the development of a "primed" phenotype, a partially activated state with exaggerated basal and evoked response to immune stimulation [173]. Of note, priming effects have recently been demonstrated in mood disorder pathology including in microglial cells exposed to psychological stress [174] and in microglia extracted from postmortem brain of suicide victims [175]. Of note, our aging studies illustrated the age-dependent vulnerability of corticostriatal glutamatergic systems to inflammation.

15.2.7.5 Inflammation-Induced Glutamate Changes in Major Depression

Given our data linking inflammatory activation, depression, and glutamate in corticostriatal regions following IFN-alpha administration, we examined if the association would be apparent in a group of subjects with major depression [176]. Based on existing literature, we used CRP measures from plasma and CSF to index inflammatory activity in depression [13–15, 159]. We classified depressed patients into high (>3 mg/L), medium (1–2 mg/L), and low inflammation (<1 mg/L) in accordance with recommendations from cardiovascular atheropreventive studies [177, 178]. Increased plasma C-reactive protein (CRP) was significantly associated with increased left basal ganglia glutamate controlling for age, sex, race, body mass index, smoking status, and depression severity. Left basal ganglia glutamate was in turn associated with anhedonia, psychomotor slowing, and information processing delays. Plasma and CSF CRP were also associated with measures of basal ganglia glutamate and the glial marker myoinositol using chemical shift imaging [176].

15.2.7.6 Immune Regulation of Glutamate-Modulating Agents

Lab animals administered bacterial endotoxin develop well-validated, time-bound, self-limiting constellation of depression-like behavioral changes including lethargy, anorexia, and apathy known as "sickness behavior" [16, 179]. Pretreatment with the noncompetitive NMDA antagonist and antidepressant agent ketamine prior to immune stimulation with endotoxin abrogated the development of sickness behavior without changing the underlying inflammatory activation [180]. Glutamate dysfunction

induced by stress has been associated with activation of the intracellular inflammasome proteins in glial cells [181, 182]. Stigmata of glutamate dysregulation including decreases in number and density of glial cells, markers of glial functioning, number of glutamate transporters, and glutamine synthase activity and altered expression profiles of glutamate-regulating genes have been consistently reported in the postmortem brain specimens of depressed suicide victims [183–187]. Taken together, these data provide support for the association between inflammation, glutamate, and glial dysfunction in depression, thus indirectly validating our findings.

15.2.8 Therapeutic Implications and New Therapeutic Targets

15.2.8.1 Anti-inflammatory Therapies

A better understanding of the above interactions can lead to selective targeting of inflammation, glutamate systems, or both systems in the management of chronicity and neuroprogression in mood disorders. Limited data support the use of anti-inflammatory agents to augment and improve efficacy of currently available antidepressant and mood stabilizers [164]. Administering immune-altering agents to a group of chronic mentally ill is an endeavor fraught with caveats and pitfalls and should not be undertaken lightly [164]. Nevertheless, increasing support derived from recent publications has made this an attractive avenue to pursue. Minocycline, a tetracycline-group antibiotic with well-documented ability to downregulate microglial activation, has been used successfully as adjunctive therapeutic agent in the treatment of refractory mood and psychotic disorders [164, 188]. Again, the current data on minocycline is limited but promising. Data from studies using nonsteroidal anti-inflammatory agents (NSAIDs) is also limited, but results of large-scale studies are pending [161, 189, 190].

15.2.8.2 Glutamatergic Antidepressants

The rapid antidepressant actions and longer-term efficacy of the noncompetitive NMDA-antagonist ketamine are under considerable investigation, and the readers are referred to expert reviews on this topic elsewhere [191, 192]. However, the utility of immune markers to predict treatment response to ketamine is just beginning to be studied. For example, antidepressant efficacy of ketamine was predicted by measures of baseline inflammatory status including CRP, interleukin-6, and adipokines [193–196]. A similar approach has not been employed to study antidepressant effects of glutamate-modulating agents, such as riluzole or memantine—both of which have shown mixed therapeutic benefits in large-scale studies [197–201]. Ketamine also has multiple off-target effects extending beyond glutamate system including effects on glucose synthase kinase (GSK)-3 system, PSD95, and AMPA receptor trafficking mechanisms—targets originally associated with mood-stabilizing medications and inflammatory activation [202].

15.2.8.3 Mood Stabilizers

Both glutamate increases and inflammatory activation have consistently been documented in bipolar disorders [203, 204]. The hypothesis that mood stabilizers and

anticonvulsants might impact glutamate has not yet been well studied—but worth studying more. In this regard, lithium is known to downregulate both inflammation and glutamate neurotransmission via inhibition of GSK3 and hence might enable concurrent targeting of both these processes [205]. Furthermore, lithium also enhances glial reuptake of glutamate from the synapses and protects neurons from NMDA-mediated calcium influx and excitotoxicity through its effects on GSK3 and PSD95 [206, 207]. Other mood stabilizers that impact glutamate neurotransmission include lamotrigine, which is believed to reduce and stabilize presynaptic release of glutamate [206, 208]. Agents such as riluzole that stabilize synaptic glutamate concentrations and glial functions might offer some promise in the future, though current studies of this agent have been disappointing, albeit not targeted to populations with increased inflammation [199].

15.2.9 Future Directions

In order to dissect the molecular mechanisms underlying inflammation-related abnormalities and their possible drug reversal, in vitro models provide valuable information. Useful data was obtained from human hippocampal progenitor cells, able to differentiate into neurons, treated with depressogenic stimuli. Two pro-inflammatory cytokines, IL-1 beta and IFN-alpha, reduce human neurogenesis and human neuronal survival, an effect that seems to be mediated by an increased production of neurotoxic tryptophan metabolites as well as increased oxidative stress [209–211]. The detrimental effects of these inflammatory stimuli can be reversed by potentially antidepressant treatments as diverse as inhibitors of the kynurenine pathways, antioxidants and mitochondrial modulators, and omega-3 polyunsaturated fatty acids [209–211].

The association between inflammatory activation and glutamate dysregulation in influencing the neuroprogressive course and outcome of depressive and related mood disorders has been summarized in the preceding paragraphs. Much more work remains to be done in this area including obtaining a better understanding of the association between glutamate and inflammatory pathology across the lifespan, disease states, and various phases of illness progression [167, 212]. It is also unclear if glutamatergic targets helpful in treating depression might be associated with the underlying pathology leading to the development of these disorders [167, 176]. Finally, multiple technological and methodological advances will need to take place to better understand the impact of inflammation and glutamate dysregulation upon mood disorder pathology [167, 176].

15.3 Concluding Remarks

The field has flourished in the last few years, and we have now several translational opportunities for psychoneuroimmunology to help patients, delivering both predictive biomarkers to implement precision psychiatry and novel pharmacological

agents that improve depression through an anti-inflammatory action. However, limitations still exist. We lack detailed information on the epigenetic mechanisms by which early life events, as early as in utero, create a long-term trajectory of increased inflammation. Similarly, questions remain on how drugs with anti-inflammatory action help in mental health disorders. While some of these issues may take years to resolve, mental health problems can no longer be seen only as disorders of the mind or indeed only of disorders of the brain; the strong impact of the immune system is undeniable.

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Interdisciplinary Collaboration in Practice: The Georgia Process and Model

16

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Abstract

The Republic of Georgia (Sakartvelo in Georgia) is a relatively small country of 69,700 square kilometers and only 3.8 million people. Being in the Southern Caucasus on the crossroads between Eastern Europe and Western Asia, it has been experiencing a tumultuous history for over 3000 years. It was subject to many invasions by stronger neighbors and maintained independence only for short periods in between. It was annexed by Tsarist Russia in 1800 and became a Soviet Republic, part of the Soviet Union (USSR) in 1921.

With the dissolution of the USSR, Georgia declared independence in 1991 and has been struggling for stability and sovereignty since then. A coup d'etat was already instigated in late December 1991. Separatist disputes over the

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regions of Abkhazia and South Ossetia were initiated already in 1992–1993 and followed up to a full-blown Russo-Georgian War in August 2008. Hostilities resulted in civilian casualties, internally displaced refugees, and continuous tensions and distress.

Georgia is currently still a nation in transition. Its internal well-being affairs are being crystalized, and it is in a process of strengthening economic and political ties with the European Union.

Since, according to the World Health Organization (WHO), health, well-being, and mental health are multifaceted processes and situations, involving the individual's physical and mental adaptation within her/his socioeconomic environment, the promotion of well-being necessitates an efficacious interdisciplinary collaboration in which each group of experts will contribute to community welfare.

Community services are of utmost importance, and family medicine practitioners are the first line of contact and clinical management. Psychiatrists are not always available, especially in the periphery. They tend to focus on the most severely affected patients in urban centers. Should this be reassessed? Georgia benefits from an active National Institute of Mental Health which promotes issues of psychiatry and addictions. Its goals are re-updated according to requirements and capabilities. The Ministry of Health, Labour and Social Affairs established health policy administration which collects and monitors epidemiological data, interprets them, and recommends actions.

A consensus was achieved that together we will be stronger and more effective. An operational group was formed, perspectives on needs were assessed, and a plan of actions is being developed.

16.1 Geopolitical and Historical Background

The Republic of Georgia is in the South Caucasus region, on the eastern coast of the Black Sea. The Caucasus is defined by the mountain ranges stretching between the Caspian and the Black Seas. As such it has been the border as well as the crossroad between Western Asia and the Eastern Mediterranean cultures and powers and Eastern Europe. Since the dawn of history, the rugged geography determined fragmentation, multiple feuding clans, and multiple languages (the Arabs called the region "The mountain of Languages"). Current Georgia-Sakartvelo, in Georgia, is a small country of only 69,700 km^2 and a population of 3.8 million people (2015). It borders with Russia on the north, Turkey on the southwest, and Armenia and Azerbaijan on the east. Currently, two areas of the small country claim autonomy, their status is in dispute, and the borders between them and the rest of the country are tense (Figs. 16.1 and 16.2).

Fig. 16.1 Republic of Georgia: Geopolitical map (from Edward Walker's blog: eurasiageopolitics.com, with permission, 6/21/2016) [1]

Fig. 16.2 The mosaic of ethnicities in Georgia (from Edward Walker, with permission)

16.2 Mental Health Care in Georgia

Georgia is a former Soviet Republic, which regained its independence in 1991, after the collapse of the USSR. Over the last decade of the last century, Georgia went through difficult social-economic and political changes, including a civil war and two revolutions. The economy was almost paralyzed. The basic health-care services needed substantial changes. The "Semashko" system (a Soviet system of state-owned health facilities and state-funded health professionals), which was unaffordable for the new independent state, had to be reorganized in a new, more adequate model [2].

Since 1995, the number of inpatient psychiatric beds has decreased significantly (from 5000 to 1490), but outpatient and community mental health care has not been developed.

Currently, inpatient mental health services are delivered through nine specialized institutions and three departments (30-bed units) within general hospitals. Outpatient care is mainly provided by soviet-type psychiatric dispensaries, so-called ambulatory units, which offer certain amount of low-quality psychotropic medication and consultations with psychiatrists (usually, once per month for 10 min). Most of the mental health services are localized in the large cities or regional centers. In relatively remote areas, neither inpatient nor outpatient services exist. Mental health care is not integrated in the primary health-care system, and primary health-care professionals, especially in rural areas, do not have appropriate knowledge and skills to manage or even recognize mental health problems.

In 2015 two mobile community-based and four multidisciplinary crisis intervention centers (only in large cities) were included in the state program and funded by government.

According to the official data on mental health in Georgia (2013):

- In outpatient clinics 68,922 cases of mental and behavioral disorders were officially registered and diagnosed. For the first time during the lifetime, 3020 of them were diagnosed.
- The prevalence of reported mental disorders per 100,000 population was 1536.0 with incidence rate of 67.3 per 100,000.

This data is likely to be an underestimate of the actual burden of mental illness. It has been suggested that only a small proportion of individuals who have mental symptoms and who are in need of mental health care actually receive appropriate services [3].

16.3 Mental Health Budget

Mental health (MH) services are financed by the state budget. The role of private and corporate insurance in MH services in Georgia is very limited.

In 1995, Georgia adopted a mental health-care program (as a part of a new general health-care program) in which mentally ill people with psychotic symptoms or significant behavioral problems receive services and treatment free of charge, both at hospitals and in outpatient clinics.

Public health allocations for MH in Georgia were somewhat increased during 2006–2011, but the volume of spending on MH as percentage (%) of the total public health expenditure did not change and was about 2.5% [4]. For the recent years, in 2012–2015, this indicator has been even dropped to 1.9%.

16.4 Human Rights and Mental Health

Recent studies carried out in Georgia reveal a strong link between mental health problems, social exclusion, and poverty [5]. Gross violations of basic rights of inpatients are stressed in special reports of the Public Defender's Office based on regular monitoring of closed psychiatric institutions.

Violations range from inappropriate involuntary hospitalization (which is forbidden by the Law on Psychiatric Care, introduced in 2007) to violations of a patient's right to privacy, information, and rehabilitation. The European Committee for the Prevention of Torture has repeatedly criticized the Georgian government for the poor conditions in the country's mental institutions.

Reports on the monitoring of mental health institutions in Georgia published by the special prevention group of the Public Defender of Georgia highlight the problem of insufficient funding that ultimately leads to lack of qualified personnel; inappropriate therapeutic environment; low-quality treatment, care, and psychosocial rehabilitation; long hospitalizations; and unavailability of community-based services.

During visits to the psychiatric institutions, the monitoring group noticed scores of cases of physical and verbal abuse of patients. They criticized placement of patients in extremely unacceptable conditions in some psychiatric institutions, frequent physical and chemical restraint, lack of privacy and use of physical restriction methods and injections in the presence of other patients, and unavailability of timely and adequate treatment for somatic diseases. Long-term hospitalizations, negligence, and involuntary medical intervention were highlighted.

16.5 The Mental Legal Framework [6–9]

In December 2013, the Parliament of Georgia adopted the "National Concept on Mental Health" as the main mental health policy document of the country. The state concept defines directions of a balanced care: "Balanced development model includes in-patient care, community-based services and strikes a balance between pharmacological treatment and psychological therapies; balance between preferences of people with Mental disorder and family and community interests; and balance between methods of prevention, treatment, and rehabilitation."

In order to implement the concept into practice, the Ministry of Labour, Health and Social Affairs of Georgia adopted "The National strategy and action plan for the years 2015–2020" in December 2014.

The renewed version of "Law of Georgia on Psychiatric Care" was adopted by the Parliament of Georgia in 2006. Some additional changes concerning human rights issues with regard to restriction, inpatient care, involuntary and compulsory treatment, forensic psychiatric expertise, etc. have been made later in 2009–2015.

This version of the "Law of Georgia on Psychiatric Care" is more in-line with the international human rights standards. In 2009, Georgia signed "the Convention on the Rights of Persons with Disabilities," and in 2013, the parliament ratified the convention.

Recently, the Ministry of Labour, Health and Social Affairs of Georgia with support of the Council of Europe has announced the urgent need of developing an internal body for monitoring and supervision of mental health institution in terms of human rights and legislation [10].

Positive trends are noticed. The service users and their caretakers are more actively involved in all aspects of mental health-care development, including discussions of policy and strategic plan, as well as treatment and other clinical guidelines. Nongovernmental organizations (NGOs) have been established by people with mental and intellectual disabilities and their family members.

16.6 Education

Since 2008, a number of clinical guidelines and treatment protocols have been developed, but due to the acute shortage of resources, both human and financial, they were not fully implemented, yet.

In 2006, the government abolished the obligatory continuing education. As a result, qualification of mental health professionals declined. For nurses, social workers, psychologists, and psychotherapists, neither specialization in mental health nor formal regulations for permission and license for clinical practice are currently applied.

The miserable financing of mental health care directly influences working environment and salaries. Medical students and other professionals are not motivated to become mental health specialists. In average, Tbilisi enrolls only two to three new residents in psychiatry each year.

However, on a positive note, after 10 years of struggling, a new residency program in child psychiatry started in 2016.

Since 2014, Ilia State University has launched the master program in mental health. Each year 10–15 students with bachelor's degree in psychology, social work, occupational therapy, and other social, humanitarian, and medical specialties apply to that program.

16.7 The National Institute of Mental Health and Its Role in Georgia Health Research, Policy, and Services

In 1925, the Research Institute of Psychiatry, named after M. Asatiani, was founded in Tbilisi, Georgia. From the very beginning, this establishment had been at a leading position in the field of psychiatric science in the former USSR. By 2010, the Institute had published almost 15 textbooks, 56 thematic collections, 70 methodological letters, more than 130 monographs, and 4200 scientific articles in Georgian, Russian, English, German, and French. In 2011, as a part of ongoing reform of psychiatric services, it was transformed into the Center for Mental Health and Prevention of Addiction and still maintains scientific strength. Along with research activities, the Center is open to under- and postgraduate education of students from Tbilisi State University, Tbilisi State Medical University, and other educational institutes.

16.8 Timeline of PTSD and Other Stress-Related Disorders in Georgia

Due to the recent turbulent history of Georgia, it is sensible that post-traumatic stress disorder (PTSD) has been of special interest to the National Institute of Mental Health and other Georgian scientists. Early studies on psychotrauma are attributed to Asatiani (1920) [11], Zurabashvili (1957) [12], Menteshashvili (1957), Chitava (1957), Svani (1963), etc. At the end of the 1980s, profound interest toward PTSD was displayed by several researchers: Naneishvili et al. (1990), Duduchava et al. (1990), Lazarishvili (1993), Naneishvili et al. (1995), Kharebava (1996), Jishkariani et al. (1997), Zurabashvili (1998) [13], and Okribelashvili (1999) [14]; the two last ones wrote and defended doctoral theses on PTSD.

The end of the twentieth century was marked by global, political, economic, and social changes. The Soviet Union (USSR), which united multiple diversified people with different backgrounds, histories, attitudes, beliefs, ethnicities, and cultures, collapsed and disintegrated. Georgia did not emerged from this process peacefully. On April 9, 1989, an anti-Soviet peaceful demonstration in the center of the capital—Tbilisi—was dispersed by the Soviet Army, resulting in 20 deaths and hundreds of injuries. From that day Georgian society was drawn into long traumatizing journey. Upon the dissolution of USSR, the breakdown of ideological archetypes, the crash of social traditions, reappraisal of spiritual values, tendency of increase of aggressive behavior, etc. expressed itself in armed conflicts and agitated Georgia for several years. In 1991–1993, ethnical cleansing in Abkhazia and "South Ossetia" caused forcible migration of almost 300,000 persons, who had started their existence in a so-called failed state with heavy political and economic crises.

In 1996–1998, the Research Institute of Psychiatry received a state grant with two main goals: elaborate pattern of adaptive and compensatory mechanisms of the person in prolonged stress situations and reveal the general mechanisms of appearance and development of mental disorders due to social and traumatic stress.

The study enrolled up to 2000 persons, living at the collective centers (random sampling), military personnel, and a control group—representative of the recipient-host society, who lived under social stress (vulnerable community).

According to that research, most of the people involved in civil war had to make hard decisions as on the other side of the fire line they had relatives, ex-neighbors, ex-friends, or simply, compatriots. In 75% of cases, investigators observed an agonizing feeling of unwarranted, unjustified war. It was also revealed that 4–5 years after forcible migration and trauma experience, in 38.9% of internally displaced people (IDPs), there was no evidence of PTSD (vs. control group 81%), while almost 60% of IDPs were diagnosed with chronic PTSD (F43.1). In contradiction with most findings, PTSD was less developed in the young population (17–25 years), while ongoing PTSD was mostly diagnosed in the age group of 36–45 years. Personal changes (F62.0) of 27.1% (vs. control group 1.8%) were closely associated with recognition of essential living problems due to forcible migration and traumatic experience. Main contributors for chronic PTSD were considered to be:

(a) Unemployment. For instance, during 5 years after displacement, in persons with ongoing PTSD, unemployment increased by 42.5% and with prolonged PTSD by 10.5%, while the employment did not correspond to previously acquired knowledge and experience (low social status).
(b) Lack of proper housing, water, electricity, and heating.
(c) Inadequate access and distribution of basic social and medical services that caused dramatic growth in morbidity and mortality.
(d) Reexperiencing of protracting negative emotions related to loosing of "Motherland," economic difficulties, social disintegration, and uncertain future.

The Russo-Georgian War of 2008 forced almost 130,000 people (about 1/3—children and adolescents under 18) to leave homes, all properties, farms, and in general focal points of existence far behind. August 2008 brought war to thousands of people, who found themselves in unfamiliar milieu, where intolerable martial law was applied to ordinary life. Moral rules, which were unacceptable, even forbidden (i.e., violence, homicide, rape, torture, etc.), became the rules for wartime life. These losses, along with a fear of being killed, created so-called massive collective stress. Even the population of nonwar-prone zones (almost 1.8 mln in Tbilisi, Kutaisi, Poti, Senaki, Zugdidi) was under psychological distress due to military attacks of Russian air raids and bombings.

In contrary to the early 1990s, when Georgia first faced the problems of massive internal displacement, the state was able to render IDPs' rescue assistance with shelter and support. The government assured IDPs' financial safety and security. Access to medical services was available but limited. Immediately after ceasefire, government started mobilization of human and other resources (parliament, NGOs, volunteers) in order to coordinate crisis intervention activities. Common problems in IDPs at rescue stage were inappropriate housing (including schools, kindergartens), lack of fundamental basic needs (e.g., food, sanitarian standards), unequal or

overlapping distribution of psychosocial support, chaotic efforts of NGOs offering emotional "first aid," lack of disaster counselors, etc. Psychologists and psychiatrists working at collective centers observed effects of psychological distress (insomnia, fears of future and health of relatives, those in conflict region, etc.), acute stress reactions, use of alcohol/drugs, and health-care problems (including physical symptoms of distress: panic attacks, high T/A, cardiovascular disorders, and headaches). Based on PTSD worldwide epidemiology and preliminary data (severity of stressors, age groups, life-threatening, etc.), the mental health professionals were expecting approximately 10–15% of IDPs to be diagnosed with PTSD; this however was not the case here [15].

16.9 Inferences (by the National Institute of Mental Health): What Should and Can Be Done During Next Crises

If symptoms and signs of PTSD are not immediately recognized at the gatekeeping point of primary health-care services, this may be due to and result in ineffective utilization of medical services, less targeted utilization of resources, reduction of quality of life, family violence and re-traumatization of youth, failed communication and education systems, disrupted social sphere, and impaired economic activities. For instance, the new villages, constructed for IDPs, might lead to continuous community-based support, but not to integration.

Therefore, most important activities for enhancement of coping abilities and resilience of vulnerable groups should be directed to identification, mapping, and coordination of NGOs and government activities; development of outreach and specialized MH services to identify those in need, establish register for pre- and post-stress vulnerable population, and provide specialized MH services for IDPs in need; education of teachers and psychologists in conflict-prone zones and among displaced populations, to develop school-based and other community services; and development of targeted economic programs for community strengthening. More actions should be collaboratively developed.

16.10 Need to Collaborate with Other Agencies

Scientific and technological advances of recent decade suggest that individual biological responses to trauma are associated with resilient phenotypes. Georgian psychiatrists would be very proud to become a part of international investigations on environmental, psychosocial, epigenetic, and neural mechanisms that underline resilience that shape emotional reactivity and social behavior. These types of investigations couldn't be done without involvement of international organizations and establishing regional projects for identification of existing resilience rates within the community. This should lead to effective disaster management at the regional and national levels.

16.11 The Initial Collaborative Process

In preparation for Halbreich's arrival at Tbilisi, the capital of Georgia, the Georgian designated coordinator—Professor Eka Chkonia—initiated discussions with leaders of the psychiatric community and major facilities. In several introductory meetings with psychiatrists, clinicians, and administrators as well as basic neuro-psycho-scientists, current resources, facilities, strengths, and limitations were discussed. Intensive schedule of meetings with potential important collaborators was arranged in a sequence that will amplify the outcome of negotiations.

First order of business was securing the cooperation and collaboration of authoritative representation of Georgia Family Medicine Association, since family primary care practitioners are the first line of entry to clinical assessment and care. Especially outside of large city centers, the setting for medical actions is community clinics; therefore, it is important to establish quality screenings and referrals in organized community services. Luckily, the Georgia Family Medicine Association and Georgia Community Services are under the same personal umbrella. Perspective and needs of primary care settings have been illuminating and informed mind-set for discussions with the Georgia Institute of Mental Health and Prevention of Addictions which is more specialized and scientifically oriented.

With the National Institute of Mental Health, national trends of epidemiology were reviewed with emphasis of influence of recent events on public health and mostly on post-traumatic stress disorder (PTSD). Research and assessment capabilities were reviewed.

Leaders of community services and the National Institute of Mental Health joined us for the meeting with the head of Health Policy Division of the Ministry of Labour, Health and Social Affairs and her team. She reviewed health and mental health processes from the government's perspective as well as decision-making procedures and powers that influence them. The professional associations, NGOs, and institutes' representatives entered into a future-oriented discourse of needs, possibilities, and realistic probabilities. Capabilities of the Ministry Division were delineated, and the group started crystallization, lobbying for the country's common interests.

The mental health professionals agreed on deficiencies and needs but were not in unison concerning actions for progress and achievement. All agreed on inclusive collaboration. Initial time frame was set by the fact that a regional Caucasus executive meeting, which included representatives from Armenia and Azerbaijan, in addition to Georgia, was scheduled for the end of that week (the meeting took place in Tbilisi, Republic of Georgia, because of the war situation between Armenia and Azerbaijan which prevents their citizens from traveling to the enemy country).

Halbreich asked the group to focus on local Georgia issues but consider generalizations so the Georgia solutions may be a model for implementation in other countries. He acted as a moderator and at that initial stage avoided suggestions of needs and Westernized solutions. The approach was: "you know your situation best, what do you think are your specific needs, what can you specifically do about the problems, learning from others but not copying them." Most of the time Halbreich was

an observer, only asked questions for clarification and then summarized an issue when he felt that it was satisfied.

The process of group forming was facilitated by a culmination of individual meetings with each of the stakeholders. These meetings were initiated as mutual introductions of the visitor-expert and the local leader. The visitor mostly listens while the institutes and their context were described. Informative questions were asked, but opinions were expressed only when they were specifically requested. From the first meeting, it was apparent that there are similarities of "complaints" and lists of deficiencies and needs. Halbreich introjected comments as "yeah, this is similar to what I heard from Dr X" to encourage more elaboration and sense of common difficulties and common interests. By the time that we arrived at the Ministry, the dynamic was such that we were a group hoping to lobby the decision-makers. However, the head of the division found support from all colleagues in her considerations of what and how to present recommendations to the political level. At that point Halbreich was somewhat more active and suggested what specific data would support the suggestions and how to present and interpret them (Fig. 16.3).

This opened a targeted discussion on the sort of data that actually is available, gaps in information, and what should and can be done. When participants expressed their wish to attend the regional meeting, it was positively agreed but mostly as observers. Eka Chkonia would be the active Georgian representative.

The group spoke in one voice about the general situation of Georgia and its impact on mental health. The impediments for solutions and the common feelings of deficiencies served as a cement for the group which became more informal by time. Halbreich channeled the "chat" toward agreement that the similar weaknesses and frustrations may point to the possibility that together the group can strengthen each other and create common and shared human and physical capital. From there the realization and hope that cooperation with the neighboring countries, who share the same civilian stressors and deficiencies, was a rational step toward progress.

Fig. 16.3 The initial Georgia group at the working meeting at the Ministry of Labour, Health and Social Affairs, August 2016

16.12 To Summarize

The guiding operational principles of establishment of the interdisciplinary collaborative process have been:

1. Determination of current problems and needs as perceived by **local** practitioners and experts
2. Definition of an optimal goal by each stakeholder
3. Assessment of resources and means of each discipline
4. Objective assessment of strengths and weaknesses of each group
5. Establishment of a **common denominator**
6. Realization that pooling resources and efforts together strengthen all
7. Agreement on a **common goal**
8. Discussion and ventilation of obstacles, frustrations, past experiences, and hopes
9. Enhancement of a group spirit
10. Structuring group priorities and their sequence
11. Planning next actions and "who is doing what"
12. **Actions** (absolutely need to follow decisions!)

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Mental Health Consequences of War Conflicts

17

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Abstract

Modern war conflicts, evolutionizing from large-scale collisions of armed forces to local, low-intensity, surrogate, terroristic and information wars, are associated with less direct mortality but with growing and long-lasting mental health consequences. These consequences can be traced in not only combatants and other military contingents and veterans but even to greater extent in the civilian populations, given that many modern war conflicts have signs of civil wars or religious conflicts. While active duty military undergo preliminary selection and resilience training, civilians in the war zone or as refugees and asylum-seeking victims are even at higher risk with the greater probability of transgenerational transmission, which implies long-lasting (decades) effects. Both military and civilians suffer from a similar set of disorders and psychological consequences caused by extreme trauma, including PTSD, depression, anxiety, addictions, somatization with chronic pain, dissociation, psychosocial dysfunctions, suicidal behavior, etc. War conflicts, terroristic acts, and information wars, amplified by technologically developing mass media, the internet and social networks, seem to add to a general feeling of instability and promote more anxiety, covering even wider contingents worldwide. Military psychiatry has accumulated knowledge and practical experience that, though not always can be applied directly, are useful for identification, management, prevention, and treatment of mental health consequences of war in wider contingents. This knowledge is a one more relevant and strong reason for advocating lowering of international tension and reducing the probability of war conflicts worldwide for the sake of preserving mental health of the humanity. It also has a potential of lowering the burden of this type of diseases worldwide.

17.1 Introduction

The impact of warfare of mental health conditions of the military and on the general population started to attract attention only in the several recent decades. Negative consequences of war have been traditionally evaluated in terms of mortality. During WW I more than 70 million of military personnel were mobilized, and 9 million of combatants and 7 million of civilians have died, almost the same number were permanently disabled and twice more seriously wounded. During WW II, which involved 62 from 73 countries existing by the moment in the world, already 130 million of the military were mobilized, while 25 million of combatants and 47 million of civilians have died. These amazing figures give an impression how little human life was valued only a century ago. No surprise that those military who survived were considered lucky, and their psychological sufferings were not in the focus. Not much attention was paid to social trauma and mental health of the civilians either.

The title of this review embraces very wide circle of issues. One can include here mental health consequences of the warfare for combatants (those who are directly involved in collisions on the battlefield); for the military in more general terms,

including support troops, reservists, etc.; for veterans of different wars; for the civil population in the region of conflict; for refugees; for victims of genocide; and even for wider contingents, which are influenced by mass media reports of war. Each of these issues has been scrutinized by many authors. Psychological and psychiatric aspects of the acute combat exposure, early management of combat stress, and preliminary selection and resilience training are the subject of the military psychiatry with its own principles and methods [1–5], while mental health of veterans is taken care of either by specialized administration (like in the USA) or by civilian specialists like in the UK [6]. Many aspects of the civilian mass trauma are discussed in the recent influential publications of WPA and UNICEF [7, 8]. Some issues of the impact of mass media exposure and information war are covered within the evaluation of mental health consequences of terroristic acts and natural disasters [9, 10].

Nevertheless, all these issues are unfortunately rarely discussed in conjunction. We consider that such combined representation is quite relevant as far as all contingents involved—acting military, reservists, war veterans, the civil population in the region of conflict, refugees, and wider contingents—are adding to the general growth of psychopathologies, mental health problems, psychosocial dysfunctions, self-destruction, and other mental disturbances that constitute burden of disease on the society as a whole. The main causative of it is war conflicts, which are spreading around the globe in a progressive manner. All this cannot but disturb both representatives of the professional community and wide public.

There is also another motivation to address this topic today. In the most modern times, the nature of war conflict has changed significantly. Modern wars may be characterized as "local," "low-intensity," "asymmetric," or "surrogate" wars where the enemy is not exposed and is not clear and where a growing number of local but constant never-ending conflicts eventually grow into global instability and chaos, associated with terrorists' attacks. Modern war conflicts have high technological level, while their location is often linked to inhabited cities and regions. They often have signs of civil wars or religious conflicts, which are characterized by especially high level of violence, embitterment, atrocities, and irreconcilability with extremely high probability of psychological distress and trauma [11]. The mental health consequences of this evolution are not assessed yet, it is a question of future decades. Nevertheless, some studies already provide relevant information. All the abovementioned issues will be discussed here by the international team of authors with consideration of the culture-specific aspects of the problem.

17.2 Combat Operational Stress Reactions

War is particularly traumatic for soldiers who most often appear in the situation of close and severe violence, including killing in a direct combat, viewing the enemy before or after killing them, and watching comrades die. Actually, from the earliest ages of mankind, the psychological impact of war on soldiers has been recognized among the other negative consequences of war, though not conceptualized in modern terms. There have been strivings for hundreds of years to apply an appropriate

name to psychological problems of soldiers exposed to extreme stressful experiences on the field. From the "nostalgia" during Napoleonic wars [12], "Swiss disease" [13], "irritable heart" or "Da Costa's syndrome" [14], "shell shock" [15, 16], and "battle fatigue" [17], there was gradual shift to combat operational stress reaction (COSR) or battle stress reaction. It should be noted that this shift took much time due to substantial stigmatization of those soldiers who suffered psychiatric disorders during World War I. Often those who broke down were labeled as "lacking moral fiber," and instead of receiving a popular diagnosis of the "shell shock," some could have been regarded as cowards with all that it implies in the wartime [1].

Finally, a concept of combat operational stress reaction (COSR) has emerged. According to recent practical guidelines, COSR refers to a reaction to high-stress events and potentially traumatic event exposure [18]. It is not considered to be an abnormal response to exposure to combat stressors and is not considered a psychiatric disorder per se, though it may result in a disorder over time. COSR has been described as a "normal" reaction to an "abnormal" experience. Modern guidelines emphasize that COSRs are "the expected and predictable emotional, intellectual, physical, and/or behavioral reactions of service members who have been exposed to stressful events in combat or noncombat military operations" [19]. As to the symptomatology, the transient problems may begin within minutes during and after the exposure and disappear within hours or days. The service member may experience physical signs, i.e., fatigue and exhaustion, psychomotor agitation, sweating, increased heart rate, nausea and vomiting, and insomnia. Difficulties in concentration, memory loss, disorientation, nightmares, and flashbacks are common cognitive disturbances, which could be experienced. On the emotional level, anxiety, fear, helplessness and hopelessness, mood lability, and anger can appear. Changes in behavior may include misconduct, careless behavior, withdrawal, and impulsivity [20, 21].

Terms associated with COSR like acute stress reaction (ASR), combat stress, and some traditional ones like "combat fatigue" or "battle neurosis" are used inconsistently. Military is stressing that combat stress is normal, generally short-term and should not be confused with regular psychiatric diagnosis. However, in psychiatric texts battle stress is sometimes uses as a synonym or subgroup of ASR. COSR is largely the result of the main principle of combat—either you kill or you will be killed. There is a direct relation between the intensity and time limits of fighting and the number of psychiatric casualty rates. In general, there is one psychiatric casualty for four wounded in action, though in different conditions, this ratio may vary. Depending on the severity of combat, the level of training and the tempo and time limits of engagement in a collision the rate of psychiatric casualties may vary from 3% to 30% of all casualties. Among troops that are defeated, the percentage of COSR and other psychiatric and psychological consequences will be inevitably higher than in those who win the battle [1, 2, 22–24].

On the other hand, evolution of the nature of war is changing the situation with COSR. In low-intensity conflicts, psychiatric presentations within operations consist mainly of adjustment reactions rather than acute stress reaction [24, 25]. Recent operations, which have usually been of a relatively fixed duration, have led to the majority of casualties presenting after return from operations; the numbers of frank intra-conflict

mental health casualties have been low. Data on admission to Czech and French field hospitals placed in Afghanistan shows that less than 1% of service members were referred to mental health professional or suffered from ASR [26]. In UK armed forces, mental health referrals represented around 0.4% of the UK force deployed [25].

17.3 Early Intervention Programs in the Armed Forces

During WW I, it was learned that mental distress needs to be managed in line with military demands to return as many men as possible to the front line [27]. The group of psychiatrists developed the concept of what has come to be known "forward psychiatry" [28, 29]. It could be summarized in the principles of proximity, immediacy, expectancy, and simplicity (PIES) and was subsequently used by the British and Americans in both World Wars [27]. Proximity is based on the principle of providing services to the soldier within his or her own unit or as close to the unit as possible. Expectancy is important as it does not focus on the soldier as a patient but as someone that is having a normal reaction to an extreme circumstance or condition. Simplicity is based on assuring that the soldiers' first-order needs (sleep, rest, food, water, hygiene) are available and provided. These principles still apply in the armies all over the world. Recently, they have been reformulated as BICEPS in US Army, which stands for brevity (refers to an initial intervention in COSR that lasts no more than 1–3 days), immediacy, centrality or contact (refers to an emphasis on the involvement of the service member's unit leaders in his/her care, in part to remind the service member that he/she continues to be part of the unit), expectancy, proximity, and simplicity [30–32].

During the eighties and nineties of the twentieth century, psychological debriefing (intervention performed by mental health professionals as soon as possible after potentially traumatic events) has been enthusiastically performed with the intention to allow either individuals or group of people to talk about their experience. During this brief crisis intervention, sufferers were encouraged to talk about their feelings and reactions to the critical incident [33]. The debriefing facilitator aims "to reduce the incidence, duration, and severity of, or impairment from, traumatic stress" [34]. Unfortunately, research revealed limited efficacy of single-session [35, 36] and multiple-session "debriefing" [3]. This intervention does not decrease the development of symptoms and in some cases, exacerbates them. Consequently, head organizations and institutes concerned with health, mental health, guidelines, and algorithms for management and treatment of posttraumatic stress reactions (i.e., the US Institutes of Mental Health, World Health Organization, Britain's National Public Health Service, etc.) have strongly recommended against the use of psychological debriefing. Psychological debriefing should not be mixed with operational debriefing, which is routine team review of a major incident from a factual perspective and has been used effectively to enable discussion.

As to medication possibilities, anxiolytics (mostly benzodiazepines) historically were the primary agent in the treatment of posttraumatic reactions. Nevertheless, there is theoretical, animal, and human evidence to suggest that benzodiazepines

may actually interfere with the extinction of fear conditioning or potentiate the acquisition of fear responses and worsen recovery from trauma [37–39]. If a service member treated with a psychotropic medication for a COSR returns to active duty, the effect of the medication on his psychomotor functioning should be evaluated.

In 2007 Hobfoll and a team of international experts have synthesized available scientific evidence and have formulated five essential principles of psychosocial care for people confronted with mass disasters, personal tragedies, or severe loss. From their perspective, the surrounding caregivers should promote (1) a sense of safety, (2) calming, (3) self-efficacy and community efficacy, (4) social connectedness, and (5) hope [31]. In relation to COSR treatment, some of these principles have been developed into several practical recommendations cited here.

1. Don't pathologize—acute stress management should not be carried out by the medical or mental health professional and should be simple and done within the unit and according to member's prior role, not as a "patient."
2. Don't psychologize—do not facilitate emotional reaction via group therapy or psychological debriefing, reactions that emerge are not indicative of a mental disorder, and interventions can be envisioned as more a correlate of physical, then psychological first aid.
3. Don't pharmacologize—there is still no evidence that any prophylactic medication treatment may prevent the development of PTSD (though such studies are in progress).
4. Educate—provide education about the broad range of normal stress-related reactions and natural course of interventions for posttraumatic stress disorders, and clarify that symptoms may be exacerbated by reexposure to traumatic stimuli or perceptions of danger.
5. Normalize observed psychological reactions to the chain of command and provide expectancy of recovery.
6. Address the basic needs by providing a wide range of psychosocial interventions aimed to facilitate contact with the caregiver, provide safety and possible comfort, ensure calming and stabilization, identify immediate needs and concerns, provide practical assistance in establishing connections with social support resources (friends, comrades, family, etc.), as well as provide information regarding coping and future opportunities of support. The last recommendation in this row is watchful waiting for those at risk for developing negative outcomes following trauma that can facilitate prevention, referral, and treatment. Specific treatment should not be commenced before 2 weeks after the trauma.

17.4 Combat-Related Prolonged Mental Health Consequences and Suicide Risk

In a certain percentage of cases, even if all positive recommendations are fulfilled, acute combat-related stress reaction will develop into more serious and prolonged condition—combat-related PTSD. For instance, data from the 1973 Yom Kippur

War show that 37% of veterans diagnosed with COSR during combat were later diagnosed with PTSD, compared with 14% of control veterans [40]. On the other hand, 16% of veterans without COSR may also develop PTSD [24]. The prevalence of PTSD among combatants and veterans varies in different cultures and warfare situations: from 16–17% among American Vietnam and Iraq war veterans and very similar figures among Soviet Army-Afghanistan conflict veterans [41–43] to 6–7% among Eelam war veterans in Sri Lanka [44]. On the other hand, it refers only full-scale PTSD, while there are studies that testify that separate symptoms of PTSD can be traced practically in all combatants [23].

PTSD is a very polymorphic and highly comorbid condition, associated not only with symptoms and syndromes that are considered "typical" (emerging after extreme stress, avoidance of the circumstances of the stressful situation, memory dysfunction, and increased psychological sensitivity and arousal) but also emotional disturbances (depressive symptoms), cognitive impairment, changes in the personality, addictive behavior, and self-harm [45, 46]. There is still a discussion if combat-related PTSD has certain peculiarities. Besides more severe manifestations, some additional psychosocial factors like a specific feeling of guilt, low social support, and rejection of the specific group of veterans by the public opinion may have an impact [23]. Though cultural peculiarities of trauma do exist especially regarding traditional rehabilitation strategies, PTSD is a phenomenon that is shared by both East and West if it comes about combat exposure [47].

Some veterans with malignant form of anxiety and a wider than the typical range of clinical symptomatology with severe psychosocial impairments may fit into the diagnostic category of DESNOS (disorders of extreme stress not otherwise specified) or complex posttraumatic stress disorder (C-PTSD). According to Herman [48], complex PTSD is a psychological injury that results from protracted exposure to prolonged social and/or interpersonal trauma in the context of either captivity or entrapment that results in the lack or loss of control, helplessness, and deformations of identity and sense of self. C-PTSD is distinct from, but similar to, PTSD, somatization disorder, dissociative identity disorder, and borderline personality disorder.

The most important feature of PTSD is that it starts to develop over time and lasts for months or years, sometimes with a tendency to chronicity. The patients with PTSD may have long-term consequences that can be divided into several groups: (1) chronic form of PTSD and enduring personality change after catastrophic experience, (2) comorbid psychiatric disorders such as depression, abuse of alcohol, or psychoactive substances, and (3) somatic diseases associated with chronic PTSD [49–56]. All this may adversely affect the ability of these patients to function in family, social, and work environment as well as interfere with the treatment and hamper recovery.

As the development of PTSD itself is affected by a number of etiological factors, including biological, social, and psychological ones, mechanisms that lead to long-term sequelae are inevitably complex. Some authors suggest that PTSD should be viewed as a heterogeneous diagnostic construct and that biomarkers should be investigated for each of the individual groups of PTSD symptoms [57]. Furthermore, the biology of routine stress response and biology of trauma are different, with the

"usual" stress causing a number of biological and physiological changes that are returning to "normal" after the stress has passed or after the body has established a new homeostasis. In contrast to that, in PTSD, biological changes last after the stressor has passed, what some authors call trauma "fixation" [58]. In addition, exposure to events that overwhelm coping mechanisms may damage self-regulatory systems essential for restoring the body to its previous state, and some studies emphasize the importance of changes in the "input filtering" in the central nervous system that helps distinguish relevant from irrelevant stimuli [58]. That could lead to a condition in which traumatized person may have difficulty in distinguishing between safe and threatening situations [58]. Some studies point out that the existence of dissociation in the early stages of acute stress disorder is one of the possible predictive factors for developing chronic PTSD [59].

PTSD is a disorder with the presence of comorbid disorders up to 80–90% [52, 60]. The most common comorbid disorders are major depressive disorder, anxiety disorders, abuse of alcohol or psychoactive disorders, and psychotic disorders. Depression is one of the most common comorbid disorders; up to 52% of patients with PTSD also have a comorbid major depression [55]. This may be due to an overlap between symptoms of PTSD and depressive disorder according to the current classification, though one cannot exclude that occurrence of depression with PTSD as a distinct phenotype [51].

PTSD and abuse of alcohol or psychoactive substances can also be found in comorbidity [61, 62]. Although there are several hypotheses that seek to explain the etiology of the connection of these two disorders, the most frequent one is that the abuse of alcohol or psychoactive substances is efforts to reduce the symptoms of PTSD, particularly hyperarousal, in an attempt of self-medication, especially among males [62–65, 146].

Furthermore, research shows that veterans who develop PTSD have a higher risk of developing certain somatic diseases or worsening existing ones, including obesity and dyslipidemia; hypertension and cardiovascular and cerebrovascular diseases; metabolic syndrome, diabetes mellitus, and ulcer; increased susceptibility to infections; and autoimmune disorders, chronic musculoskeletal disorders, osteoarthritis, chronic pain, fibromyalgia, and chronic fatigue syndrome [49, 53, 54, 66–70]. These conditions with a strong psychosomatic component may have multiple underlying factors, including biological factors (dysregulation of the hypothalamic-pituitary-adrenal axis, autonomic nervous system dysfunction, and inflammation), behavioral risk factors (substance use, obesity, decreased physical activity, medication nonadherence, and sleep disturbance), and psychosocial risk factors (comorbid psychological disorders and impairments in social functioning) [69, 71, 72].

Besides all abovementioned polymorphic manifestations, PTSD-suffering veterans often have a wide range of cognitive impairment, psychosocial disturbances, and dysfunctional behaviors including loss of the pre-traumatic personality structure, altered self-perception and distorted social interactions, alterations in the own system of values and meanings, dissociative flashback-driven violence, sexualized behaviors, sense of foreshortened future, self-harm, and suicide. With concomitant family problems, drinking, gambling, and somatization, such traumatized veterans constitute a very complicated contingent for treatment and rehabilitation [23, 47].

Early recognition of PTSD symptoms, working through the trauma, psychotherapy, and/or psychopharmacological treatment can help reduce long-term consequences and the occurrence of comorbid psychiatric and somatic conditions. If they occur, an integrated approach is needed for the treatment of both mental and possibly existing somatic conditions. It is necessary to provide an individual approach to the patient and individually evaluate best psychotherapeutic and pharmacological treatment for the patient, including socio-therapy procedures and rehabilitation, with the aim of remission of symptoms, stabilization of the condition, and improvement of the quality of life.

All abovementioned psychosocial and mental health problems of war veterans, but mostly depression, PTSD, alcohol and other substance use disorders, pain, and traumatic brain injury, constitute factors of enhanced risk of suicide [73–78, 147]. War veterans in many countries are an important part of the society that attracts the attention of mass media, politicians, and a wide public; thus, suicides among them are often scrutinized, and prevention programs are evaluated [73, 79].

Suicide in veterans is a controversial issue. Veterans are a heterogeneous group that is not easy to reach, which impairs objective studies. Nevertheless, according to the data collected among 17 NATO and Partnership for Peace (PfP) nations, it is apparent that in many countries suicide ranks highly among the leading causes of death within the military personnel, often much higher than in the general population. Moreover, in several countries, the military suicide rate (per 100,000) is higher compared with the suicide rate in the general population [80]. An example is the USA, where suicide rate among army members has increased strikingly during the last decade and exceeds since 2008 the rate in the general population [75, 81], and the rate of suicide in veterans is higher than expected [74, 82].

The most significant protective factor against suicidality seems to be a social support that enhances resilience—from the partner, from family, from friends, and also from military leaders and buddy soldiers [74, 76, 83]. In addition, positive attitudes and appreciation by society for serving in the military and participating in deployments provide protection against suicidality [83, 84]. Besides, individual-level protective factors are post-deployment sense of purpose and control [74, 76], sense of coherence and meaningfulness [83], self-forgiveness (i.e., being kind and generous toward oneself) [85], and spiritual health and well-being [86].

Some specific risk factors related to the context of military service include having been in active duty during military service [78], involuntary repatriation from service [87], witnessing violence, perceiving powerlessness, and having pointless tasks during deployment [83, 84]. Within the military system, the availability of firearms, as well as knowledge and skills in using them, is a relevant factor [73–75]. Early life stress and dysfunctional family relations [84] as well as negative life events may be important precipitating factors [87]. Suicide risk is also elevated if the barriers to care exist: lack of psychological resources [74], longer time from the last deployment to screening for mental health problems, and geographical distance from care facilities [78].

Different stages in the military life cycle comprise some specific vulnerabilities. For example, during the post-deployment stage, the service members have to redefine their role both in the military system and in the family. They may encounter

false perceptions, inadequate expectations, societal disapproval of the mission, lack of social support, and other psychosocial difficulties. When combined with limited access to mental health services and the tendency to self-medicate with substances (alcohol, drugs), these vulnerabilities may increase the risk of suicide. The final stage of the military life cycle—end of military service—means psychosocial tension due to difficulties in finding one's position and identity as a civilian, mental (and physical) health impairment due to experiences during deployment or during the military service in general, etc. [80, 88].

Among different theories of suicide, the Joiner's interpersonal-psychological theory has been found as the most appropriate one to explain suicidal behaviors among military personnel [79, 80, 89, 90]. According to this theory, three variables should be present for a person who eventually die by suicide—sense of thwarted belongingness, perceived burdensomeness, and acquired capability for suicide. The first two variables generate the desire to die by suicide (psychosocial vulnerability), and the third variable enables to reach to the lethal suicidal act by acquired habituation of self-injury or witnessing/engaging in violence (e.g., exposure to a combat situation). The Joiner's theory has been tested in several studies within the military system with good confirming results [89, 91, 92].

17.5 Military as Occupation: Preliminary Selection and Psychological Resilience Training

To diminish the deteriorating effect of combat stress, two principal strategies may be involved—to implement selection procedures that may rule out vulnerable personalities and to develop and introduce approaches and methods of special training that may attenuate the possible impact of trauma, i.e., to build resilience of the military personnel. Nevertheless, although preventing the war pathology sounds attractive, it is, at the same time, very controversial, as it is disclaimed by some armies and sustained by others.

17.5.1 Preliminary Selection Principles

This type of activity has been one of the first systematic attempts of preventing and limiting the occurrence of traumatic stress reactions. The huge number of psychological victims during the WW I stimulated search of methods to create a combat force invulnerable to psychiatric injury, so as by the beginning of WW II, the American army considered that a successful fighter could be predicted and thus selected. However, the reality showed that the screening could not select "the best and the brightest who could make insuperable warriors" [93] and neither rejects those whose psychological profile could make them prone to developing psychological disorders. Quite the contrary, during the WW II, US psychiatric casualties were more than twice compared to those of the previous war. It appeared that prediction methods were not sufficiently precise and of those recommended for

rejection due to psychiatric reasons, only 18% were later discharged on this reason [94], so US Army gave up the screening program.

The fact that there is not enough evidence that screening using psychological questionnaires could have a predictive value was the reason for stopping mental health screening before deployment also in the Armies of Australia, Canada, Netherland, UK, and the USA. Other discussed reasons were that screening could have negative effects on the career and mental health and well-being of service personnel [95, 96] and that results of the screening for psychological disorders may have counterproductive effect on manpower, often rejecting those who would have made good soldiers [97]. Besides, "there are extensive selection processes in selection for combat corps and most frontline roles that are a form of screening itself" [5].

In other countries, such as Austria, Bulgaria, or Romania, as well as in the Armies of the countries of the former Soviet Union, psychologists are still using the psychological testing or screening before deployment in order to exclude soldiers who might put themselves or others in danger during combat or peacekeeping operations and soldiers who have a low stress tolerance and adaptation capabilities [23, 98, 99]. The focus in these selection activities is on cognitive abilities, personality structure and specific traits, trauma and suicidal behavior history, and psychopathological clinical symptoms. In these Armies, the reduced number of psychiatric casualties after participating in combat missions and exposure to war trauma is supposed to be due to this selection stage and psychological support programs before, during, and after deployment [98, 99].

It is already well established that unresolved childhood trauma (existential, attachment, or loss trauma), highly stressful life events, lack of internal locus of control, and low intelligence are factors that increase the risk of PTSD [100–104]. Thus, mental health professionals should consider assessing the military personnel for vulnerability, exploring before deployment prior exposure to traumatic events, current or past psychopathology, and familial susceptibility. Moreover, recent recommendations of the Group NATO RTO HFM-081 admit that the military personnel selection solely at the beginning of the career is not enough and therefore support psychological evaluation before deployment as a possible measure of prevention of posttraumatic war pathology.

17.5.2 Enhancing Resilience in Combatants

Resilience is the ability to maintain a stable equilibrium in the face of adversity [105], which means that the person preserves a relatively stable behavior, emotions, and cognition within the range of healthy levels of psychological and physical functioning or quickly returns to normal functioning after extreme stress. In order to enhance the resilience, the training should begin by developing the motor abilities, so that in combat, the soldier can perform with maximum safety and mental energy and the time necessary to perform an action is reduced. Combat often implies extreme reactions of the sympathetic nervous system within acute stress reactions so that the performance can be altered. Building resilience by training

before missions is supposed to allow militaries to perform in stressful situations, helping them to recognize their physiological and emotional reactions and control their stress level.

The most frequent and efficient practice used in many armies before combat missions is stress inoculation training (SIT). As described by its founder, Donald Meichenbaum, in the 1970s, stress inoculation therapy (SIT) targeted a diverse population of individuals. Meichenbaum argued that in order to defend, or "inoculate," against potential traumatizing stressors, trainees must be taught preemptive strategies on how best to deal with them [106, 107]. In 1988, the National Research Council verified this approach, finding that stress surrounding an event can be diminished by first giving an individual knowledge of what to expect [108]. Thus, while new tasks can induce stress responses, SIT presents these tasks, often via mental imagery, in controlled settings in order to enhance the trainee's self-efficacy and facilitate performance improvement. According to this approach conceptualized as "cognitive-behavioral modification" every aspect of the battlefield is repeated over and over again so that soldiers can perform in the extreme stress conditions of combat. Thus, SIT diminishes the risk of a potential negative reaction of the soldiers, and it is done by gradual, controlled, and repeated exposure to highly stressful situations, similar to those on the battlefield, in order to desensitize the respective situation, so that the flight or freeze response would not appear.

Technological advancements over the past 20 years have introduced novel approaches to SIT, such is virtual reality SIT (VR-SIT). In this method, a military personnel is introduced to stressors via virtual reality (VR) while their physiological responses are monitored. Soldiers are trained in virtual environments by means of scenarios that contain elements related to the war zones, so that these trainings could be transferred in real environments, with specially created tactical exercises**.** Ultimately, repeated exposure to physiologically and psychologically tasking situations progressively desensitizes the trainees, equipping them with a set of coping strategies from which they can choose those that best suit their needs in a specific occasion. This ensures the transfer of the training from the virtual world to the real world and the remediation of the insufficiently learnt abilities, which has, as a direct effect, the improvement of the troops [109].

Recently SIT has been extended also on the medical staff, who are often members of the initial assault forces and whose mental health is also under threat. This is based on the so-called injury creation science (ICS), which is an injury simulation tool that provides both the programs and prosthetics necessary to adjunctively train medical professionals in a variety of interventions. Now ICS is a validated tool for US Army combat medics that has both important first aid skills training and stress resilience hardening components [110, 111].

Besides SIT, which is a technique that helps soldiers become resilient to potential future stress factors, another way of enhancing resilience before combat may be psychological treating previous trauma, which is known as a predictor of severity of PTSD symptoms in combatants [104]. This constitutes a promising direction that may be the subject for future studies.

While there are obvious achievements in the field of pre-deployment resilience training, enhancing resilience during combat still remains a questionable issue. The empirical evidence indicates that people experience disruptive psychological symptoms immediately following violence. It is well known that acute stress disorder can lead to PTSD and chronic PTSD ([112–114]. It highlights the importance of providing early psychological intervention (EPI) to victims of interpersonal violence [98, 115]. EPI can take many forms, and it is very controversial, as there are contradictory studies about its efficiency [3]. However, it is important to remember that intervention in crisis situation does not mean trauma psychotherapy and that its role is to prevent the development of PTSD and stopping the posttraumatic symptoms from becoming chronic.

Recent studies [116, 117] report the success the eye movement desensitization and reprocessing (EMDR) method has in different crisis situations, from natural disasters to terrorist attacks. Early EMDR intervention (EEI) may be used to treat acute distress and also can prevent complications and strengthen resilience in short interventions, which suggest their possible application in the war zone.

Though there is a progress in SIT and other computerized technologies of resilience training, one must keep in mind that resilience to combat is a very complex feature, which is far beyond these technological approaches. Individual variability in how humans respond to stress and trauma depends on numerous genetic, developmental, cognitive, psychological, and neurobiological risk and protective factors, which implies the whole life trajectory in which special training is only a part [118].

17.6 Mental Health Consequences of War in the Civilian Population

Civilians have always suffered immensely during wartime, but in contrast to traditional wars of the past, in recent wars civilians have been the main target of violence. In previous wars, 90% of casualties were military, while recently 90% are civilians [119]. This is especially true for mental health casualties and long-term mental health consequences. Recently accumulated data from different parts of the world (Afghanistan, the Balkans and former Yugoslavia countries, Cambodia, Iraq, Israel, Lebanon, Chechnya, Palestine, Rwanda, Sri Lanka, Somalia, Uganda, and others) report about severe trauma and inevitable mental health disorders and psychological sequelae in civilians. In different populations percentage of depression ranged from 16% to 68%, while of PTSD – from 25% to 60%, other prevalent conditions were anxiety, somatization, alcohol and drug abuse, different signs of functional disability, and a variety of psychosocial impairments [120]. Rather typical picture of war-related trauma in civilians (Sri Lanka experience) looks as follows. Nearly one-half had experienced between five and nine war stresses and one-quarter experienced over ten (mean 6.66). Only 6% had not experienced any. Sixty-four percent had developed psychosocial sequelae, including somatization (41%), posttraumatic stress disorder (27%), anxiety disorder (26%), major depression (25%),

hostility (19%), relationship problems (13%), alcohol and drug misuse (15%), and functional disability (18%) [121].

It is well established that women and children are at greater risk, that the severity of experienced stress correlates with psychological and psychiatric outcomes, that early life adversities and personal and family psychiatric history are associated with higher risk, while social and psychological support is the main factors that may attenuate war-related traumas, especially with the special role of cultural traditions and religions [47, 104, 120]. Posttraumatic symptoms may be noticed in children aged 1.5–5 years if exposed to daily war-related trauma, with certain peculiarities and usually associated with developmental regression, which implies long-lasting consequences [122].

War conflicts inevitably lead to a massive migration of the civilian population, either trying to escape from direct bombing and shooting inside the country or looking for better economic and secure conditions abroad. Estimations for the year 2013 report that more than 50 million people in various parts of the world were being forced to flee from war, of them 33.3 million were internally displaced persons, 16.7 million refugees worldwide, and 1.2 million asylum seekers [123]. This is associated with a variety of stressful life events, like loss of a family member, loss of a home and shelter, hunger, low access to medical resources, anxiety about future, and many others. Though outcomes of migration may vary, migrants and refugees often find themselves in the situation of lower socioeconomic status, frequent unemployment, cultural conflict, hostility, rejection, etc. Recent studies report of prevalence rates of depression among refugees ranging from 3% to 80%; PTSD, from 5% to 86%; and anxiety disorder, from 20% to 88% [124]. Other frequent consequences are obsessive-compulsive disorder, somatization and persistent pain, complex PTSD, prolonged grief reactions, substance abuse, dissociation, and eating disorders [47]. Mental health disturbances in refugees are long-lasting (years) and depend on post-migration socioeconomic status [124].

Many modern war conflicts have signs of civil or religious wars, which are often associated with atrocities, tortures, sexual violence, extrajudicial killings, captivity, and generally higher level of violence, than interstate conflicts, in which war crimes are more restricted. Moreover, moral justification in the form of dehumanizing of the opposing part is often present. Victims of civil wars experience similar mental health problems as other war victims, with the high prevalence of PTSD, anxiety, sleep disorders, psychological impairment, and paranoid ideation [125, 126]. Historical examples also suggest that rehabilitation and overcoming the consequences of civil conflicts and collective trauma caused by it take decades; several generations have to pass until memories of such conflicts may fade (though they seem to exist for centuries and may be very easily revived).

The mental health consequences are even more severe if wars are associated with acts of genocide [127]. Genocide by definition is an intentional action to destroy the ethnic, religious, or racial group. A number of studies have confirmed that victims of political violence are suffering from severe psychological and mental health problems including PTSD, sleep disturbances, anxiety disorder, mental distress, and suicidal behavior, the severity of which reflects the level of

violence [127]. Tortures are reported as a strong factor that accounts for higher rates of mental health disturbances in populations exposed to mass conflicts with genocide [128].

The civilian population exposed to a war of different type, due to gender and age distribution, which is rather different from the military, may have specific mental health consequences. It is well established that under similar conditions women and children are at greater risk of psychopathologies and mental health disturbances [120, 127]. Children growing in wartime have a higher probability of worse mental health, lower education, impaired cognitive abilities, and lower subjective well-being in older age [129]. Moreover, negative mental health effects may be transgenerational. It is suggested that conflict-driven health harms may be transmitted due to persistent complex environmental factors and feedback loops between sources of harm and individual weaknesses or societal vulnerabilities [130]. Other possibilities of transgenerational effects are associated with severe early life stress (including in utero effects) on developing brain with subsequent mental health problems in children and young adults [131].

In overall, existing studies provide strong evidence that civilian populations subjected to war stressors caused by different types of conflicts, including civil or religious conflicts, genocide, tortures, and political violence, or associated with migration, asylum seeking, and refugee status have severe long-lasting negative mental health consequences. They include all typical trauma-driven disorders and psychological consequences, often in a more severe form than in war veterans, with higher frequency and with the greater tendency toward the transgenerational transmission. It makes an impression how war-related mental health problems propagate in wider populations, thus adding to the general burden of mental health problems in the modern world.

17.7 Global Impact of Instability, Terrorism, War Threat, and Information Wars

One of the signs of modernity is prevailing of local conflicts spreading across the planet and growth of the number of terrorist acts, which are associated with existing war conflicts. This is coinciding with the unprecedented influence of mass media providing extensive coverage of these events and making them globally evident. It should be noted that after the event 9/11, many commentators consider that the world remains in the state of the global terrorist war. This is confirmed by total world count of incidences of terrorist acts, which has grown from 2–3 hundreds in 70–80s to several thousand per year in the first decade of the twenty-first century [132]. There is no doubt that massive media portrayal of terrorism and war becomes a potent source of stress for the wide public. Surveys have revealed that media exposure to 9/11 and Iraq war-related TV images predicted an increase of PTSD symptoms 2–3 years after 9/11 in general population sample [133]. Mental health consequences were mostly inherent to vulnerable individuals with pre-existing mental health problems [133].

It is worth noting that modern mass media themselves are the source of anxiety, sleep problems, and mental health disturbances, for instance, screen time in children [134] and in adults [135] predicts higher depression and anxiety. On the other hand, disaster media coverage, both in the context of terrorism and warfare, is associated with such outcomes as PTSD caseness, posttraumatic stress reactions, depression, anxiety, and substance use [136]. In children, negative outcomes are linked to family context—lower socioeconomic status of the family, a lower educational status of parents, high parental stress, and poor coping being most prominent risk factors [137]. Risk factors for negative outcomes of media coverage of the mass shooting are female gender, pre-existing emotional problems, and lower social support [138]. In some cases (Boston Marathon Bombing) prolonged media exposure (6 or more hours a day) appeared to cause even higher distress in a distant population than direct exposure to the bombing, i.e., inhabitants of Boston [139].

One of the features of the modern war is that it turned into "War Live." It has become technically possible with launching modern satellites that are covering all geographical parts of the world. Another technical achievement in this field—drones and quadrocopters equipped with high-resolution cameras—has made the picture even more spectacular. Moreover, recent conflicts have revealed the availability of mobile means of video recording in the battlefield, due to which there is a growing volume of video streams of martial clashes, which appear in the social media, YouTube, and subsequently in the leading information agencies. All this makes a new reality and adds new destructive quality to the information warfare. Such development may be responsible for more mental health outcomes in the society in general and, largely, in those who are mostly involved in social networks as alternative channels of information distribution. The Internet, social media, and networks are domains, where positive and negative, rational and irrational discourse flourishes without boundaries, where professional comments and moral evaluations do not exist, while anonymity prevails. It may have specific consequences so far as psychological observations suggest that people have a tendency to believe in negative information easier than in positive and our attitudes are more heavily influenced by bad news than by good ones [140]. Moreover, it is already clear, that emotional states can be transferred to others in social networks via emotional contagion, leading people to experience the same emotions without their awareness, and this is true for both depression and happiness [141]. There are many signs that it promotes further differentiation of feelings, attitudes, and evaluations and may contribute to general embitterment, hostility, and animosity in the web. It is just one more manifestation of the conflict that moves emotions, feeling, and attitudes from TV screens to the personal level.

As to the concept of information warfare, it started to develop in the beginning of the 1990s together with the development of the information society [142]. Information warfare has two main strategic components—technical, aimed at computers and information networks, and psychological, aimed at peoples' minds, and can, therefore, be applied in military and civilian context [143]. The psychological information warfare is understood as influencing military and civil population of the

enemy side by distributing quite specific, often distorted, and manipulative information. On the other hand, in the modern world due to global information distribution, such information opposition quickly captures huge contingents, adding to the general feeling of the approaching war or inducing a premonition of the war, which influences the general psychological status of the peoples.

Information warfare is the logical product of the information society, where power and authority are based on communications and management of information flows. Means of communication, which are transforming and dosing information, become the main tool of influence in modern society. Moreover, manipulative information distributed by modern mass media, based mostly on TV, but also utilizing internet, social networks, and other available sources and covering many different aspects of political, economic, and spiritual life of the society has become a powerful weapon in global policy and a tool in achieving geopolitical goals of different warring parties. It is of fundamental importance at the present time that realizing the unreality of a global war, which can lead to the destruction of humanity, opposing parties rely on maintaining low-intensity local conflicts and information opposition. These conflicts may occur on their own on the basis of interethnic, religious, territorial, or other contradictions or may be provoked artificially, which is one of the features of the modern surrogate war. Media coverage of these events is a prerequisite of the general efficacy of hybrid strategy when mutual accusations and statements of the politicians, international organizations' evaluations, political commentators' opinions, and social media groups and individuals' posts, images, and videos create an information mosaic of the conflict.

It is suggested that such information pressure may have both psychological and psychiatric consequences [144]. All these activities often remain covert and are not perceived by the public as specifically aimed actions. On the other hand, they are obviously adding to the general feeling of instability and anxiety, both regionally and globally, and may induce cognitive dissonance, which in turn may contribute to exacerbation of different psychopathologies. In general, reaction to the information warfare may have something in common with the mass psychogenic epidemic, associated with exacerbation of existing psychological and mental health problems, like accentuated traits exasperation and enhancement of neurotic, depressive, histrionic, or anxiety symptoms [144]. Objective evaluation of mental health consequences of information warfare is not an easy task and still waits for being developed.

Conclusion

Another world war did not happen since WW II, but the number of local conflicts is growing, causing accumulating public health problems, mostly long-lasting negative psychosocial outcomes [120, 145]. Moreover, modern wars and conflicts seem to be aiming societies in general rather than military forces of the opposing part. While military may have preliminary selection and training and professionals better understand their mental health problems as veterans, civilians remain almost unprotected. As a result, many thousands of international refugees and internally displaced families, children, women, and older people,

deprived of their homes and shelters, are experiencing severe stress with very high probability of mental health consequences.

Moreover, there is another quality that makes modern situation special. Modern wars have all signs information wars with information becoming the factor of damage. Modern wars, terrorism, online representation of warfare on TV and on the web have an impact on much bigger contingents, which are not directly involved in the conflict, producing fear, anxiety, depression, uncertainty about future, and other psychosocial consequences. Thus, war consequences can be traced even in a wider context, considering huge contingents and populations. War and terrorism, civil wars and religious conflicts, forced migration, and people seeking refuge and asylum all around the world—all this contributes to the general feeling of instability and threat of a bigger and more global war. All this influences psychiatry too and means new challenges for this medical profession.

In March 2016 by the initiative of WPA, an anti-war declaration was formulated and published, which states "War is the worst of human-made disasters and has tragic and unacceptable consequences on the mental health of its victims. The catastrophic impact of war on mental health is longitudinal, transgenerational, and amplified by refugee crises both in countries of origin and elsewhere." The declaration, among other measures, calls for "termination of war conflicts wherever they occur" and has been supported by more than 100 organizations and entities, including military psychiatry section of the WPA. Military psychiatry has accumulated knowledge and practical experience that, though not always can be applied directly, may be useful for identification, management, prevention, and treatment of mental health consequences of war in wider contingents. This knowledge is a one more relevant and strong reason for advocating lowering of international tension and reducing the probability of war conflicts worldwide for the sake of preserving mental health of the humanity and diminishing of the burden of this type of diseases worldwide.

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Challenges for Old Age Psychiatry

18

Gabriela Stoppe and Carlos Augusto de Mendonça Lima

Abstract

The increase of life expectancy worldwide leads to a demographic challenge. The aim to reach old age in good mental and physical health comes closer, when prevention throughout the life course takes place and the health-care structures provide integrative and person-centred care and cure. According to the available evidence, education, physical activity, social integration, low or adequately treated cardiovascular risk factors and more reduce the risk for, e.g. dementia or depression, the most frequent mental disorders in late life. The article focuses on four relevant areas: the role of psychiatry in dementia care, the problems of suicide and assisted suicide (prevention), the situation in nursing homes and hospitals and finally, the development of service structures and reflects recent developments in research and policy.

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18.1 Introduction

The World Health Organization definition of health is "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" [1]. At that time this formulation was groundbreaking because of its breadth and ambition. It overcame the negative definition of health as absence of disease and included the physical, mental and social domains. This means that mental health is essential to overall health and well-being and should be recognized in all older persons with the same importance as physical health. Although the definition has been criticized over the past 60 years, it has never been adapted. Criticism is now intensifying as populations age and the pattern of illnesses changes. Various authors propose changing the emphasis towards the ability to adapt and self-manage in the face of social, physical and emotional challenges and, also, to include spiritual aspects of health [2]. Regarding old age, a new definition would not only allow most of the elderly population to stay healthy per definition but also to include gerontological knowledge developed during the last three decades on successful ageing [3]. These authors nicely showed that the ability to select and optimize what is relevant and to compensate effectively for deficits and losses is crucial for coping with the ageing process. And this new concept of health might also fit better with those of biological ageing [4].

By 2050, the world population over the age of 60 is estimated to be 2 billion [5]. A rapid growth of older persons will occur in low- and middle-income countries (LMIC) with huge consequences for these vulnerable economies. In LMIC, this is the result of huge reductions in mortality at younger ages (mainly during childhood and childbirth) and from infectious diseases. In high-income countries, continuing increases in life expectancy are now mainly due to declining mortality among those who are older. The consequences for health, health systems, their workforce and budgets are strong.

Each older person is unique, as well as each own ageing process. The resulting diversity in the capacities and health needs of older people depends in events throughout the life course that can often be modified, underscoring the importance of a life-course approach. Though most older people risk to have multiple health problems, older age does not imply necessarily dependence. Otherwise, ageing has far less influence on health-care expenditures than other factors, e.g. technological progress.

The increase in life expectancy adds years to life: this has profound implications for each of us, as well as for the societies we live in. They offer opportunities and have a fundamental impact on the way we live our lives, the things we aspire to and the ways we relate to each other. This fact of the global ageing process is a predictable trend, and we can plan to face to it in the best way possible.

The success of the demographic transition will be heavily dependent on our health. If people are experiencing these extra years in good health, their ability to enjoy their lives will have few limits. But if these added years are dominated by declines in physical and mental capacities, the consequences for all will be much more negative.

There are international initiatives which pave the way for an ageing society in good health. The WHO has developed a *Global Strategy and Action Plan on Ageing and Health*, a detailed report on the web-based consultation, and other information about the process and earlier drafts can be accessed in English at http://www.who.int/ageing/consultation/en/. *The World Report on Ageing and Health*, which was released just prior to the global consultation, provides much of the conceptual framework for the strategy [6]. There are also other initiatives to be mentioned, e.g. the statement of eight European academies from 2014 *Mastering Demographic Change in Europe*, which between others focuses on the relevance of education and health [7]. And there are others focusing on major health issues like dementia and suicide.

More than 20% of people age 55 years or older may have some type of mental health problem [8]. Biological changes may interfere with the brain's functioning. Social changes can lead to isolation or attribution of worthlessness. Somatic diseases are often important contributory factors, too. Mental disorders may exacerbate the symptoms and functional disabilities associated with medical illnesses and increase the use of health-care resources, length of hospital stay and overall cost of care.

In the following chapters, we will highlight new developments for the major mental health problems in old age and finally focus on the problems to develop adequate service structures.

18.2 The Role of Psychiatry in Dementia Care

In 2012, the WHO and Alzheimer's Disease International (ADI) jointly published a report *Dementia*: *A Public Health Priority* [9]. According to this, the total number of people with dementia worldwide in 2010 is estimated at 35.6 million and is projected to nearly double every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. The total number of new cases of dementia each year worldwide is nearly 7.7 million, implying one new case every 4 s. The total estimated worldwide costs of dementia were US$ 604 billion in 2010. In high-income countries, informal care (45%) and formal social care (40%) account for the majority of costs, while the proportionate contribution of direct medical costs (15%) is much lower. In low-income and lower-middle-income countries, direct social care costs are small, and informal care costs (i.e. unpaid care provided by the family) predominate. Changing population demographics may lead to a decline in the ready availability of extended family members in the coming decades.

Dementia is overwhelming for the caregivers, who have been shown to have an increased risk for own (stress induced) physical and mental morbidity, especially when they are at middle or higher age themselves. They want to be acknowledged in their role and need adequate support from the health, social, financial and legal systems. WHO and ADI postulate that countries must include dementia on their public health agendas. Sustained action and coordination are required across multiple levels and with all stakeholders at international, national, regional and local

levels. People with dementia and their caregivers often should be involved in formulating the policies, plans, laws and services that relate to them.

During the last years, epidemiological studies showed that the incidence of dementia might decrease significantly [10, 11]. It is not yet clear, which factors are relevant, but a greater investment in education and cardiovascular health in younger age seem to be major factors. However, stressful life events are also highlighted as preventable risk factors. These results support initiatives to prevent or better delay the onset of dementia. Prevention of dementia is also good for other health conditions. However, biological treatment trials for Alzheimer's have revealed disappointing results until now [12, 13].

Not only because cure is not available yet, the care of dementia is remaining of major importance. What is the role for psychiatrists, if they are or were available in adequate numbers?

- *Diagnosis*: the early diagnosis of dementia requires careful anamnesis and neuropsychological investigation. The most frequent and also difficult differential diagnosis is depression. It requires mental health competence.
- *Assessment of competence*: dementia threatens autonomy of the individuals affected. When can a demented person express a valid will, drive a car and more? To assess the competence in demented patients should include the examination of personality, mood and behaviour, too [14].
- *Treatment of behavioural and mood symptoms*: the symptomatic treatment of the non-cognitive symptoms requires a tailored psychopharmacological and non-drug treatment (e.g. music therapies, physical trainings, group interventions). This kind of treatment is typical for nearly all mental disorders and "daily business" for a psychiatrist.
- *Support for the caregivers*: stress-related symptoms affect not only the caregiver but also the interaction between patient and caregiver and profit from an involvement of mental health professionals. This applies also to the interaction between the demented individuals and the staff in institutions.

However, most patients are not even diagnosed for their dementia. This is even true in developed countries. So access to care is still limited for most dementia patients [15]. The development of the WHO Mental Health Gap Action Programme is helpful in this situation (http://www.who.int/mental_health/mhgap/evidence/dementia/en/).

18.3 Old Age Psychiatry in Nursing Homes and General Hospitals

Physical and mental health are very strongly connected in old age. This is well known for depression, which is much more frequent in patients suffering from chronic health conditions and affects their course and prognosis. Impairment of hearing or vision like macular degeneration leads to problems in communication

and social isolation. In general hospitals delirium is a frequent problem. Meanwhile there is much progress to be seen for the assessment and prevention of delirium by structured care and intervention plans, which may reduce the incidence of delirium by more than 60% [16, 17].

At nursing homes the situation might differ largely between regions. However, as far as studies are available, they consistently show high prevalences of mental disorders in nursing homes. Clearly, problems connected to mental health problems like a lack of a helpful social network or family increase the probability to be admitted to a nursing home [18]. Dementia affects more than two thirds of the population, and depression more than a third, respectively; suicide and other mental health problems have been mainly disregarded yet [19, 20]. Psychoactive drugs are prescribed in the majority of cases and are reported to increase the risk to fall and also to die [21, 22]. The staff of nursing homes is often not adequately trained how to interact with mentally impaired elderly. Supervision and training should be provided. Meanwhile there is much research interest to develop psychosocial alternatives to drugs (e.g. [23]).

18.4 Suicide and Assisted Suicide

In most countries suicide rates are highest in the elderly, especially in elderly men. As a comprehensive report of the WHO in 2014 shows, its title *Preventing Suicide: a Global Imperative* holds especially true for the elderly population [31]. However risk factors and strategies differ partly from those in other age groups. Psychiatric disorders—often insufficiently treated or even unrecognized—are the underlying condition; however in up to 90% of the elderly cases, it is depression. Newer research revealed that chronic sleep disorders and beginning dementia are other conditions in old age [24, 25]. Shared risk factors for suicide and depression in the elderly are the onset of physical disorders, especially when these somatic conditions go along with pain and impair activities of daily living. However, as in younger age, factors related to the personality play a crucial role, e.g. hopelessness, hostility and a lack of trustful relationships. Bereavement is associated with an increased risk of suicide during the first 6 months following the death of a loved person.

Strategies for prevention include the access to suicidal means. Multifaceted interventions against depression in the European Alliance Against Depression have been helpful to increase the awareness for depression and reduce suicides [26]. Overall there is good evidence that depression in the elderly might be prevented, when risk groups are targeted [27]. New models based on primary care may pave the way to a better integrated care of the elderly with depression and suicide [28, 29].

What is urgently needed are knowledge and skills concerning depression and suicide risk in the elderly. Nurses, physicians, pharmacists and other health and social care workers often do not know much about this and other mental health problems in the elderly. So information and education should be provided. Ideally this should also antagonize common stereotypes that ageing goes along with lower life satisfaction and the wish to die.

In some countries the issue of assisted suicide gains support dramatically, e.g. at the Netherlands or Switzerland. The ethical debate is ongoing [29]. The individual decision to control circumstances of death as sign of autonomy challenges societies, which regard chronic disease and impairment as conditions which might mean a loss of dignity. Authors hope that the discussion might lead to a debate on caring communities and societies facing demographic change with solidarity.

18.5 Organizing Mental Health Care for Older People: A Public Health Issue

Mental health problems can have a high impact on an older person's ability to carry out the basic activities of daily living, reducing their independency, autonomy and quality of life. The first step to reduce these negative consequences is simply making a diagnosis. Unfortunately, although some progress can be seen, too often mental health problems are undiagnosed and untreated, and many older people struggle on without the proper help—or any help at all.

Today's older adult population has been less likely to acknowledge mental illness or access mental health services. Many stigmas exist regarding the meaning of mental illness. Several elders view mental illness as a sign of weakness and are unlikely to admit to problems, especially when they fear loss of independence. Too many persons consider that symptoms of dementia and depression are a normal part of ageing. Many elders lack availability of and access to services [30].

Other difficulties concern the work force: few mental health providers have had specialized training in providing care for older adults, and many come with a set of societal-transmitted biases themselves. The therapeutic pessimism allows health professionals believe that older people cannot change and that it is too late for psychiatric care. In consequence, there are few investments in the development of policies, strategies, programmes and services for older persons with mental health problems. No country today has enough programmes to educate a number of health and social service professionals at the same speed of their own population ageing.

Health systems are too often poorly aligned with the needs of the older populations they now serve; in many parts of the world, it is unsafe and impractical for an older person to leave his or her home, caregivers are often untrained and not supported, and at least 10% of older people is a victim of some form of elder abuse. Besides some progress these last years, "there is low priority within health policy to the challenge of the demographic transition"; "there are low levels of training in geriatrics and gerontology within the health professions, despite increasing numbers of older persons"; and "care and support for care givers is not a priority focus of government action on ageing" [6].

So which is the most appropriate public health response to the population ageing?

The maintenance of functional physical and mental well-being has the highest importance. The greatest costs to society are not the expenditures made to foster this

functional ability, but the benefits that might be missed if we fail to let older people in good health. A transformation of health systems away from disease-based curative models and towards the provision of integrated care that is centred on the needs of older people is a high priority.

This transformation is underpinned by three main reasons to act on ageing and health:

- The recognition of the rights of older people to the highest attainable standard of health.
- The understanding that ageing, health and development all come together. In order to build societies that are cohesive, peaceful, equitable and secure, the development strategies have to take account of the demographic transition and actions will need to include the contributions that older people make to development and ensure that they are not left behind.
- The economic imperative to adapt the expenditures associated with population ageing while maximizing the many contributions that older people make directs participation in the formal and informal workforce, through taxes and consumption, through transfers of cash and property to younger generations and through other benefits that accrue to their families and communities.

A new framework for global action to promote a better global health in old age is required and has to include mental health aspects. It will need to encompass the great diversity of older populations and address the inequities that lie beneath it. It must drive the development of new systems for health care and long-term care that are more in tune with the needs of older people, and it must ensure that all sectors focus on common goals so that action can be coordinated and balanced. It will also need to transcend outdated ways of thinking about ageing, foster a major shift in how we understand ageing and health and inspire the development of transformative approaches [6].

Services will have to be redesigned to deliver the comprehensive and coordinated care that has been shown to be more appropriate and more effective. They should put older people at the centre of health care, focusing on their unique needs and preferences and including them as active participants in care planning and in managing their health states. Health services have to be better integrated between levels and across specialist groups.

Although transforming health systems requires action on several fronts, three key themes emerge as priorities:

- Shifting the clinical focus from disease to intrinsic capacity
- Rebuilding health systems to provide more person-centred and integrated care to older people
- Transforming the health workforce so that it can better provide the care that these new systems will require

18.6 Outlook: The Potential Role of the Digital Society

We live in a rapidly changing world, which brings new technologies to be connected and exchange information. The elderly of today and tomorrow have problems with rapid changes, because flexibility and velocity are mainly youth related. However, these competencies might be trained throughout life. Patients suffering from mental health problems have a major—let's say intrinsic—disadvantage in the information society. This must be taken into account when developing health technologies.

On the other hand, new technologies might help to inform and educate people on mental health issues. They provide chances to promote models of good care and exchange experiences made with them. They should also help to develop mental health and ageing literacy in the public and start initiatives of laypersons and communities providing better mental health for the elderly.

Overall, the situation of old age psychiatry is serious, but not hopeless.

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Advances in Treatment for Personality Disorders

19

Robert Biskin and Joel Paris

19.1 Defining the Problem

Before discussing treatment of personality disorder (PD), clinicians need to know that this construct has been classified in different ways in different diagnostic manuals. In all systems, PD is a complex construct, describing abnormalities in personality that broadly affect functioning over many years.

The overall definitions in the *International Classification of Diseases*, 10th edition (ICD-10) [1], and in Section I of the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) [2], are similar. Both define PDs in terms of enduring patterns of cognition, affect, behavior, and relationships, manifesting themselves as inflexible responses to a broad range of life situations. However, while ICD-10 and Section II of DSM-5 describe a series of specific PD categories, Section III of DSM-5 and the proposal for ICD-11 [3] use dimensional scores of trait profiles or hybrids between the dimensional and categorical models. While the DSM-5 Section III provides some limited guidance in how to reconstruct categories from these scores, the ICD-11 proposal replaces categories entirely with dimensions. The new model introduced in DSM-5 Section III received some empirical support and justification for its use [4], but it remains the alternate model until further research demonstrates superiority over the current model for the multiple users of the DSM system.

The vast majority of research on the treatment of PD has concerned the category of borderline personality disorder (BPD), a severe form of psychopathology which is a frequent subject of clinical concern [5]. Even studies that eschew using this category, but describe treatment for severely ill PD cases in clinical settings, may be describing the same patients. As such, the majority of this section will focus on BPD.

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19.2 Efficacy of Treatment in BPD

For many years, pessimism about the treatment of PD was common among clinicians. This sense of hopelessness certainly applied to BPD. Many had the impression that these patients kept returning to clinics and emergency rooms, but almost never got better. A few clinical trials suggested that medications such as antipsychotics have some effect in reducing some of the more distressing symptoms of BPD [6]. But there were hardly any long-term follow-ups, and remission from the disorder was never observed. The literature on psychotherapy for BPD was also very limited. Although therapists wrote books focusing on their own experiences and understandings of these patients, there were no clinical trials.

Two discoveries changed these perceptions. In the 1980s it was shown that most BPD patients improve with time. The impression that they do not improve was what has been called a "clinician's illusion" [7], created by the tendency for remitted patients to stop coming, while unremitted patents continue to ask for treatment. Then, a series of follow-back studies found that most BPD patients improve enough to no longer meet diagnostic criteria by age 40 [8]. These findings have later been confirmed by prospective studies [9, 10].

The two major prospective studies have compared BPD to other personality disorders or major depressive disorder and several specific personality disorders [9, 11]. Beyond the cautious optimism regarding remission from the diagnosis for all patients with PDs, these studies have also demonstrated that impairment in functional status does persist for a significant minority of patients with PDs, even up to 16 years later [10]. Patients with BPD are also higher service users of both psychiatric and medical care, with high rates of physical health problems and poor health behaviors that may be inadequately treated and followed [12, 13]. It is important to note that these community studies generally do not include patients who have received specialized psychiatric care or specific treatment programs, suggesting that many patients with BPD seen in the community may have even milder forms of BPD.

In the 1990s it was shown that specific psychotherapies for BPD are efficacious. This literature is now sufficiently mature that several clinical guidelines have been published using meta-analysis to measure the strength of this evidence. Guidelines have been published by the Cochrane reports [14], favoring the use of cognitive therapy (Cochrane has long been famous for its conservatism, setting a high bar for any recommendation). The National Institute for Health and Clinical Excellence (NICE) in the UK reached very similar conclusions [15]. Thus strong evidence supports the use of specialized therapies for these patients.

It should also be noted that the American Psychiatric Association, as part of a series of clinical guidelines for mental disorders, published one on the treatment of BPD [6]. However, its conclusions, dating from 2001, are now seriously out of date, and the guidelines are not recommended for current use.

19.2.1 Dialectical Behavior Therapy

Dialectical behavior therapy (DBT) is an adaptation of cognitive behavioral therapy using an eclectic mix of interventions derived from several other approaches [16]. DBT

is specifically designed to target the mood instability of BPD that leads to self-harming and suicidal behaviors, i.e., emotion regulation. DBT also addresses impulsive behaviors and management of interpersonal relationships. DBT consists of a combination of weekly individual and group psychotherapy, in addition to team consultation meetings. The approach used in DBT relies on a balance of "validation" of the patient's thoughts and emotions, with change-oriented skills training to help patient develop skills to improve emotion regulation and interpersonal relationships. Developing mindfulness skills also serves as the foundation on which many of the other skills are developed. One of the important skills in DBT is behavioral analysis, which was designed to help patients understand the life events that lead to self-injury and suicidality and identify different ways in which they can act in the future.

DBT was the subject of the first randomized controlled trial (RCT) of a psychotherapy designed for BPD [17]. The method was compared to "treatment as usual" (TAU), i.e., the limited and variable interventions that most patients receive in community clinics. After a year of treatment, the sample receiving DBT was less likely to make suicide gestures and spent less time in hospital. The gap narrowed at 1-year follow-up, but patients treated with DBT continued to show a higher functional level [18]. DBT may also be effective in BPD patients with substance abuse [19].

In the first RCT [17], over 90% of patients treated with DBT stayed in therapy for the full year—a remarkable finding in a patient population known for low compliance. However, patients who enroll in clinical trials and who receive free treatment may not be typical. Moreover, TAU can be variable and disorganized, particularly in comparison to a well-structured program like DBT. Replications in other centers have confirmed the efficacy of DBT, although overall these studies had higher rates of attrition than the initial study [20].

While the efficacy of DBT is well documented, its specificity remains to be determined. A second RCT [21] showed that DBT is superior to a range of "treatment by experts in the community" (who provided psychodynamic and client-centered therapies, but not cognitive behavioral therapy). But this time the advantage of DBT was narrower. The outcomes that differentiated the groups were overdoses and subsequent hospitalizations within the first year of treatment, although there were no differences in the frequency of self-harm. A third study [22] presented evidence that the group skills building component of DBT, which teaches specific skills, is crucial for improvement.

All studies of DBT have used small samples, and results may have been affected by selection biases. Since not every BPD patient will enter a clinical trial, we do not know whether DBT can be applied to the larger clinical population. We also do not know the long-term outcome of DBT. While the first cohort received therapy over 25 years ago, the patients were never followed up, nor have other studies followed patients over several years. Thus we do not know whether treated samples maintain their gains and continue to improve or whether they at risk for relapse.

Linehan [16] suggested that a full course of DBT could take several years, so that only the first stage (in which parasuicidal behaviors are targeted) has been formally described and tested. But because DBT is lengthy and involves a team, it is resource-intensive and expensive. Where it is available, there are usually long waiting lists. To improve access, one needs to determine whether DBT can be dismantled, shortened, and streamlined [23]. Unless costs can be brought down, DBT, like psychoanalysis,

will remain a treatment for the wealthy. That makes little sense since BPD affects a population who tend to fall within a lower socioeconomic level [24].

DBT has become very popular as a brand name. The question is whether it has specific effects that are stronger than other treatments. This issue was addressed by a study by McMain et al. [25] in a comparative trial of DBT and "general psychiatric management" (GPM), a manualized version of standard clinical care that included both regular psychodynamically informed psychotherapy and pharmacotherapy. There were no differences whatsoever, either at the end of the study or on 1-year follow-up [25]. It is possible that DBT's superiority in other trials is attributable to its highly structured approach to this clinical population.

19.2.2 Other Forms of Cognitive Therapy

Linehan developed DBT after concluding that classical cognitive behavioral therapy (CBT) was ineffective for BPD. But Davidson et al. [26] found that manualized CBT was superior to TAU. Since the mean number of sessions was 26 sessions provided over a 1-year period, the results also suggested that briefer therapies can be effective. This is an important issue because the price of both the individual and group components of DBT (and most other current therapies) puts treatment out of reach for most patients and families.

The best example to date of a brief intervention is the *Systems Training for Emotional Predictability and Problem Solving* (STEPPS) program [27]. This program provides 20 sessions of psychoeducation and skills training in a group format and is designed to be an add-on to all types of existing treatment, including both nonspecific individual therapy and medication follow-up. Its brief group format makes it accessible, and the method has most often been applied in small communities. The method has been supported by clinical trials when compared to TAU alone [28, 29].

19.2.3 Psychodynamic Therapies

Psychoanalysts have long been interested in treating BPD. But therapists using this model have adapted their methods, becoming increasingly active in session and employing more specific interventions that are helpful for patients with BPD [30].

Transference-focused psychotherapy (TFP), developed by a group of psychoanalysts [31], aims to correct distortions in the patient's perception of significant others by pointing out how they affect a relationship with the therapist within the setting of a strong treatment frame. However, TFP does not put as much emphasis on the past as classical psychoanalysis. In a comparative trial comparing TFP to DBT, results were generally similar [32]. There is also one trial showing that TFP for BPD is superior to treatment by community therapists [33]. Unlike some of the other therapies for BPD, TFP does not incorporate group therapy elements, instead opting for twice weekly individual therapy for a fixed period of time.

19.2.4 Methods Combining CBT and Psychodynamic Therapy

Mentalization-based therapy (MBT), developed by two psychoanalysts, Bateman and Fonagy [34], adds particular cognitive therapy elements to a psychodynamic framework and conceptualization. MBT is based on the theory that BPD patients have a deficit in the capacity to "mentalize" (i.e., to stand outside their feelings and accurately observe thoughts, actions, and emotions in self and others). This deficit is hypothesized to arise from a disorganized attachment with the primary caregiver [34]. This idea bears some similarity to mindfulness in DBT and CBT, as both are reflective processes focusing on developing alternate or more nuanced understandings of what is observed in the present moment within and around oneself. The first RCT on MBT was carried out in a day hospital setting [35], with the second in an outpatient clinic [36]. Both studies found MBT to be superior to structured clinical management, although differences were narrow. The day hospital sample had an improvement in symptoms that remained stable after 8 years [37], a rare example of long-term follow-up of an RCT. However, a replication in another center failed to find differences between MBT and structured standard clinical care [38]. While MBT is a lengthy and resource-intensive treatment, Bateman and Krawitz [39] have proposed that it could be shortened and adapted for a variety of clinical settings, with the advantage that training for MBT is shorter than other specialized psychotherapies.

Schema-focused therapy (SFT), developed by Young [40], is also a hybrid of CBT and psychodynamic therapy. It focuses on maladaptive schema deriving from adverse experiences in childhood. Thus far the full SFT program has only been supported by a comparative trial with TFP [41]. Another relative limitation is that SFT is designed to last as long as 3 years, incorporating both group and individual psychotherapy, which makes it costly and potentially difficult to access.

Good psychiatric management [42] is an attempt at developing an integrative model that is also open to pharmacotherapeutic interventions, adapted from the control condition in a study by McMain et al. [43]. This method has not yet been subjected to RCTs compared to TAU, but is offered as practical model that adds some specific techniques and an improved structure to what most clinicians do in practice.

19.2.5 Psychotherapy Integration

There is a strong movement to replace separate, acronym-based therapies with a single integrative model [44]. One rarely finds evidence in the literature that any method of psychotherapy for any disorder is robustly superior to any alternative [45]. Instead, factors common to all approaches are important than specific technical interventions. These findings suggest that clinicians are misguided in attending workshops or buying books describing the latest forms of treatment. We should be practicing evidence-based therapy, but sometimes end up with "eminence-based therapy."

There is also little evidence that any of the current methods for treating BPD are any better than any other [46]. In head-to-head comparisons, few differences emerge. There is also no evidence that lengthy treatments such as DBT, MBT, TFP, and SFT are superior to briefer interventions such as STEPPS or standard CBT.

Clinicians might therefore consider abandoning the search for specificity, and apply an *integrative* perspective, combining the best ideas from many sources. Many basic principles can be applied to this patient population [46, 47]. For example, therapy needs to be well structured. It also needs to focus on current problems, not on the past: Linehan's [16] concept of "radical acceptance" implies that patients should be encouraged to reduce their often painful efforts to live their lives focused on past experiences; to put their past, however traumatic, behind them; and to focus their efforts on changing their current life.

Each of the specific methods includes aspects that are idiosyncratic to its developers. One example is the use of pagers or mobile phones and messaging in DBT [16], intended to coach patients who can call in for reminders of distress tolerance skills to stop themselves from carrying out impulsive actions at any point. There is no evidence that this procedure adds to the treatment package. Given the burden of treating these difficult patients, and the difficulty of finding clinicians who are committed to treating them, it is not practical to ask therapists to sacrifice personal time to their work.

19.3 Psychopharmacological Treatment in BPD

Psychiatric practice has moved away from the use of psychotherapy [48]. PDs, traditionally treated with psychotherapies, are also now likely to be managed with one or several medications [49, 50]. Yet up to now, no drugs have been formally approved as indicated for BPD. Research also needs to establish whether medications have specific effects on the disorder. This question has been addressed in a Cochrane report [14], in a NICE report [15], and in other systematic reviews [51, 52]. The overall conclusion from all these reviews is that the value of medication in BPD remains to be proven.

Unfortunately, there are other limitations in the literature that raise questions about the generalizability of the existing literature on pharmacotherapy for BPD. Most studies use long lists of exclusion criteria such that patients enrolled in research represent much milder forms of the illness. Studies are often short term, rarely lasting beyond 12 weeks of blinding, which makes interpretation for a chronic condition such as BPD hard to interpret. The dropout rate in many studies is also unreasonably high which limits the interpretation of the results and applicability to clinical practice, particularly in the context of the very small samples used. Finally, the outcome measures used rarely assess for improvements or remission in BPD, preferring to focus on improvements in mood, anxiety, anger, or impulsivity. Another consideration is that pharmacotherapy is rarely without notable adverse effects, such as marked weight gain and potential lethality in overdose. In a population with higher rates of obesity and related medical complications, as well as poorer health behaviors, further adding to the burden is questionable [12, 53].

19.3.1 Antidepressants

Patients with BPD are often comorbid for major depression [54]. Thus it might seem logical to offer them antidepressants. However, consistent evidence shows that the presence of a personality disorder makes drug treatment of depression less effective [55]. Even in depressions not complicated by a PD, there is only a small advantage of drug over placebo in mild to moderate depression [56].

An older literature examined the effects of tricyclics and mono-amine oxidase inhibitors on BPD [6]. However, these agents are rarely used today, as they have many side effects and are dangerous in overdose.

Specific serotonin reuptake inhibitors (SSRIs) are safe drugs that have been used widely in BPD. However, clinical trials suggest that their efficacy for mood symptoms is doubtful [57]. Some studies have suggested that these agents have more effect on aggression [58]. Recent literature has not, however, supported an earlier claim that SSRIs could be effective for self-harm [59]. Finally, even if SSRIs can "take the edge off" symptoms, they do not lead to remission of the disorder.

19.3.2 Mood Stabilizers

BPD is associated with marked affective instability [60]. Some have thought that BPD lies in the bipolar spectrum and should therefore respond to the same drugs [61]. This hypothesis is not supported by research and may be one reason why patients with BPD take so long to receive [62] the diagnosis and referral to appropriate treatment [50]. Mood stabilizers do not yield remission in BPD, as they often do in bipolar disorder types I and II [63]. Like SSRIs, these agents seem to have more effect on anger and impulsivity [64, 65]. In spite of a lack of evidence for controlling mood instability, anticonvulsive mood stabilizers have been widely used "off label" in BPD. The terms "antidepressant" and "mood stabilizer" have led clinicians to assume that these agents have effects that are not dependent on diagnosis. This turns out not to be the case.

19.3.3 Antipsychotics

These agents, particularly olanzapine [66], have a more robust evidence base in BPD, although the overall findings when compared to placebo are less and less impressive as the size and quality of the studies increase. Short-term clinical trials [15, 49, 57] suggest that the most consistent effect is a reduction in impulsivity, without full remission. Similarly, a recent trial of quetiapine reported short-term reduction in impulsive symptoms [67], but there may have been methodological problems with the research. Only one trial of aripiprazole has been published [68], and although the results are very promising, they have not been replicated by other teams.

The question is whether antipsychotics should be used long term or short term. Gains may or may not be maintained on follow-up, and compliance can be limited by

side effects. While atypical neuroleptics are better tolerated, these agents put patients at risk for metabolic syndrome associated with weight gain and/or diabetes [69]. While low doses of atypical antipsychotics are usually tolerated, results can best be described as reduction in a few specific symptoms without remission.

19.3.4 Other Agents

Naloxone, an opioid antagonist, may specifically reduce dissociative symptoms [70] and reduce the urge to self-harm. One study has reported symptom reduction in BPD using omega-3 fatty acids [71]. Both of these agents need substantially more research before they can be recommended in clinical practice.

19.3.5 Polypharmacy

None of the drugs used for BPD lead to remission of the disorder. When short-term improvements do not last, as is often the case, clinicians may add a new drug—without subtracting the minimally beneficial treatment that the patient is already taking. This helps explain why so many BPD patients are on a polypharmacy regime of 4–5 drugs [50], with at least one agent from each major group.

The use of algorithms for drug treatment, with a sequence of prescriptions, each of which would target different symptoms, encourages this practice. This approach was recommended by the American Psychiatric Association guidelines [6], but with remarkably weak evidence, and algorithms were not recommended by Cochrane [57] nor by NICE [15].

Notably, there has been no research on drug combinations in BPD. Moreover, the observation that different drugs have similar effects on BPD suggests a common mechanism of action. Any drug with sedating properties can reduce anger and impulsivity. We need to develop more specific agents, as opposed to nonspecific "stopgaps" that were developed for other purposes. Further research on the sustained effects of existing, frequently used treatments would also help us understand the long-term benefits of these medications, particularly considering the long-term risks related to side effects. Finally, the combination of medication and specialized psychotherapies, such as DBT, should be evaluation. One study of patients receiving DBT found that the addition of pharmacotherapy to psychotherapy led to lower response rates compared to not adding any medications [72]. This finding has significant implications particularly for some structured treatments that combine psychotherapy and pharmacotherapy, such as GPM.

The NICE guidelines [15] concluded that there is insufficient evidence to recommend the prescription of *any* drug for BPD. Similarly, conservative conclusions appeared in a report published by the World Federation of Societies of Biological Psychiatry [73]. Some years ago, Tyrer and Bateman [74] emphasize the lack of specificity of current pharmacological therapies for PD, and the situation has not changed.

19.4 Treatment of Other PDs and of Mixed PD Populations

There is surprisingly little research on the treatment of categories of PD other than BPD.

Only a few studies have examined therapy for antisocial personality (ASPD), which is a high prevalence disorder [75], or the closely related construct of psychopathy [76]. These patients rarely come to mental health clinics and drop out of research and clinical follow-up quickly, and most reports come from correctional samples. Moreover, follow-up data in this population is rare. Derefinko and Widiger [75] concluded: "….treatment for psychopathy and ASPD remains a very controversial subject; while meta-analytic findings demonstrate positive results, considerable evidence also indicates that these disorders are resistant to typical interventions." This conclusion seems relatively unchanged in recent decades, with the exception that treatment of comorbid substance use disorders is increasingly recognized as important for long-term improvement [77].

Schizotypal personality is often considered to be a milder form of schizophrenia [78]. There is some evidence that antipsychotics [78] as well as the sympathomimetic drug guanfacine [79] can help control symptoms, although the studies are fraught with the same challenges as the pharmacotherapy studies in patients with BPD.

Avoidant personality overlaps with social anxiety disorder, of which it may be a more severe or persistent form. But due to lack of suitable studies, Cochrane withdrew its protocol to examine treatment methods for this condition in 2014. At this point, with respect to both pharmacology and psychotherapy, there are only scattered case reports and small sample studies [80].

The lack of research applies to the other categories in DSM-5 and ICD-10. For example, while there has been research interest in narcissistic PD [81], there are no studies of treatment, probably because these patients rarely present to clinics. It is also possible that future classifications may eliminate current categories entirely [3].

Some studies of psychotherapy in PD have been applied to clinical populations that have a mix of categories. This approach is more common in the UK where categorical diagnosis is not given the same weight. For example, a recent report found that psychoeducation and brief therapy in community clinics alone was not superior to standard care [82]. Another report found that therapeutic communities supported the effectiveness of an inpatient population [83]. These findings may not, however, be generalizable to countries where community care is weak and/or where hospital admissions tend to be brief.

19.5 Future Directions

At our present state of knowledge, there is much stronger evidence for the effectiveness of psychotherapy in specific PDs than there is for *any* pharmacological intervention. The main reason psychological therapies are not more widely used is their cost and lack of specialized therapists. However, scarce resources can be used more effectively by providing brief treatment for most patients while reserving expensive rehabilitation programs for more chronic and severely disabled patients [84].

Since PDs are by definition chronic, research on treatment has to move beyond short-term studies and examine long-term effects. Treatment effects also need to be shown as superior to naturalistic remission. Second, there are striking common factors in all therapies that help patients. Much of the literature suggests that improvement occurs with different methods rooted in different theories. This gives clinicians the impression that they mainly need to learn technical procedures. Yet as has been consistently shown in the psychotherapy research literature, common factors are more efficacious than any specific technique.

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Positive Psychiatry: Neuroscience of Brain Health and Resilience

20

Keri-Leigh Cassidy and Beverley Cassidy

Abstract

Positive psychiatry is dedicated to the science and promotion of biopsychosocial health and resilience. Positive psychiatry has broad relevance for patients with serious mental or physical illness as well as for the general public. In this chapter, the evidence base of applied positive psychiatry for mental health promotion is reviewed. Domains of human behavior with more robust evidence to promote brain health and resilience include physical activity, social connectedness, and cognitive stimulation, proactively taking care of mental health and cultivating a balanced, optimistic outlook. Practical considerations for the integration of positive psychiatry practice are reviewed. Suggested targeted questions and measures to assess mental wellness and resilience and specific interventions shown to promote brain neuroplasticity and resilience are outlined. Early models of successful practice applications are described, with current examples of successful applications in clinical practice and in the community, including resilience-enhancing community initiatives. The Fountain of Health Initiative for Optimal Aging is highlighted as an example of applied positive psychiatry both in healthcare and in community settings.

20.1 Introduction

Positive psychiatry is a new branch of psychiatry dedicated to the science and promotion of biopsychosocial health and well-being. Led internationally by Dr. Dilip V. Jeste and outlined in his seminal book *Positive Psychiatry* [1], this branch of

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psychiatry strives to understand the biopsychosocial underpinnings of resilience and to enhance factors that contribute to mental and physical well-being. Like positive psychology, positive psychiatry focuses on wellness but emphasizes an understanding of the neurobiological correlates of mental health, including brain neuroplasticity. It also seeks to understand the impact behaviors and attitudes can have on biology and health across the lifespan and offers a paradigm shift away from pathology and toward resilience and wellness promotion within healthcare. Positive psychiatry is relevant for patients with mental or physical illnesses as well as for the general population, and in this regard, it offers an opportunity to bring psychiatry to the fore of the healthcare system and of society in general.

Our profession is ideally positioned to forward resilience and well-being as an overarching goal of the healthcare system. Rooted in medicine, with its dual focus on brain neurochemistry and psychotherapy, the field of psychiatry has a significant role to play both in brain health research and in the application of cognitive-behavioral and other psychotherapeutic strategies to optimize health behaviors and attitudes in practice [2]. Through positive psychiatry, healthcare providers can promote resilience in patients by focusing on individuals' strengths and capacities and by inviting behavior and attitude change. Similarly, translation of positive psychiatry science directly to the public can promote understanding about brain health and resilience within our communities. Resilience is fundamentally defined as the ability to "bounce back" in the face of adversity, a dynamic capacity that involves cognitive, physical, and emotional skills that can be cultivated. But there is more to resilience than recovery from serious adversity; resilience skills are vital to enriching the quality of our everyday lives as well. Psychological resilience involves a mindset that allows one to think flexibly, accurately, and thoroughly and to focus on that which can be changed [3].

Perhaps more than any other medical professionals, psychiatrists understand the vital role of resilience in our patients. In assessments and in formulations, psychiatrists routinely consider the biopsychosocial protective factors of patients. Psychiatric treatments include non-pharmacological approaches, in addition to medications, notably the psychotherapies aimed at relapse reduction and improving patient insight, function, and quality of life. Multidisciplinary mental health workers use a recovery, strengths-based model, even with the most severely and persistently mentally ill. Psychiatry appreciates the difference between mental illness and mental health, including that it is possible to foster positive psychosocial adaptation to living with serious mental illness including schizophrenia and other psychotic disorders [4].

In terms of the role of positive psychiatry in severe mental illness, a recent study by Edmonds et al. [5] evaluated 135 outpatients with schizophrenia and 127 healthy comparison subjects for mood, stress, resilience, and other psychosocial factors. The authors found that 38% of people with schizophrenia reported levels of happiness similar to healthy counterparts. More positive scores were not correlated with disease severity but with psychosocial factors such as lower perceived stress, higher resilience, optimism, and personal mastery. Higher positive psychosocial scores were also associated with better mental and physical health including improved values of biomarkers such as inflammation and insulin resistance. These findings

raise the possibility that positive psychosocial interventions might improve health measures and outcomes in patients with severe mental illness [4]. Many of the medications needed to treat mental illnesses such as bipolar disorder and schizophrenia improve psychiatric symptoms but do not foster physical health [6]. In fact, many of the medications used to help regulate mood and psychotic conditions adversely affect physical health outcomes, such as cholesterol and glucose regulation and body mass index [7, 8]. Positive psychiatry can promote health behaviors and attitudes to minimize the physical harms of such necessary psychiatric treatments.

In the context of an aging world population, positive psychiatry's focus on resilience in the second half of life will be increasingly relevant. An increasing percentage of the global population is now over age 65: in Canada, for example, approximately 17% of Canadians are over 65 years of age, with this number expected to double in the next 20 years [9]. The same trends are seen around the world, with a resultant increased need for mental and physical healthcare and residential care for elderly living with chronic medical conditions, including dementia. Adversity over the course of a long life is often of a chronic or repeating nature, with or without mental illness, such as coping with repeated attachment or interpersonal losses as well as medical illnesses that challenge our ability to remain mentally and physically healthy over time. These demographic shifts and accumulative adversity over very long lives make it essential to focus on primary and secondary prevention. Positive psychiatry seeks to highlight key dimensions of well-being across the lifespan including physical, social, and cognitive activation.

As the role of epigenetic factors in determining health and human longevity becomes clearer, so does the reality of improving health and health outcomes through outlook and behavior. The coefficient of heritability of human longevity found in twin studies is only about 0.25 [10–12]. This finding means that only 25% of human longevity is determined by inherited family genes and that much more is determined by epigenetic factors such as attitude and lifestyle. Evidence-based interventions that support epigenetic factors of behavior and attitude change that further well-being and longevity [13–15] are relevant for positive psychiatry research and practice.

In terms of positive psychiatry research, Jeste highlights the following key research areas for further investigation: neuroplasticity, epigenetics, brain health, healthy aging, health/longevity biomarkers, positive emotions, resilience, health-promoting cognitions and attitudes (such as optimism, wisdom, empathy, positive views on aging, life satisfaction), health-promoting behaviors (such as social activity, physical activity, mindfulness practice), and health behavior change theory and practice (such as cognitive behavioral and values-based therapeutic approaches) [16]. Domains of human behavior and outlook with the most robust evidence for brain health promotion, resilience, and longevity include (1) having a balanced, optimistic outlook [17], (2) physical activity [18], (3) social connectedness [19], (4) cognitive stimulation [20] and (5) proactively taking care of mental health. In this chapter, the evidence base for the above five key areas of behavior to improve mental health and resilience are reviewed. Practical considerations for integrating positive psychiatry practice are discussed, including targeted questions and measures of

assessment. Specific interventions shown to promote psychosocial wellness as well as brain neuroplasticity are also reviewed. Early models of successful applications are described, as well as current examples of positive psychiatry interventions in clinical practice and in the community.

20.2 Positive Psychiatry: Evidence for Five Key Epigenetic Factors on Positive Health Outcomes

20.2.1 Outlook, Attitude, and Positive Self-Perceptions

Interventions that promote a positive cognitive set (including optimism, gratitude, and kindness) have been shown to impact positively on self-rated happiness and to promote psychosocial resilience [21]. A positive cognitive set also is associated with healthy longevity in humans [22]. Positive attitudes and perceptions foster emotional and cognitive resilience in situations of adversity. While resilience expresses itself visibly in the face of serious hardships, its underpinnings include a mindset that allows individuals to think accurately and flexibly. It involves optimism but not of a "rose-colored glasses" variety but rather an ability to see goodness in the self and in others, as well as to see problems objectively and focus on what can be changed. One of the most profound examples of positive cognitive set in resilience can be found in Viktor Frankel's *Man's Search for Meaning* [23], a book he wrote while in a German concentration camp. He wrote lucidly about how he survived each day by focusing on small meaningful interactions with other prisoners and even guards that gave him a sense of purpose and the strength to go on. Flexible, clear, and positive thinking are key psychological ingredients repeatedly found in resilient prisoner-of-war survivors, as well as adherence to personal and group ethical codes [24]. As well, optimism and cognitive flexibility have been repeatedly shown to lower the risk of major depression, suicidality, addictions, and post-traumatic stress disorder in adults exposed to traumatic events. A positive cognitive set is also correlated with other key protective factors such as higher reported happiness, strong relationships, and problem-solving skills [25].

The theoretical framework for both positive psychology and positive psychiatry is cognitive behavioral therapy (CBT). CBT has been effectively applied to the general population through positive psychology, aiming to improve awareness and self-direction of thought habits in the normative population. CBT is a model of psychotherapy based on the principle that thoughts impact emotions and behaviors and that improving thoughts improves emotional and behavioral states. Within psychology and psychiatry, CBT currently has the broadest evidence base among the psychotherapies, effective for the treatment of mental illnesses across a range of disorders including mood disorders, anxiety disorders, and addictions [26, 27], and across age groups. Positive psychiatry might also help redress stigma of mental illness and agism and their negative impact on health and health outcomes. For example, positive self-perceptions of aging have been shown to benefit mental and physical health outcomes and to increase lifespan [28] as well as to increase health behaviors over time, even in

the face of physical illness [15]. "Enhanced CBT" specifically modified to better meet needs of older adults including addressing negative thoughts on aging [29] and "strengths-based CBT" to promote resilience [30] are promising new approaches.

20.2.2 Physical Activity

Many contemporary illnesses such as cardiovascular disease, stroke, and diabetes mellitus are directly linked to sedentary behavior, while optimal levels of physical activity are highly protective for physical health [18]. The direct health benefits of physical activity in regulating blood glucose, lipids, blood pressure, and body weight are well known in those with mental illness as well as the general population. The benefits of physical activity on brain health and mental wellness are only more recently being appreciated. As the evidence stands, there is no better promoter of brain neuroplasticity than physical exercise. Physical exercise also has been shown to slow progression in mild cognitive impairment to dementia [31, 32]. The likely mechanisms include stimulating neurogenesis, increasing cerebral blood flow, and increasing production of important proteins such as brain-derived neurotrophic factor [32].

Regarding improvements in mood, even moderate physical activity (180 min/week of walking or other moderate activity) improves depressive symptoms. In a Cochrane Review of 32 randomized double-blind studies (n = 1858), exercise was of significant benefit, especially in mild to moderate depression [33]; meanwhile, sedentary behavior has been correlated with a 25% increased risk of depression (193,166 subjects) [34]. Exercise is now recommended as a first-line non-pharmacological treatment for depression in national guidelines such as the Canadian Network for Mood and Anxiety Treatments (CANMAT) [35]. With the inclusion of exercise in national guidelines, psychiatrists and other physicians will increasingly be prescribing physical activity to patients and will need to find ways to help them follow through. Positive psychiatry uses current data to inform and develop the use of evidence-based tools such as cognitive-behavioral therapy to engage, shift, and maintain health behaviors such as physical activity to minimize disease burden.

20.2.3 Social Connectedness and Attachment Relationships

Research shows that social relationships and especially close attachment relationships in which a person feels emotionally safe are extremely important to mental health and well-being. The longest-running study of healthy longevity is the Harvard Longitudinal Study of 724 American men, which is now in its 76th year. The results of this study showed that warmth of early childhood family relationships predicted secure attachments and well-being up to 60 years later [36]. As well, data on the impact of loneliness and social isolation show that this variable is as powerful a risk factor as smoking in terms of impact on overall health [37, 38]. Given the

importance of social connection and attachment on both physical and mental health, positive psychiatry seeks to inquire about relationship strength and social engagement when interviewing patients. Individual and groupbased psychotherapies across modalities offer evidence-based methods to reddress attachment issues and improve outcomes across age groups. As well, positive psychiatry seeks to advocate for resilience-friendly communities where social activities that promote intergenerational connection are organized and available. Resilience and well-being do not occur in a vacuum: it is essential that social cohesion is valued and forwarded in practical and affordable ways for individuals and communities to thrive.

20.2.4 Cognitive Activity

Another key promoter of brain neuroplasticity, health, and well-being across the lifespan is new learning. More complex, novel activities are stronger promoters of brain neuroplasticity, such as learning a new language or musical instrument. Staying cognitively active throughout life through social engagement or intellectual stimulation is associated with a lower risk of dementia. Having fewer years of education has been associated with a higher risk of dementia, while attaining a higher level of education is associated with an increased "cognitive reserve" or ability to operate effectively even when damaged and a decreased risk of developing dementia risk. Formal cognitive training also seems to have cognitive benefits. In the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial, healthy adults 65 and older who participated in memory training, reasoning training, or processing-speed training sessions had improved mental skills that persisted 10 years after the training was complete [39]. The potential for cognitive training to benefit patients with mild cognitive impairment and depression is currently being investigated through the Brain Canada Foundation by Dr. Benoit Mulsant and colleagues in the Preventing Alzheimer's Dementia with Cognitive Remediation plus Transcranial Direct Current Stimulation in Mild Cognitive Impairment and Depression (PACt-MD) study [40]. Previous research has indicated benefit of cognitive training in older adults with mild cognitive impairment in improved cognitive and functional performance [41].

20.2.5 Caring for Mental Health, Mindfulness, and the Relaxation Response

Undiagnosed and untreated mental illness negatively impacts well-being, resilience, and quality of life and worsens prognosis of medical illnesses and other health outcomes. Robust national anti-stigma public awareness campaigns and well-funded mental healthcare resources are needed to improve mental healthcare access in every corner of the globe.

Particularly in Western culture where fast-paced efficiency is highly valued, learning how to "switch tone" in the nervous system is a key element for mental wellness. Dr. Herbert Benson, founder of Harvard's Mind/Body Medical Institute, describes the "relaxation response" as a state of deep relaxation that engages the

parasympathetic nervous system and increases blood flow to the brain [42]. The response can be achieved through visualization, progressive muscle relaxation, massage, breathing techniques, meditation, yoga, and prayer, practices generally more prevalent outside of North America and Europe. Common elements are removal from everyday thought and focusing on your breath, a word, a sound, phrase, or prayer. In his book *The Relaxation Response* [43], Dr. Benson outlines research showing that regular use of the relaxation response can help health counteract the physiological effects of chronic stress. Benefits of routine practice include improvement in stress-related problems including fibromyalgia, insomnia, hypertension, and anxiety disorders while promoting better health, lower stress, increased well-being, and reduced blood pressure and heart rate.

Newer research on the impact of meditation and mindfulness practice at the cellular level is promising. A recently discovered biochemical marker in healthy aging is an enzyme called telomerase that can lengthen our chromosomal telomeres [44]. Telomeres are the DNA protein structures found at the ends of our chromosomes that play a vital role in protecting the genetic material in our genome. Telomere length is correlated with onset of age-related diseases. Telomere shortening is associated with aging and with chronic diseases including depression, stroke, heart disease, diabetes, and cancer as well as with chronic stress. In a meta-analytic review by Schutte and Malouff [45], meditation in 190 subjects increased telomerase activity in peripheral blood mononuclear cells. A recent study by Duraimani et al. [46] showed that a 4-month meditation exposure decreased blood pressure in hypertensive patients and increased telomerase gene activation. The relaxation response appears to be an important approach to promote biological and mental health, and interventions that induce the relaxation response—including meditation, mindfulness, and yoga—could be readily included in patient care plans in psychiatry and across healthcare.

Other vital dimensions of physical well-being include nutritional and dietary status (and especially to address malnutrition), addictions including excess alcohol and cigarette smoking, and the psychosocial correlates of poverty. These factors have also been clearly demonstrated to affect physical and especially brain health, including mood and cognitive functioning over time, and are important to include in the assessment phase and treatment plan in patients with mental illness around the globe.

20.3 Bringing Positive Psychiatry Into Clinical Practice

Positive psychiatry has important contributions to make to our field and to medicine regarding the practical application of strategies to optimize patient resilience and well-being. Evidence-based tools are needed for frontline clinicians to optimize attitudes and behaviors for health and resilience across the lifespan. Health behavior and attitude change can be accomplished through cognitive behavior therapy-informed interventions and can be learned by clinicians in psychiatry, in primary care, and on the front line of community mental healthcare. Practical applications of positive psychiatry in clinical care mean adding targeted questions and measures to assess mental wellness and resilience and using specific evidence-based techniques and interventions to promote mental wellness and quality of life.

Aspects of mental wellness and resilience often are included in the standard psychiatric approach. The psychiatric multiaxial formulation includes a resilience domain of "protective" factors: the biological, psychological, and social resources that promote patients' mental well-being. In terms of existing treatments, standard psychiatric approaches aligned with the goals of positive psychiatry include the recovery model, strengths-based care, patient-centered care, and standard psychotherapeutic treatments, such as cognitive behavioral therapy (CBT), problem-solving therapy (PST) [47], and acceptance and commitment therapy (ACT) among others [48].

Given the protective psychological effects of resilience across the lifespan, it is a capacity deserving of careful assessment in psychiatric evaluations and of focus in psychotherapeutic treatment to promote mental health and prevent illness relapse. For those suffering from the most chronic and severe mental disorders, positive psychological attributes when present can be highly protective [5]. Positive psychiatry seeks to promote these psychological factors even in the face of serious mental illness. Positive psychiatry practice is an invitation for psychiatrists and mental health workers to move beyond pathology identification or symptom reduction, to expand clinical attention to patient strengths and use a more thorough, systematic, and scientific approach to assess and build on strengths. In addition to individual patients, positive psychiatry interventions carried out by the multidisciplinary mental health team members will benefit patients, families, and caregivers alike.

The following are recommendations to support all clinicians in the practical integration of positive psychiatry into frontline care:

- During the *patient assessment*, spend a few extra minutes assessing patient strengths and protective factors using relevant questions and questionnaires (see examples below).
- In providing a *clinical impression*, highlight patient strengths in more detail within the biopsychosocial case formulation.
- In making *recommendations/management plans*, include evidence-based wellness/resilience promotion plans (see Caring for Mental Health section, and see Specific Techniques to Promote Wellness for details).
- In *follow-up*, continue to monitor beyond initial psychiatric symptom improvement, and aim to improve wellness and protect against future relapse. Help the patient/family and caregivers to set specific health behavior goals shown to promote mental wellness, and track their progress.

20.4 Measures and Questions to Assess Resilience in Clinical Practice

Five core psychological attributes have been associated with resilience in adults [2]. These include self-awareness, self-regulation, mental agility, character strengths, and strong relationships. *Self-awareness* includes the ability to identify one's thoughts, emotions, and behaviors as being either helpful or counterproductive.

Self-regulation refers to the ability to modulate impulses, emotions, thoughts, and behaviors, especially to achieve important goals. *Mental agility* refers to the ability to think flexibly and accurately, including the ability to take perspective and try new strategies to problem-solving. *Character strengths* include identifying one's own strengths to overcome challenges and stay focused on goals. *Connection* refers to the ability to build strong relationships through positive, clear communication, empathy, and a willingness to ask for and to offer help as needed [49]. Fortunately, resilience is a dynamic capacity that can be learned and improved upon [50].

Targeted questions directed to the six core competencies of resilience as outlined above are useful to ask about as a basic frame during an assessment to help evaluate resilience factors:

1. *Self-awareness*: Do you feel able to judge the strength and weakness of your own ideas and behaviors? Can you think of an example when you found it useful to review the pros and cons of your own ideas and actions? (This is a jumpstart evaluation of the individual's capacity for insight and ability to self-reflect on specific situations).
2. *Self-regulation*: How hard is it to regulate your impulses and moods? Do you get angry/depressed/anxious easily and find it hard to stop thinking about certain problems? What do you do if anything to manage feelings and thoughts?
3. *Optimism*: Do you find it easy or hard to notice what is good about other people and yourself? Is it a struggle to see the glass as half full?
4. *Mental agility*: Do you find that you can get around problems by being flexible in how you think of them? Are you good at coming up with different solutions to problems?
5. *Character strengths*: What would you consider to be a key strength in yourself and in other people who are important to you? Can you use those strengths to help you in problem-solving and trouble shooting in your life?
6. *Close relationships*: How strong do you feel your personal relationships are? Do you find it a struggle to empathize with other people or does that come easily to you? Are you able to ask for help when you need it? Does someone have your back? Are you able to help other people close to you?

The above questions in clinical interviewing help unlock and develop core psychological competencies to support resilience. Using these questions, psychiatrists and other mental health clinicians can evaluate individual perceived and actual psychological strengths that form part of a biopsychosocial formulation and help patients to identify and articulate their own capacities.

In terms of specific measures to assess mental wellness and resilience in frontline care, a variety of tools are available to measure resilience in the context of the biopsychosocial assessment. The ten-item Connor-Davidson Resilience Scale (CD-RISC) [51] can be used in evaluations pre- and posttreatment of adults, and the two-item CD-RISC 2 is an even briefer version to measure resilience in terms of "bounce back" [52]. The Psychological General Well-Being Index (PGWB) [53] and the World Health Organization–Five Well-Being Index (WHO-5) [54] are

recommended well-being scales with content validity and clinical relevance for positive psychiatry [1], (p. 129).

20.5 Specific Techniques to Promote Resilience: Importance of CBT to Positive Psychiatry

Cognitive behavior therapy (CBT) offers the theoretical underpinning of positive psychology and positive psychiatry: personal influence on our own happiness is based on the CBT theory that our thoughts impact behaviors and mood states and that our thoughts are changeable. The goal of CBT is to promote constructive, adaptive thinking in order to improve mood and promote constructive behaviors. Among psychological treatments, CBT has the broadest empirical evidence, found to be as effective as medications in the treatment of mild to moderate depression [55, 56], more effective than antidepressants in relapse prevention [57, 58], a gold-standard treatment for anxiety disorders, and helpful in a range of other psychiatric disorders from psychotic disorders to addictions. Other psychotherapies derived from CBT, such as problem-solving therapy (PST) and acceptance and commitment therapy (ACT), also offer techniques to promote resilience and mental wellness in patients through goal setting and alignment of behaviors and beliefs.

In considering psychotherapy to promote relapse prevention, Dr. Christine Padesky's strengths-based CBT to promote resilience [30] offers promise in those with chronic medical illness and/or psychiatric disorders. An "enhanced CBT" model has been specifically modified to meet needs of older adults with depressive or anxiety disorders and also to address negative thoughts on aging [29]. The enhanced CBT approach offers an 8-week manualized program with therapist and participant guides, most recently modified to include an extra week to challenge negative age stereotypes and negative automatic thoughts about aging.

20.6 Positive Psychiatry and Resilience-Friendly Communities

Relevant to global demographic changes, communities will increasingly benefit when resilience is supported across the lifespan. A paradigm shift is needed away from interventions simply at an individual level toward prevention-focused, community-based approaches. The World Health Organization (WHO)'s Global Age-Friendly Communities (AFCs) Network [59] is a global initiative to actively involve and value older adults in communities.

Positive psychiatry can play a key role in maximizing the ability of adults to remain in their homes and communities over time, where necessary with additional supports and services. In his seminal paper, "Age Friendly Communities Initiatives: Public Health Approach to Promoting Successful Aging" [60], Dr. Jeste and authors suggest that academic geriatric psychiatry must play a key role to ensure that "mental healthcare is considered and delivered on par with physical care". The authors

assert that one of the largest societal barriers is pervasive agism and that in order for Age-Friendly Communities (AFCs) to thrive, entrenched negative age stereotypes need to be replaced with positive, realistic expectations, both at individual and societal levels. In support of this assertion, research suggests negative beliefs about aging are almost universal and tend to become self-fulfilling prophecies, associated with worse health outcomes and reduced longevity [61], while positive attitudes are associated with improved outcomes [28, 62].

In terms of negative age stereotypes, positive psychiatry and the psychotherapies have much to offer in addressing underlying attitudes and their impact on health behaviors and health outcomes. As well, positive psychiatry can help advocate for the underlying resources and community structures that support "resilience-friendly" communities including access to physical activities, social, and lifelong learning opportunities.

Jeste offers examples of resilience-friendly initiatives in Nova Scotia, Iowa, and California in which community-based seniors' mental health promotion is supported by government and private funding. In San Diego, University of California, San Diego's Center for Healthy Aging has recently received a grant from the San Diego Foundation to conduct a pilot study of training for advocacy to make neighborhoods more walkable. In Johnson County, the University of Iowa Center on Aging is helping with surveys of older residents' unmet needs. In Halifax, Nova Scotia, the Fountain of Health Initiative for Optimal Aging has several projects applying positive psychiatry tools in clinical practice and in the community, with further details outlined below.

20.7 The Fountain of Health Initiative: Applied Positive Psychiatry from Community to Clinic

Founded by Dr. Keri-Leigh Cassidy at Dalhousie University in Nova Scotia, Canada, the Fountain of Health (FoH) Initiative for Optimal Aging is an example of positive psychiatry applied across age groups and across the continuum, from the clinical to the community level. The FoH is a national Canadian nonprofit organization to increase public awareness about brain health and resilience across the lifespan and to provide clinician tools to promote brain health and resilience primary/secondary community care to tertiary care settings. The FoH targets the following groups:

- *General public (primary prevention)*: Since outlook and lifestyle patterns in early, mid- and later adult life can determine health and resilience, it is crucial that more members of the general public know this information and apply it across the lifespan.
- *At-risk/ill population (secondary prevention)*: For those at increased health risk or stress, such as caregivers or those with preexisting mental or physical health problems, the Fountain of Health information offers tools to promote resilience in the face of stress or ill health, to potentially offset significant human and healthcare costs.

- *Healthcare providers*: Healthcare providers are offered practical evidence-based health promotion information and tools to use for primary and secondary prevention, help patients set and meet health goals, and help clinicians in busy practice settings to deal with patients' psychological barriers to health behavior change.

Fountain of Health aims to activate mental and physical health across the lifespan with a focus on the underpinnings of resilience and mental well-being. The FoH has several goals: to shift negative attitudes about aging and mental illness; to improve health behaviors and outcomes by translating the science of resilience to clinicians and the public; to help catalyze a collective and meaningful investment in resilience and well-being across the lifespan, particularly within the healthcare system; and to support resilience-friendly communities. The FoH supports individuals, clinicians, and communities to become more aware of the current science of healthy and active aging and promotes translation to action in a variety of ways. In terms of clinician tools, the FoH specifically addresses stigma and agism. Using cognitive behavioral principles, clinicians can learn how to invite behavior and attitude change in brief office contacts and provide follow-up on goal setting.

The FoH website is designed to provide education and current research on wellness and health promotion at *fountainofhealth.ca*. The website condenses the current science of resilience and healthy aging into the main five key domains: (1) positive thinking, (2) social activity, (3) physical activity, (4) mental health, and (5) lifelong learning. Online resources include:

- *Positive psychiatry clinician tools* for health professionals to use with patients to promote changes in outlook and health behaviors. The FoH tools include a patient self-assessment questionnaire, a 3-minute educational video for patients, a 4.5-minute instructional video for clinicians, several downloadable tools for use in frontline care, and a *Clinicians' Guide* to support clinicians in helping patients set an achievable health goal and to address barriers that arise in behavioral change. (See Clinicians' Corner under the Resources section of the website).
- *FoH app* to further support positive psychiatry health behavior change in physical, social, and cognitive domains.
- *Evidence base* with a listing of key literature.
- *Speakers' bureau* with experts on topics of resilience, emotional well-being, and healthy aging (see "Speakers' Bureau" under the resources section of the website).
- *International positive psychiatry* through affiliations with World Psychiatric Association (WPA) and the World Aging and Brain Health Institute (WABHI) (see "Our People").

The FoH program materials have been piloted in primary care, as well as in the community. The primary care projects found FoH to be well received and useful in frontline care, leading to increased patient knowledge, health behavior goal setting [63], and health behavior change. A recent study found the majority of patients who received the FoH education not only set health behavior goals but also followed through on them over a 4-month period, and longer-term follow-up is underway to

evaluate the efficacy of interventions to support health behavior change in clinical settings. Meanwhile a community project found that 6-week community FoH education run by senior lay leaders improved community-dwelling seniors' knowledge, attitudes to aging, and confidence in health behavior goal setting [64].

20.8 Positive Psychiatry Movement: Potential Impact Around the Globe

The positive psychiatry movement is at its inception and carries the potential for influence on the field of psychiatry for decades to come. Major national and international psychiatric organizations have established positive psychiatry in the past year most notably the American Psychiatric Association's Caucus on Positive Psychiatry and the WPA's Section on Positive Psychiatry, its inaugural newsletter published Summer 2016 [65]. The Association for Positive Psychiatry of Canada has emerged in the past year as an organization that aims to support the academic positive psychiatry movement in Canada.

Through the WPA section, countries from around the globe will be able to join and participate in the global section and/or pursue their own national organizations as well. There is a need for further development of standards of training, as well as training opportunities, in positive psychiatry. There is also the potential for the development of "self-reflexive" positive psychiatry, which considers wellness and resilience in healthcare providers and offers meaningful contributions to the "physician wellness" movement. The emergence of mindfulness programs for medical students, residents, and healthcare practitioners in university centers in North America and Europe provides a concrete example of evidence-based wellness promotion for healthcare providers.

Further research is needed around the world in positive psychiatry to build evidence and academic credibility within the field. The University of California, San Diego Center for Healthy Aging is providing significant leadership in academic positive psychiatry. The center formed an international-level think tank comprised of experts in aging, from different relevant fields on topics important to the aging population such as technology, housing, and built environment. The center also has started a new positive living workgroup, in collaboration with child psychiatry, public health, and undergraduate and graduate education programs across the USA and Canada to focus on positive living themes (i.e., resilience, optimism, social engagement, well-being, happiness) across the lifespan and to plan strategies for incorporating those concepts into clinical care, training, and research. The workgroup is developing research projects to enhance training and education programs and to work toward interventions and intergenerational activities to promote well-being.

Another recent development in positive psychiatry research is the establishment of a research network in positive psychiatry: the World Aging and Brain Health Institute (WABHI) hosted the first International Think Tank on Optimal Aging in 2016. Founding members include Dr. Dilip Jeste among other internationally renowned researchers in brain health. WABHI's think tank brought together leading

international researchers from Canada, the USA, the United Kingdom, and Europe with interests in resilience, brain neuroplasticity, cognitive behavioral therapy, and health behavior change.

In terms of future directions, positive psychiatry offers a major paradigm shift away from pathology and toward resilience and wellness in the healthcare system in general. Our current medical model focuses much more on the science of pathology and the treatment of disease rather than on the science of health and wellness. Positive psychiatry promotes health and wellness at the level of primary and secondary prevention of chronic disease including dementia, depression and anxiety disorders. Positive psychiatry will have a significant role in serious mental illnesses such as schizophrenia and other psychotic disorders [4]. Emerging areas such as "lifestyle medicine" [66] are gaining traction in medicine and will synergize with positive psychiatry. Positive psychiatry also has relevance beyond formal healthcare for society as a whole. In addition to promoting education for the general population about the science of brain health, mental wellness, and resilience, positive psychiatry advocates for resilience-friendly communities and for the promotion of human longevity through lifestyle and attitude change.

Regarding the potential impact of positive psychiatry on a global scale, the social and economic disparities around the world are vital to consider. Given that positive psychiatry promotes health and wellness in the context of inadequate human resource to meet population mental healthcare needs, positive psychiatry has the potential to impact locations where mental health human resources are most scarce and community resilience is most greatly needed. Countries with the fewest psychiatric resources and greatest poverty stand to benefit from evidence-based community approaches to supporting resilience and mental wellness among its people. In war-torn regions of the world, positive psychiatry can offer evidence-based approaches to frontline workers to promote resilience in individual patients, families, and their communities and even for themselves in the face of adversity.

To realize the full potential of positive psychiatry, wide knowledge transfer and implementation of evidence-based positive psychiatry practices are required. Specific techniques to promote wellness and resilience in patients and their families need to be systematically and broadly applied both in psychiatry and throughout primary care and allied health as well as implemented within communities. Emerging successful techniques and practices in positive psychiatry could be more widely scaled up and utilized. Research is needed at a large scale to meaningfully assess the impact of positive psychiatry health promotion approaches in regional and global contexts.

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Mental Health and Sexual Medicine: An Update

21

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Abstract

In this chapter of the WPA Section on Psychiatry and Human Sexuality are presented two interesting articles on sexual dysfunctions, a crucial clinical concern in Sexology – one deals with female sexuality and its dimensions and the other on the adequate and efficient treatments offered in these days. One other concerns the important matter of sexual violence.

Kevan Wylie, sexologist and president of the World Association for Sexual Health presents a very actual reflection on female sexuality on different dimensions, namely women, sexual well-being, mental health, religion and sex and sexual diversity.

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A revision on the treatment of sexual dysfunction is done by T. S. Rao and et al. Navarro Cremades et al. the authors of the last article present an overview of the dramatic problem of sexuality violence against women starting in the definition and in sexual rights. This theme of sexual violence and PTSD is another dimension considered in what concerns to prevalence, genetic and epigenetic classifications and sexuality. The last point treated in this paper is the dimension of public health, prevention and public policies.

The authors intended to follow a clinical orientation since the important issue of sexual history and how to do it in different treatments that can be prescribed, psychological and biological treatments.

The human sexuality section believes in the importance of sexuality dimension in Psychiatry and Mental Health.

António Palha

Chair of the P.H.S. Section of WPA

21.1 An Update on Female Sexuality

21.1.1 Introduction

Societies have been changing significantly over the last two decades with the impact of the Internet and of technologies, in particular smartphones, having influence by informing women and their partners about opportunities available to them. An increasing awareness of individual opportunities and rights to a fulfilling and enjoyable sexual life has become prominent in many countries where discussion and exposure to sexual images and activity were previously absent or even forbidden. Psychosocial interventions are beneficial in supporting women with sexual difficulties although new pharmacological agents remain limited in development and clinical practice.

21.1.2 Changing Attitudes Toward Sex Among Women

The shift in sexual attitudes is highlighted by the findings from the consecutive UK National Surveys of Sexual Attitudes and Lifestyles (NATSAL) conducted over the last three decades. The most recent survey of individuals aged 16–74 years who lived in Britain (England, Scotland, and Wales) was completed between 2010 and 2012 and has data available for 6777 women and 4913 men [1]. Some of the key findings for women was that low sexual function was associated with increased age and, after age adjustment, with depression and self-reported poor health status. Low sexual function was also associated with experiencing the end of a relationship, an inability to talk easily about sex with a partner, and not being happy in the relationship. Associations were also noted with engaging in fewer than four sex acts in the past 4 weeks, having had same-sex partners, and having ten or more lifetime

partners. 51.2% of women reported one or more problems in the past year, although self-reported distress about their sex lives was much less common. For women in a sexual relationship for the past year, 27.4% (and 23.4% of men) reported an imbalance in the level of interest in sex between partners with 17.1% of women reporting that their partner had also some sexual difficulties.

21.1.3 Sexual Rights and Advocacy

The World Association for Sexual Health (WAS) [2] promotes sexual health throughout human life spans all over the world by developing, promoting, and supporting sexology and sexual rights for all. WAS accomplishes this by advocacy, networking, and facilitating information exchange of ideas and experiences while concurrently advancing scientifically based sexuality research, sexuality education, and clinical sexology with a transdisciplinary approach.

The World Association for Sexual Health Declaration of Sexual Rights was updated in 2014 and calls for a number of sexual rights with regard to sexual health. The full text is available on the Association website (www.worldsexualhealth.org). Right 7 is the right to the highest attainable standard of health, including sexual health, with the possibility of pleasurable, satisfying, and safe sexual experiences. Everyone has the right to the highest attainable level of health and well-being in relation to sexuality, including the possibility of pleasurable, satisfying, and safe sexual experiences. This requires the availability, accessibility, and acceptability of quality health services and access to the conditions that influence and determine health including sexual health.

21.1.4 Models of Sexual Response and Classification

The early models of sexual response were linear in nature incorporating concepts of sexual drive, sexual desire and libido, excitation and plateau, orgasm, and resolution. More recently, an intimacy-based model of a women's sexual response cycle was introduced by a team of experts led by Rosemary Basson [3]. This model reflects the key roles of emotional intimacy and sexual stimuli as motivators to find or be responsive to sexual stimuli. The basis of the more cyclical model is that the goal of sexual activity in women may not necessarily be physical satisfaction (by attaining orgasm) but rather emotional satisfaction (a feeling of intimacy and connection with a partner). Although Basson has continued to modify the model over time to accommodate additional factors that may impact on a woman's sexuality, there are additional models that may be important when considering sexual function and dysfunction, and these are offered in a recent review [4]. Reclassification of desire and arousal problems into female sexual interest/arousal disorder (FSIAD) in the DSM-5 remains controversial with some professionals criticizing such a move based on clinical judgment and expert opinion rather than empirical evidence [5].

21.1.5 Psychosocial and Psychosexual Factors and Sexual Well-Being

The expert committee reviewing psychological and interpersonal dimensions of sexual function and dysfunction of the fourth International Consultation on Sexual Medicine (ICSM) made a number of recommendations for women presenting with sexual problems [6]. Exploration of the attachment style of the woman, her personality, her cognitive schemas, any infertility concerns, and sexual expectations should all be noted. Assessment of depression, anxiety, stress, substance use, and posttraumatic stress (and their medical treatments) should be carried out as part of the initial evaluation. Clinicians should attempt to ascertain whether any anxiety or depression is a consequence or a cause of the sexual complaint, and treatment should be administered accordingly.

The assessment of multiple aspects of sexual functioning, including, but not limited to, subjective aspects such as sexual self-esteem and sexual satisfaction, not just sexual dysfunction should occur. A developmental approach to assessing the onset of sexual activity is recommended including self-focused as well as partnered activity ranging from non-genital to genital expressions, the context around those experiences, as well as any associated beliefs and emotions associated with them. Crucially, there should be an attempt to explore their possible role in the individual's current sexual function and behavior. Clinicians should explore sensitively childhood experiences including sexual abuse. A number of specific life stage stressors are evident for women including infertility, postpartum experiences, aging, and menopause, and these can have a specific impact on psychosocial and psychosexual experiences. Assessment of physical and mental illnesses that commonly occur in later life should be included as part of the initial evaluation in this age group.

21.1.6 Physical Factors and Sexual Well-Being

A substantial number of factors can interrupt the normal process of sexual activity and can be regarded as endocrine factors (typically androgens and estrogens), neurological factors, vascular factors, and iatrogenic factors. Cardiovascular risk factors have recently emerged as the main contributors to the onset of problems of sexual arousal. The role of metabolic syndrome (MetS), diabetes mellitus, hypertension, and dyslipidemia requires assessment in women with problems of sexual desire or arousal.

There are a number of common gynecological conditions in women where interruption to usual sexual function can occur such as cervical, ovarian, and other gynecological carcinoma, prolapse, incontinence, interstitial cystitis, and surgical procedures such as hysterectomy. Dermatological conditions such as lichen sclerosus and eczematous rash can cause a number of sexual problems including sexual pain. These can all have a significant impact on a sense of self and completeness for

a woman and impact on feelings of attractiveness to both self and partner and overall desire to engage in sexual activity.

The contribution of hormones, including estrogens and androgens on female sexual function, remains a contentious area for debate, but other specific endocrinopathies in women are associated with female sexual dysfunction (FSD) including hyperprolactinemia (a common clinical scenario with some treatments for psychosis), polycystic ovary syndrome, and obesity [7].

21.1.7 Mental Health, Religion, and Sex

Religion and culture are inherently intertwined. Sungur and Bez [8] argue in their recent review that while many practitioners will now aim to understand and recognize the cultural diversity of their patients when it comes to religion, most do not feel competent or do not wish to address the subject specifically in a mental health setting, particularly with respect to sexual problems. The authors remind us that an evaluation of 30 research studies identified 14 suggestive of a favorable relationship between religion and mental health, 9 that showed no association, and only 7 indicating a non-favorable relationship. This review summarizes the similarities among Muslims, Christians, and Jews and offers some insights into provision of specific couple-tailored treatment programs.

Searching of 13 electronic databases identified a number of controlled trials (randomized or non-randomized) comparing the effectiveness of sexual health risk reduction interventions with usual care for individuals living in the community with severe mental illness [9]. Unfortunately, there is insufficient evidence at present to fully support or reject the identified sexual health risk reduction interventions for people with severe mental illness. However, given the serious consequences of high-risk sexual behaviors, there is an urgent need for well-designed trials as well as training and support for staff implementing sexual health risk reduction interventions for women (and men) with mental health problems.

21.1.8 Sexual Diversity

Psychiatrists and other mental health practitioners should strive to offer a nonjudgmental approach when exploring and understanding with a woman her sexual and gender identity regardless of any sexual dysfunction. The principal issues involve sexual orientation, gender identity, and the presence of any paraphilic patterns of sexual arousal. Although many women will describe themselves as “straight” or heterosexual, around 15% of women in one study reported some same-sex attraction or sexual experiences, while only around 1% would describe themselves are exclusively lesbian. Mental health issues associated with experiences of discrimination and marginalization from family, friends, and wider society should be regularly assessed in women reporting sexual problems [10]. With increasing age, there is

likelihood of being alone and more isolated, and across age groups, there is reporting of self-harming. Mental health issues are as high as 88% in transgender people, and the sexual needs of patients undergoing gender transition and thereafter are often poorly attended to within clinical services [10, 11].

With the increasing acceptance of diversity over recent decades, many of the conditions historically described as paraphilias are no longer considered such and have been removed from the recent revision of the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5). There is clear distinction between the behavior itself (e.g., receiving of pain for sexual pleasure—sexual masochism) and a disorder stemming from that behavior (i.e., sexual masochism disorder) [12]. Most of the behaviors observed and enjoyed by women would not be classified as a disorder within the new classification system.

21.1.9 Clinical Interventions

The interventions that may be of use in helping women with sexual problems are diverse and are predominantly psychological and/or educational. These include psychosexual therapy, relaxation training, mindfulness training, and self-focus work on body exploration and experience. A detailed review of interventions is beyond the scope of this section; however, a review of psychosocial and pharmacological interventions (including the recently approved agent flibanserin in the USA) is provided by Brotto et al. [6] and Parish and Hahn [5]. The interested reader is also referred to the proceedings of the ICSM4 and other substantial resources that can be accessed from the International Society for Sexual Medicine (ISSM) university website (http://issm.university/).

21.1.10 Conclusions

This chapter section has identified a number of factors that impact on the sexuality for an individual woman. The limited space means that only some of the factors have been considered and presented in detail to the reader. Other issues such as the impact of non-monogamous relationships, use of Internet-based dating sites, and access to pornography may continue to have a bearing on a woman's sexuality. The impact for a woman (and her partner) necessitates careful nonjudgmental and supportive enquiry and has become a necessary part for evaluation in the clinical setting.

Comprehensive history taking can elicit the contributions from the physical, psychological, and relationship perspectives to allow a biopsychosocial formulation and to propose a treatment plan. An awareness of the interventions that may be helpful for the woman (and her partner) is valuable, and the MHP can assist in signposting women to the appropriate healthcare professional(s) if expertise or time does not allow direct support to the women in the clinic where the issues have been identified.

21.2 Management of Male Sexual Dysfunctions: Current Evidence and Emerging Vistas

The interface between mind and body though known from ages has been emphasized in modern medicine only in the recent times. Sexuality is the ultimate union of mind and body. Many diseases are fully described based on their effects on specific organs, but the impact on sexuality has not been emphasized.

Human sexual response cycle is mediated by neurotransmitters and hormones. Neurotransmitters like serotonin, acetylcholine, and nitric oxide and hormones like testosterone acting in specific brain structures like the hypothalamus, limbic system, and cortex mediate sexual response cycle.

Prevalence of male sexual dysfunction varies from 3–40% according to different studies. Men suffer from various sexual problems, which include hypoactive desire disorders, premature ejaculation, delayed ejaculation, retrograde ejaculation, painful ejaculation, anejaculation, erectile dysfunction, and postorgasmic illness syndrome. Different professional bodies have classified sexual dysfunction in different ways, like the International Society for Sexual Medicine, International Classification of Diseases-10 (ICD-10), and Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5).

In order to simplify, several authors have conceptualized sexual problems arising from illness as primary, secondary, or tertiary. Primary sexual dysfunction refers to dysfunction that is organic in nature directly related to the illness; secondary sexual dysfunction relates to physical changes that cause indirect impairment such as fatigue, weakness, bowel, and bladder incontinence; and tertiary sexual dysfunction refers to psychological impact of the illness like depression, fear, and low self-esteem.

Making a Diagnosis Male sexual dysfunction is an important public health issue, but the diagnosis of the same can be a bit dicey. A patient-centered approach to diagnosis is one of the most accepted concepts in sexual medicine. This approach takes into account the various cultural variations and age factors so that the diagnosis and treatment aspects can be individualized. Some patients may not be comfortable while talking about their sex partners and sexual practices. The clinician should be nonjudgmental, maintain privacy, and first focus on building a strong rapport and simultaneously be sensitive toward the patient. Detailed history (particularly medical, sexual, and psychosocial history) should be taken followed by a thorough physical examination in the entire cases [13]. Personal, social, and cultural aspects of the patient are equally important. Young men may particularly become uncomfortable to admit problems with erection, which undermines their masculinity. Culture defines gender roles, influences sexual behavior, elaborates on explanations of sexual dysfunctions, and defines personal beliefs for healing. Hence culture defines the point at which normal variation in sexual functioning becomes a disorder [14]. With a proper history, one should be able to differentiate between organic and psychogenic causes of sexual dysfunction, identify underlying comorbid medical disorders, and use of any medications/drug use or abuse leading to sexual problems.

It is necessary to understand the ongoing relationship problems in the couple, whether the partner is supportive or not, and their expectations and motivation for treatment [15]. Sexual functioning is a complex biopsychosocial process; evaluation and treatment of sexual disorders in an individual require commitment and interest from both the partners. Usually, psychogenic potency problems are situation specific, begin suddenly, and are accompanied by normal nocturnal and early morning tumescence. However, organic erectile dysfunction presents consistently and starts gradually, and there would be loss of early morning erections; libido and ejaculatory function may be normal in men with erectile dysfunction. Anticholinergic drugs, antidepressants, antihypertensive, histamine H2 receptor antagonists, and other drugs may be associated with sexual dysfunction. Hypogonadism may present with loss of interest in sexual activity.

Sexual History A comprehensive sexual history and evaluation of the patient's overall sexual function are essential in confirming the patient's diagnosis. An ideal time would be 45–60 min for taking the sexual history [16]. While obtaining the sexual history, the clinician needs to enquire how the patient obtained information about sex. Due to deficits in basic knowledge about human sexuality, many sexual problems may surface up. Basic principles of sexual history taking are given in Table 21.1 [17].

Both partners are asked to make a timetable in terms of time spent in different categories: work time (both at work and work in the house), family time (with children and partners, extended family time—with parents and relations), relationship time (time spent together), social time, and personal time. The "timetable" needs to be made for different times in life and compared with periods of good sexual functioning [24, 25].

Table 21.1 History taking for male sexual disorders

(I) Identifying data	Patient's name, age, sex, job, relationship status, orientation (heterosexual, homosexual, bisexual)
(II) Current sexual functioning	Satisfactory or not, whether partner feels satisfied; frequency and libido
	Description of sexual interaction; the problem and its duration; its relation to time, place, or partner [16]. Interest, performance problems, ejaculation, orgasm, and satisfaction related to sexual functioning [17–23]
(III) Past sexual history	
Childhood	Childhood sexuality (parental attitudes, learning about sex, self-stimulation)
Adolescence	Onset of puberty, masturbation (fantasies associated with masturbation), homosexual activities, dating, first coitus
Adults	Premarital sex/cohabitation details; marriage: frequency of sexual interaction; birth control, protected sex; extramarital sex, conflicts in marriage if any; current relationship; partner's view of the problem
Special issues	• Fertility problems, miscarriage, abortions, or illegitimate pregnancies • Paraphilias, gender identity problems • Chronic illnesses, sexually transmitted infections • Sex after, separation, widowhood, divorce • History of rape, incest, sexual abuse

Examination A thorough physical examination including the neurological and the vascular systems and systems related to other etiologies should be undertaken [26–28].

Investigations Laboratory studies as and when indicated may include a urine analysis, blood tests for complete hemogram, kidney function test, lipid profile, fasting blood sugar, thyroid function, and other endocrinal tests. Nocturnal penile tumescence, intracavernous pharmacologic injection (using a vasodilating agent like papaverine, phentolamine, and prostaglandin E1), dynamic infusion pharmacocavernosometry, and duplex color ultrasonography are the other tests in some selected cases [18, 29].

Treatment The treatment can be broadly classified as (a) psychological treatment, (b) pharmacotherapy for sexual dysfunctions, and (c) lifestyle management. Specific psychological treatment approaches may vary depending on the type of sexual dysfunction.

21.2.1 Psychological Treatment Approaches

Masters and Johnson's Short-Term Sex Therapy Before Masters and Johnson's published *Human Sexual Response* in 1966 and *Human Sexual Inadequacy* in 1970, psychological treatment of sexual dysfunctions was similar to other disorders and focused on repressed emotional trauma and childhood conditioning. Research published in *Human Sexual Inadequacy* formed the basis of short-term therapy (similar to behavior therapy) as we know it today. The treatment is useful in impotency, nonorgasmic response, premature ejaculation, and ejaculation incompetency [30]. During therapy the couple is treated as a unit with a male-female therapy team. Hence the couple has someone of their own sex, a therapist who can understand their problems better.

The first step is taking a detailed medical and sexual history from the patient by the therapist of the same sex (male therapist takes history from the male patient and female therapist from the female patient). During the second appointment, the same process is reversed, and the male therapist takes history from the female patient. The second step particularly helps in understanding the attitudes of patients and as a check point. Before moving to a specific therapy, a round table discussion is made to understand the attitudes, opinions, and actions of the couple toward each other. At this point, the couple has the option of opting out of the therapy, if they are not comfortable with the idea that, for a successful treatment, changes will have to take place in the relationship itself [30].This is followed by a program of sexual tasks. The first stage of this program is the "sensate focus." This is helpful in a couple irrespective of the presenting problem. In "sensate focus," the couple learns to touch each other erotically and simultaneously communicate their likings and dislikings. During this stage, touching of genitals and breasts of female or having intercourse is not allowed. The purpose of this stage is to facilitate discovering of various

sensual parts of the body. These help the couple in recognizing that "pleasuring" and "receiving pleasure" are enjoyable without being regarded as part of sexual intercourse [31].The next stage is mutual genital stimulation while communicating to each other what feels good. After completion of these two stages, further treatment depends on the presenting problem [30].

In case of erectile dysfunction, the female learns how to stimulate the penis in specific ways. When her partner has an erection, the female initiates the insertion and movement first. Hence performance pressure on the male is allayed and the responsibility gets shared.

For premature ejaculation, the "squeeze technique" is effective. Here both partners need to communicate effectively; the male lets his partner know when he is about to ejaculate. At this juncture, the female squeezes the tip of the penis, thereby inhibiting ejaculation. This process has to be followed for several weeks before when improvement is seen.

The important aspects of Masters and Johnson's therapy are to improve communication and relationship of the couple along with the physical therapy. Reeducating the couple to get sexual satisfaction while removing any fears and misconceptions is at the core of the therapy [30, 32].

Behavioral Techniques The assessment and treatment needs to be tailored according to one's professional setting and type of problem the patient is facing. The intensive therapy involves primarily sensitization and desensitization techniques [15, 33]. The general principles are applicable to majority of the inadequacies.

Annon (1974) proposed a graded intervention popularly called as *PLISSIT model* of sex therapy, highlighting the fact that most people with sexual dysfunction may not need an intensive course of therapy [34, 35]. As the level of intervention goes up, greater knowledge, training, and skills are required during the therapeutic process [36].

The PLISSIT model is as follows:

P = Permission giving—Defining one's own sexuality. During this stage, the therapist gives permission to the patient to voice their sexual concerns. The therapist may simply give permission to the patient to do whatever he/she is already doing, which can improve a range of sexual problems. (e.g., guilt feelings associated with masturbation)

LI = Limited information—Educating the couple about the functioning of the body based on the anatomy and physiology may sometimes be sufficient to restore their sexual functioning. This can alleviate wrong notions about sexual functioning, and hence the client can avoid unrealistic expectations.

SS = Specific suggestion—Includes behavioral techniques and exercises tailored to the individual case. Mutual exercises by Masters and Johnson fall in this category.

IT = Intensive sex therapy—Long-term intervention for complex cases. According to Annon, these cases are relatively rare. During this phase, the patients may require referral to medical professionals.

In the *Ex-PLISSIT* model of therapy, permission giving is taken as a core component of each of the other stages. As per this model, interventions during the other stages also should begin with permission giving. Other features are requirement to review all interactions with the clients and using reflection as a means of increasing awareness of self by challenging assumptions [35].

Systematic Sensitization and Desensitization This includes the "Start-Stop Sensitization" technique, very helpful in premature ejaculation and can be part of Masters and Johnson's therapy. Here the female provides manual stimulation and is stopped when the male signals orgasm is imminent. When the couple is able to achieve some degree of control, the partners should try intravaginal containment, usually in female-superior position. During the act, the rhythmic movements are increased until the man gives the signal to stop. After a pause, the couple can restart again while containing the urge to ejaculate; this prolongs the pleasure of intercourse [37]. Similar sensitizing and desensitizing techniques can be utilized in treating erectile dysfunction of psychogenic etiology and orgasmic dysfunctions in men. There is evidence that focused sex-group psychotherapy may improve erectile function [38].

A five-part model primarily for psychogenic erectile dysfunction in couples, which can also be applied to single males and those with organic erectile difficulties, has been proposed: this includes cognitive and psychoeducational intervention, sexual and performance anxiety reduction, script assessment and modification if required, resolution of conflicts and relationship enhancement, and relapse prevention training [36].

21.2.2 Pharmacotherapy for Sexual Dysfunction

Phosphodiesterase (PDE)-5 inhibitors (*sildenafil*, *tadalafil*, *vardenafil*) act on the nitric oxide mechanism by blocking phosphodiesterase (PDE)-5. PDE-5 hydrolyzes cGMP (cyclic guanosine monophosphate) in the corpora cavernosa. With accumulation of cGMP, there is smooth muscle relaxation and increased arterial blood flow which compresses the subtunical venous plexus and increases penile erection. These drugs don't initiate an erection and require sexual stimulation to facilitate erection [39].

Sildenafil (launched in 1998) is rapidly absorbed after oral administration. However there is prolonged absorption with fatty food; hence, efficacy is reduced. Efficacy is defined as an erection with sufficient rigidity for vaginal penetration; peak plasma concentrations are reached about an hour later. The terminal half-life is 3–5 h. The clearance is reduced in the elderly, in severe renal insufficiency patients, and in those suffering from hepatic disease. It has been shown to be effective in individuals irrespective of the cause of the erectile dysfunction (ED). Individuals with ED due to psychogenic causes, diabetes mellitus, post-prostate surgery, and spinal cord injury have shown benefits. Patients have been benefitted irrespective of age and baseline severity of symptoms. The magnitude of the

benefit however varies. Sildenafil improves the strength and duration of erection and the number of occasions on which the erection is satisfactory. It is available in doses of 25, 50, and 100 mg. The recommended starting dose is 50 mg which can be titrated depending upon the patient's response. Efficacy can be maintained for up to 12 h [40].

Common side effects include headache (12.8%), flushing (10.4%), and dyspepsia (4.6%); nasal congestion, dizziness, and abnormal vision may be seen in 1–2% cases [41]. The adverse effects are usually mild and transient, lasting a few minutes to a few hours after drug administration.

Tadalafil is effective 30 min after administration of the drug and has much longer duration of action (36 h) [42]. Its absorption is not affected by food. The recommended starting dosage is 10 mg; 10 mg and 20 mg doses are used for on-demand treatment of ED. Tadalafil has been found to be useful in difficult subgroups of patients. Adverse effects include headache (14.5%), dyspepsia (12.3%), back pain and myalgia (5–7% cases), flushing and nasal congestion (approximately 4 % cases), and dizziness [41]. In 2007, 2.5 and 5 mg dosage of tadalafil have been approved by the European Medicines Agency (EMA) for daily treatment of ED. The recommended dose is 5 mg at approximately the same time of the day. Chronic tadalafil treatment has been shown to improve endothelial function which is sustained after its discontinuation [43, 44].

Vardenafil is effective 30 min after administration; absorption is reduced by fatty food with recommended starting dose being 10 mg for on-demand treatment of ED and titrated as per the response (5, 10, and 20 mg tablets are available). Side effects include headache (16%), flushing (12%), nasal congestion (10%), dyspepsia (4%), and dizziness and abnormal vision in around 2% cases. Orodispersible tablets are available in few countries [41]. Sildenafil, tadalafil, and vardenafil have demonstrated no increase in myocardial infarction rates in patients receiving PDE-5 inhibitors compared to expected rates in age-matched male populations. PDE-5 inhibitors are contraindicated in patients on concurrent organic nitrates as it potentiates the hypotensive action of such drugs. If a person on PDE-5 inhibitors develops angina, nitrates should not be given for a period of 24 h (in case of sildenafil and vardenafil), and 48 h in case of tadalafil and other drugs should be used for the time being. It should be used with caution in persons with anatomical deformities of the penis, and in patients at risk for priapism (e.g., patients with sickle cell anemia), PDE-5 inhibitors are relatively safe in combination with antihypertensives. Combined use of PDE-5 inhibitors and α-blockers may lead to hypotension. CYP3A4 inhibitors (ketoconazole, erythromycin) may increase levels of PDE-5 inhibitors, whereas with CYP3A4 inducers (rifampicin, phenytoin, carbamazepine), higher doses of PDE-5 inhibitors may be required [41].

Intracavernous Injections Alprostadil (dose of 5–40 μg) was the first and only drug approved by the European Medicines Agency (EMA) for use as an intracavernous injection in the treatment of ED. Erection appears in 5–15 min and lasts depending upon the dosage. Efficacy rate of greater than 70% has been found in ED

population; however, compliance has been found to be poor. Complications include pain, priapism, prolonged erections, and fibrosis. Papaverine (40–80 mg) and phentolamine may be used in combination to achieve better results. Prostaglandin EI is an effective agent.

Pharmacotherapeutic agents used in treatment of premature ejaculation include:

- Tricyclic antidepressants (TCA): Clomipramine (25 mg 4–24 h pre-intercourse).
- *Specific selective serotonin reuptake inhibitors (SSRIs)*: Dapoxetine is a potent SSRI, structurally similar to fluoxetine, and the first compound specifically developed for the treatment of PE (30–60 mg 1–3 h) before intercourse.
- *Nonspecific SSRIs*: Fluoxetine, 5–20 mg/day; paroxetine, 20 m; 3–4 h, pre-intercourse; sertraline, 50 mg 4–8 h pre-intercourse
- *Topical therapies include* lidocaine/prilocaine cream—Lidocaine 2.5% 20–30 min. Pre-intercourse.

21.2.3 Other Methods

Testosterone can increase the desire and is definitively effective only in case of hypogonadism. *Hormone replacement therapy (HRT)* with estrogen is helpful for vaginal function, particularly lubrication in case of menopausal women. *Bromocriptine* is helpful in hyperprolactinemia. *Yohimbine* is a central alpha-2 adrenoreceptor blocker and increases sympathetic drive with doubtful effectivity. *Trazodone* inhibits serotonin uptake and also influences alpha adrenergic and dopaminergic function; results are inconsistent in erectile disorders [45]. *Others* include apomorphine, a dopamine receptor agonist [46]; L-arginine, a nitric oxide precursor; naltrexone, an opiate antagonist (can antagonize the inhibition of sexual functions) [47]; and Ashwagandha, Shatavari, and Korean red ginseng. *Topical pharmacotherapy* includes nitroglycerine (2% ointment) and papaverine gel, vasodilators; minoxidil, a vasodilator for arterial smooth muscles; and alprostadil cream (MUSE) (prostaglandin EI) used intraurethrally [48].

Vacuum erection devices do not use physiological pathways and help in passive engorgement of corpora cavernosa with a constrictor ring placed at the base of the penis. Satisfactory erections occur in up to 90% cases. Common side effects include inability to ejaculate, bruising, and rarely skin necrosis. These devices are contraindicated in individuals with bleeding disorders.

Shockwave Therapy Low-intensity extracorporeal shock wave therapy has been shown to have a short-term positive effect on erectile function in men who respond to PDE-5 inhibitors.

Penile Prostheses Patients not responding to pharmacotherapy may go for surgical implantation of a penile prosthesis. Classes of penile implants available include inflatable and malleable devices.

Lifestyle Management in ED Modification of reversible risk factors and lifestyle changes are likely to help ED; these will also benefit cardiovascular and metabolic disorders [49].

21.3 Sexuality and Violence Against Women: Selected Milestone and Some Related Questions Especially in Europe

21.3.1 Foreword

21.3.1.1 Preliminary Information

Most of the presented information is open access from public webs and it can be presented as textual one. Many of the contents of the different documents and reports of the organizations have relevant coincidences between them.

21.3.1.2 Introduction

This work focuses on sexuality and violence against women, including relevant aspects as definitions; human rights; selected documents as European Union Charter for Fundamental Rights; sexual rights and the World Health Organization; WAS Declarations of Sexual Rights; Directive EU for victims' protection; Istanbul Convention of Council of Europe; WHO-specific reports and contributions; health consequences of sexual violence against women; trauma exposure, PTSD, and sexual violence; prevalence; genetic and epigenetic factors and PTSD; main classifications of PTSD; posttraumatic sexual stress; PTSD in the criminal justice area; personal posttraumatic growth; and sexual PTSD spectrum proposal and ending with public health, prevention, and public policies' aspects.

21.3.1.3 Definitions

Sexual violence (SV) definition in the world report on violence and health [50] includes many behaviors: rape, sexual coercion, and not true consent. Violence against women (VAW) and domestic violence (DV) are defined differentially by Istanbul Convention [51]. VAW is understood as a violation of human rights and a form of discrimination against women as physical, psychological, sexual, or economic acts. Doings of DV occur within the family or domestic unit. Intimate partner violence (IPV) refers to current or former partners or spouses.

Human Rights (HHRR), Sexuality, and Violence Related

HHRR are fundamental rights of the human being (HB) as such, usually being defined and guaranteed in the constitutions of the states [52]. The Universal Declaration of Human Rights (UDHR) of UN (1948) [53] is a milestone document in the history of HHRR, as a common standard of achievements for all peoples and all nations. They proclaimed the recognition of the inherent dignity and of the equal and inalienable rights of all human beings without distinction of any kind.

Human Sexuality and VAW

Selected documents on especially in Europe are presented as *European Union (EU) Charter for Fundamental Rights* [54] (2007) which contains rights and freedoms related to sexuality and violence as:

- Dignity: human dignity, right to life, prohibition of trafficking in human beings, and others
- Freedoms, such as the right to liberty, security, marry, and found a family and respect for private and family life
- Equality: equality before the law and between women and men and nondiscrimination based on sex or sexual orientation
- The child's best interests
- Right to justice

Sexual Rights (SR) and the World Health Organization [55]

SR embraces HHRR recognized in laws, documents, and consensus statements. They include the right of all people to sexual health, information, and education, respect for bodily integrity, choose their partner, decide to be sexually active or not, consensual sexual relations and marriage, have children, and pursue a safe, satisfying, and pleasurable sexual life, free of violence, coercion, and discrimination.

World Association for Sexual Health (WAS) Declaration of Sexual Rights and the Guidance Document for the Implementation of Young People's Sexual Rights

The WAS Declaration of Sexual Rights [56] revised in 2014 includes 16 rights, recognizing that sexual rights are human rights pertaining to sexuality, based on the inherent freedom, dignity, and equality of all human beings, and including a commitment to protection from harm. The first two are the right to equality and nondiscrimination and the right to life, liberty, and security of the person. The Guidance Document for the Implementation of Young People's Sexual Rights (IPPF and WAS, IPPF) provides guidance for young people's sexual rights within five areas: freedom of sexual expression, sexual and reproductive health services and commodities, comprehensive sexuality education and SRHR information, protection from sexual violence, and remedies and redress [57].

Victims' Protection in EU

Directive 2012/29/EU establishes minimum standards on the rights, support, and protection of victims of crime [58]. It includes physical, sexual, psychological, or economic types and could result in physical, mental, or emotional harm or economic loss.

Istanbul Convention [51]

The Council of Europe Convention on preventing and combating violence against women (VAW) and domestic violence (Istanbul 2011) includes physical, psychological, and sexual violence, female genital mutilation, forced marriage,

harassment, forced abortion, and forced sterilization. The signatory states will incorporate its contents into national laws [51].

WHO Reports and Contributions

Selection of relevant contents on sexual violence (SV) especially on women and children victims includes:

1. Types of Sexual Violence [50]. Relevant factors are offender(s) intimate or not, place (home), and others (war, workplace, school, prisons). Other forms include sexual slavery and harassment; trafficking for purposes of forced prostitution; forced pregnancy, sterilization, abortion, marriage; and genital mutilation.
2. Risk Factors (RF) of SV [50]. Many factors are RF of SV. Some RF are related to the attitudes, beliefs, and behaviors of the individuals, social conditioning, and the environment. Some people may be more vulnerable including past history of SV, intimate or dependent relationship, armed conflict or war, and others.
3. Health consequences of SV [50] include physical and psychological effects, short term and long term, altering a person's life course.
   Physical consequences include injuries, genital or not, and death. Risk is increased from STIs/HIV/AIDS, sexual dysfunctions (SD), unwanted pregnancy, unsafe abortion, infertility, pelvic pain and pelvic inflammatory disease, genital injuries, and urinary tract infections (UTI).
   Psychological consequences such as no typical reaction to the experience of SV excepted frequent rape trauma syndrome (RTS) and posttraumatic stress disorder (PTSD). Psychological effects vary considerable individually. They are suspected in individuals who present, particularly repeatedly, with RTS, PTSD, and other psychopathologies and also longer-term sexual difficulties and nonspecific symptoms. Adult survivors of child sexual abuse may present PTSD and others. Prevalence and health effects [50]. SV affects millions of people worldwide, women, children, and men in all countries, cultures, and history and in all levels of society. Reliable statistics are very limited and cases are underreported. SV can take many different clinical and criminal forms. Majority of victims of SV are females and males are the perpetrators. Most cases of SV perpetrator is intimate partner or a relative. SV has both physical and psychological effects on health and well-being. These effects can vary related to factors as individuals and nature abuse (frequency, severity, and perpetrator) and others.
4. Forensic and medicolegal points [59]. People who are sex assaulted often seek medical help but may not disclose the assault. Optimal acute management is the provision of all necessary services in place. Management includes treatment of injuries; emergency contraception; prevention of infections, including HIV; and psychosocial support. Collection of evidence may be crucial in identifying and prosecuting perpetrators.
5. Child sexual abuse (CSA) [59, 60]. Violence against infants and younger children is a major RF for psychiatric disorders and suicide and has lifelong sequelae including depression, anxiety disorders, smoking, alcohol and drug abuse,

aggression and violence toward others, risky sexual behaviors, and posttraumatic stress disorders. Preventing violence against children contributes to preventing a much broader range of noncommunicable diseases [60].

Trauma Exposure, PTSD, and Sexual Violence

Trauma exposure is associated with alterations of biological systems as the neuroendocrine response to stress [61] and can result in variation in stress adaptation, susceptibility, or resilience for mental disorders [62]. Exposure to chronic or severe psychosocial stress, particularly during early development, is one of the major RFs for developing a mental disorder [62]. Half of the cases of PTSD become chronic and persist for many years [62].

Sexual Violence (SV) and Its Prevalence

SV in the World (WHO) [59]

SV affects millions of people worldwide, mainly women and children in all countries, cultures, and history and in all levels of society. Reliable statistics are very limited, underreporting as in sexual assault (rape) of women and men and child sexual abuse.

Global and regional estimates of violence against women, prevalence and health effects of intimate partner violence (IPV), and non-partner sexual violence: Life time prevalence of IPV violence among ever-partnered women is 30.0% with differences between WHO regions [59] which is about 25% in European, American, and Western Pacific WHO regions (average 23.2% for high-income regions) and about 35% for African, Eastern Mediterranean, and Southeast Asian WHO regions.

Sexual Violence in EU

Violence against women (VAW) EU-wide survey of the EU Agency for Fundamental Rights, FRA 2014 [63]. Selected results are as follows: (1) The overall prevalence of physical and sexual violence is that one in three women (33%) has experienced physical and/or sexual violence since she was 15 years old. (2) Some 8% of women have experienced physical and/or sexual violence in the 12 months before the survey interview. (3) Out of all women who have a (current or previous) partner, 22% have experienced physical and/or sexual violence by a partner since the age of 15.

Characteristics of sexual violence: In total, 11% of women have experienced some form of sexual violence since they were 15 years old, either by a partner or some other person. Five percent of women has been raped since the age of 15. Of those women who are victims of sexual violence by a non-partner, almost 10% indicates that more than one perpetrator was involved in the most serious incident of sexual violence they have experienced. Under notification is systematic.

Sexual Violence in the USA [64]

Data from 2011 reported in 2014 indicate that in estimated %, 19.3% of women and 1.7% of men have been raped during their lifetimes; 1.6% of women reported

that they were raped in the 12 months preceding the survey, and the % of men was too small to produce a statistically reliable prevalence estimate. 43.9% of women and 23.4% of men experienced other forms of sexual violence during their lifetimes.

On sexual violence and stalking, female victims reported predominantly male perpetrators, and male rape victims predominantly had male perpetrators.

Adolescents [65]. Adolescence is the period of highest risk of exposure to potentially traumatic events (PTEs), including interpersonal violence. Over 60% of US adolescents have experienced a lifetime PTE event. PTSD can develop following potentially traumatic event (PTE) exposure. PTSD is associated with important role impairment and increased risk of secondary mental and physical disorders. Lifetime prevalence of PTSD (DSM-IV criteria) in the USA was 4.7% and was 7.3% among females and 2.2% among males.

Children as victims [66]. Traumatic events including SV are associated with high risk for different psychopathologies as PTSD, depression, and anxiety. These risks can be mitigated by protective factors and worsen by interpersonal violence.

Genetic and Epigenetic Factors and PTSD

There is a challenge for genetic and epigenetic factors [67].

People experiencing certain types of trauma, even the same trauma, can have important interindividual variability in their risk of PTSD and resilience, most likely due to underlying differences in biological processes, presumably associated with genetically or/and epigenetically underlying processes [67].

For the role of genetic and epigenetic factors in trauma, studies of PTSD indicate a relatively high heritability explaining up to 45% (ranges from 13 to 69%) of the variability in risk looking at individual PTSD symptoms. Some factors are considered related to them as personality traits that can influence behavior and lifestyle choices that can be partly mediated by genetic factors [67].

Relevant studies on genomics and epigenomics of PTSD are genome-wide association studies (GWAS) of PTSD and epigenome-wide association studies (EWAS). Both investigate many thousands of loci across the genome simultaneously. The epigenome is the collection of potentially reversible modifications that regulate the activity of genes without influencing the DNA sequence [67]. Epigenome is being regulated by genetic factors, and much of the epigenome is responsive to external influences throughout life [67]. Exposure to certain traumatic events in childhood alters affective and neurobiological development [66, 67]. Mechanisms clearly play a role in the pathways linking child trauma to psychopathology, including changes threat processing in stress hormones and epigenetic factors [66, 67]. Vulnerability to the effects of trauma and the risk of PTSD result from multiple environmental and genetic factors interacting between them [67].

Trauma exposure is associated with epigenetic modifications as influencing a particularly sensitive period of biological vulnerability, e.g., critical periods of development in utero and early childhood, with long-term consequences including a major risk for later PTSD [67]. Epigenetic changes can potentially occur throughout the life span and even be passed on to future generations [68].

Evidence is growing for familial influences on PTSD studies of parental and offspring PTSD through trauma-exposed samples. Psychosocial factors and genetic differences are important in the variability in risk [69].

Epigenetic processes are dynamic and highly sensitive to environmental cues, opening ways to appropriate interventions on negative effects of trauma [67]. Life transitions are linked to the development of psychological distress and can be a source of personal growth and development [70]. Research results provide support for PTSD as a valid phenotype to study in both men and women but may be important gender differences in the pathophysiology of, or mechanisms underlying, the PTSD [71]. There are links between PTSD and anger/aggression [72].

Increased risk of developing PTSD is caused by a combination of victim vulnerability and the severity of the current assault [73]. Sexual trauma can lead to long-standing effects on individuals' intimacy functioning [74].

Sexual aggression in female rats (SCAR model) significantly reduces learning and the development of maternal behavior. Women exposed to severe childhood sexual and/or physical abuse oftentimes suffer from PTSD, which is associated with brain changes and learning deficits. Children of mothers with PTSD are at a greater risk for traumatic experiences, which contribute to their poor developmental prognosis [75].

PTSD is related to the rape trauma syndrome (RTS) post assault, with partial overlapping between both. Many victims of SV experience RTS with very frequent changes in a person's sex life including SD (sexual aversion, flashbacks of the rape during sex, vaginismus, orgasmic dysfunction). Often, the person may conclude an existing relationship with the offender [76].

Posttraumatic stress disorder (PTSD) in main classifications selected as:

DSM-5. PTSD is included in DSM-5 chapter on "Trauma- and Stressor-Related Disorders". In the DSM-IV, PTSD was included in the "Anxiety Disorders" chapter. The diagnostic criteria include exposure to traumatic events as actual or threatened sexual violence (Criterion A: stressor) [77, 78].

ICD-10. PTSD is classified in the chapter "Neurotic, Stress-Related, and Somatoform Disorders" and may develop after an exposition to one (or more) traumatic events, e.g., sexual assault [79].

ICD-11 PTSD. The proposed ICD-11 grouping of disorders specifically associated with stress includes PTSD and complex PTSD [80, 81].

Diagnostic Manual in Sexology, third edition (MDS III). It is a sexual-specific diagnostic manual including chapter "C11 Posttraumatic Sexual Stress (PTSS)" as PTSD related with sexual stressors [82].

Sexual violence related to posttraumatic sexual stress (PTSS) and other. Females are at an increased risk of developing PTSD in response to physical assault compared with males. Physical assault is possibly a contributor to the overall female increased prevalence of PTSD. Forms and contexts of sexual violence are multiple, e.g., rape, sexual harassment, sexual abuse of children or disabled people, forced marriage or cohabitation, forced abortion, violating sexual integrity of women,

forced prostitution and sexual trafficking, forced sexual initiation, and sexual violence against sex workers.

The consequences of sexual violence are multifold, e.g., unwanted pregnancy and gynecological complications, STIs, mental health and behavioral problems, social ostracization, injuries and death, suicide, and homicides [83].

Interest in PTSD developments in the criminal justice area includes PTSD and a criminal defense and civil (and administrative) plaints, PTSD diagnosis items (stressors, symptoms, functional impairments), and increased potential for fraudulent claims. The insanity defense in criminal cases and PTSD can be associated with criminal issues: PTSD and violence [84].

Personal Posttraumatic Growth (PPG/PPTG)

Highly stressful experiences are a possible facilitator of personal change processes and established the notion of posttraumatic growth (PTG) for this phenomenon, which has also been referred to as stress-related growth, adversarial growth, and benefit-finding [85]. The THRIVE model combines three key factors extracted from posttraumatic and postecstatic growth theories, facilitating positive development after major life events. The three contributing factors of the model are positive emotions, supportive relationships, and meaning making [85]. Pretrauma predictor variables for PTSD can be included within the next categories: pretrauma vulnerability, etiology factors, cognitive abilities, coping and response styles, personality factors, psychopathology, psychophysiological factors, and social ecological factors [86]. Most individuals exposed to trauma do not develop PTSD: many variables, previously considered outcomes of trauma, are pretrauma risk factors (RF) [86].

Sexual PTSD Spectrum

Diagnosis of "posttraumatic sexual stress spectrum" (PTSSS) has been recently proposed [87]. PTSSS would include three diagnoses that extend to three levels the posttraumatic sexual stress (PTSS, MDS III) [82] with a dimensional perspective. From lowest to highest severity, they would be:

1. Subthreshold or partial PTSSD, specification of partial/subthreshold PTSD
2. PTSSD, as described in MDS III
3. Complex PTSSD, sexological specification of complex PTSD

A robust literature provides support for these three diagnostics.

Public Health, Prevention, and Public Policies

VAW is preventable and programs to reduce IPV need to address risk factors at multiple levels: individual, relationship, community, and societal [88].

Preventing IPV and sexual VAW [89] stresses: The public health approach to prevention approach emphasizes the primary prevention of IPV and SV, complementing criminal justice-based approaches. The HHRR approach is based on the obligations of states to respect, protect, and fulfill HHRR, addressing to prevent,

eradicate, and punish VAW and implementing appropriate public policies, from the perspective of public health [90] with psychosocial orientation in a humanistic way with the irrevocable goal to finally eradicate this complex social pandemic.

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Sleep Disturbances Among Patients in Primary Care: Psychiatric Practice

22

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Abstract

Insomnia, hypersomnia, and disturbed diurnal sleep-wake cycle are among the main complaints of psychiatric patients. On the other hand, disrupted sleep is a risk factor for the emergence of psychopathology. The intention of the authors of this article is to improve psychiatrists' awareness of the clinical importance in considering disturbed sleep among patients suffering from various psychiatric disorders.

22.1 Introduction

Large-scale epidemiological studies demonstrate that about 30% of individuals in the general population present with sleep complaints or they are prone to develop sleep problems within a given year [1–7]. Obviously, this occurrence has a considerable negative impact on the general health status and quality of life of the affected individuals. Moreover, sleep-related problems cause a substantial socioeconomic burden due to an increase in absenteeism, accidents, etc. [8–12].

On the other hand, chronic sleep disorders have been associated with comorbid psychiatric disorders, such as major depression, alcoholism and substance abuse, or multiple medical conditions [13–21]. Despite the overall toll of sleep disorders to society, however, they usually remain under-recognized and therefore untreated.

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22.2 The Interrelationship Between Sleep Disorders and Psychopathological Conditions

The ICD-10 and DSM-5 classifications include disturbed sleep as a characteristic symptom among the diagnostic criteria for several psychiatric disorders, including major depression, bipolar disorder, generalized anxiety disorder, separation anxiety, post-traumatic stress disorder, etc. [22, 23].

Population surveys report that up to 50% of individuals with complaints of insomnia or hypersomnia show evidence of primary psychiatric disorders [17, 24–26]. Anxiety in particular has been found to be quite common (in 25–40%) among insomniacs, compared to the general population (in 10% of individuals with no sleep complaint) [5, 17, 27]. Also, based on referrals to sleep disorder centers, a psychiatric disorder is found to be the most frequent cause of insomnia [15]; moreover, certain sleep-wakefulness disorders (e.g., sleep apnea, narcolepsy) are often accompanied by secondary psychopathology [28–30].

22.3 Sleep in Affective Disorders

Sleep problems are considered a cardinal symptom of affective disorders. During episodes of depression, patients have difficulty with sleep induction, sleep maintenance, and early morning awakening; however, during episodes of mania, although patients sleep less, almost invariably they do not complain of insomnia [31].

In approximately 30% of patients with major depression, sleep disturbance (i.e., insomnia, hypersomnia, and/or nightmares) may be the presenting complaint. It should be emphasized that insomnia in depressed patients is associated with the symptom of fatigue [32] and is a predictor of suicide tendencies; in fact, several studies have suggested that patients with both depression and insomnia are particularly at risk of committing suicide [33–38]. Also, sleep disturbance is the most common prodrome of mania and the sixth most common prodrome of bipolar depression [39, 40]. Thus, reduced sleep duration may have a predictive value in the early diagnosis of an affective episode [41–43]. Furthermore, it has been suggested that sleep-wake cycle instability caused by psychosocial stressors may trigger an episode of either depression or mania in bipolar patients [44, 45]. Last but not least, induced sleep deprivation and phase advance of the sleep-wake cycle are frequently associated with mood improvement, and they have been proposed for the therapy of depression [46].

22.3.1 Major Depression

A large percentage of patients with depression complain of insomnia: delayed sleep induction, frequent nocturnal awakenings, and early morning awakening 2–4 h earlier than desired [47]. In a 3-year longitudinal epidemiological study of 979 young

adults (aged 21–30 years) over a 3-year period, the relative risk of developing major depression was four times higher in subjects with insomnia, while subjects with hypersomnia presented with a 2.9 relative risk for major depression when compared to subjects without sleep complaints [48]. In addition, the history of previous periods of insomnia remained a significant predictor of subsequent major depression, while a recurring complaint of insomnia for 2 weeks or more signaled the onset of major depression [48]. Apart from insomnia and hypersomnia, other sleep abnormalities have also been reported in association with depression. In the Wisconsin Sleep Cohort study of 812 participants, depression was associated with a twofold increase in hypnagogic hallucinations and automatic sleep behavior and a fivefold increase in sleep paralysis [49].

Insomnia may subside with the treatment of depression, even with non-sedating antidepressants [50]. Trazodone, mirtazapine, and agomelatine can be used as the starting treatment in patients with severe insomnia, or they can replace or be added to other treatment modalities later on if needed [51, 52]. In a review by Alberti et al. [53], it was shown that lower rates of insomnia were associated with the use of agomelatine while higher rates of insomnia with the use of desvenlafaxine and bupropion.

22.3.2 Bipolar Disorder

Disturbed sleep is a quite prominent symptom both during depressive and manic episodes of bipolar disorder [54, 55]. Within the context of bipolar disorder, disrupted sleep has been implicated in the pathogenesis of manic episodes [56], and it may be considered as an early marker for the occurrence of a depressive episode [40]. In addition, residual insomnia during euthymic periods is associated with an increased risk of relapse and/or with inadequate recovery from the previous episode [57]. Finally, Harvey [58] in a comprehensive review found that 69–99% of patients with bipolar disorder experience reduced need for sleep during the manic phase, with more variable rates of hypersomnia (23–78%) and insomnia (up to 100%) observed in the depressive phase.

22.4 Sleep in Schizophrenia

In schizophrenia, insomnia is a common clinical feature during the acute psychotic state and the exacerbations of the disease; actually, severe insomnia is one of the prodromal symptoms associated with psychotic decompensation [47]. In addition, reversal of the sleep-wake cycle with concomitant severe insomnia, nightmares, and terrifying hypnagogic hallucinations is quite frequent in schizophrenic patients [59].

Benzodiazepines and benzodiazepine-like drugs are often used for the treatment of insomnia in patients with schizophrenia [60, 61]. In a recent RCT study by Tek et al. [62], eszopiclone improved insomnia symptoms in schizophrenic patients

without affecting cognitive functions; moreover, sleep remained improved during the single-blind placebo phase after eszopiclone was discontinued. Improvements in total sleep time and sleep efficiency have been observed with the use of antipsychotic medication [63], but sleep problems may also persist [64]; newer antipsychotics (olanzapine, risperidone) are shown to enhance slow-wave sleep, while older antipsychotics (haloperidol, thiothixene, flupenthixol) shorten sleep latency and increase sleep efficacy [65].

22.5 Sleep in Anxiety Disorders

Anxiety disorders are the most frequent psychiatric causes of sleep disturbance. Most notably, patients with generalized anxiety disorder and panic disorder frequently present with insomnia [66, 67]. Common sleep disturbances associated with anxiety disorders are delayed sleep onset or problems with sleep maintenance; additionally, some anxiety sufferers develop sedative or hypnotic drug abuse, further complicating their sleep disturbances [47].

Nearly a third of the patients with panic disorder suffer also from recurrent nocturnal panic attacks [68]. These attacks typically occur during the transition from Stage 2 to slow-wave sleep with an abrupt arousal from sleep, which is accompanied by intense anxiety and autonomic nervous system hyperactivity.

In post-traumatic stress disorder, specific sleep disturbances (i.e., re-experiencing of the traumatic event in the form of recurrent nightmares and symptoms of hyperarousal such as difficulty initiating and maintaining sleep) are among the diagnostic criteria of this disorder. Furthermore, nightmares or anxiety arousals are reported by 60–70% of patients with post-traumatic stress disorder [31, 69–71].

22.6 Sleep in Alcoholism

Alcoholic patients commonly suffer from insomnia, diurnal hypersomnolence, polyphasic sleep-wake cycles, and several parasomnias [72]; furthermore, alcohol increases the likelihood of sleep-related breathing disorders, such as obstructive sleep apnea-hypopnea syndrome, as well as the risk of developing periodic limb movements [66, 73]. Notably, sleep disturbances persist for months or even years following recovery and continued abstinence from alcohol [73].

22.7 Sleep in Substance Abuse

Stimulant-dependent sleep disorder consists of reduction in sleepiness or suppression of sleep by central stimulants, with alterations in wakefulness following abstinence [74]. Polysomnographic recordings during acute intoxication with stimulants demonstrate increased sleep latency, decreased total sleep time, increased spontaneous awakenings, and increased body movements during sleep. Stimulant withdrawal

is associated with reduced sleep latency and increased total sleep time as well as with hypersomnia and prolongation of nocturnal sleep duration [74–76].

Hypnotic-dependent sleep disorder presents with excessive sleepiness or insomnia associated with tolerance to or withdrawal from sedative-hypnotic medications [65]. Sleep complaints and objective measures of sleep are affected by the differences in duration of action and half-life of various sedative-hypnotic agents. During acute intoxication, sedative-hypnotic drug use is accompanied by hypersomnolence and decreased wakefulness. Polysomnographic sleep recordings during withdrawal demonstrate reduced sleep duration, increased sleep disruption, and REM sleep rebound [75, 76].

22.8 Sleep in Personality Disorders

Sleep impairments are relatively common among patients with borderline personality disorder (BPD) and possibly antisocial personality disorder; however, these impairments are comparable to those associated with other psychopathological states or various sleep disorders [77].

In an epidemiological study ($N = 5692$), BPD symptoms were significantly associated with self-reported difficulty of initiating and maintaining sleep, early morning awakenings, and negative consequences of poor sleep; however, these sleep problems were similar to those reported by individuals with Axis I disorders [78]. Based on 16-year longitudinal follow-up data, recovered BPD patients ($n = 105$) reported shorter sleep onset latency, less fatigue-related dysfunction [79], and less severe maladaptive sleep-related cognitions relative to non-recovered ($n = 118$) BPD patients [80]. These data suggest that as BPD symptoms ameliorate, sleep problems may also get better.

22.9 Concluding Remark

The purpose of this article is to improve psychiatrists' awareness in considering the importance of disturbed sleep among psychiatric patients as well as to emphasize the need for incorporation of knowledge from sleep medicine into primary psychiatric practice. To this end, basic principles regarding evaluation and skillful management of sleep disorders should be incorporated into the curriculum of psychiatric specialty programs and continuing psychiatric education programs.

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Integrating Mental Health into Primary Care: Training Current and Future Providers

23

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Abstract

In this chapter the authors will discuss an important aspect of the integration of behavioral health (specifically psychiatry) and primary care from a global perspective. The chapter examines this topic through the continuum of medical education, from medical student to psychiatry residency, and concludes with a discussion of post-residency continuing education opportunities. Current psychiatry residents share their experience in working in an integrated primary care clinic, highlighting the challenges and rewards. The need to fully integrate this concept into all aspects of medical training is the primary goal of the authors. This will require a change in culture from the existing specialty-driven approach to patient care. It will also help address the current crisis in limited access to mental health care around the world. There will never be an adequate number of psychiatrists given the current model of mental health-care delivery. This is not a new problem, but altering current training experiences has the potential to begin this necessary transition in mental health-care delivery. Achieving this goal will improve the overall quality of life for patients worldwide.

23.1 Introduction

The integration of mental health into primary care delivery is not a new concept but one that has become increasingly discussed as a global priority. In fact, the theme of the 2016 World Psychiatric Association Congress held in Cape Town, South Africa, was centered around integration of care [1]. Despite an extensive body of literature

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highlighting the need to integrate mental health care in the primary care setting, little progress has been made in altering or augmenting existing clinical and didactic opportunities for physicians at all levels of training. "As health care is redesigned and primary health care reemphasized, the move toward integrating behavioral health care with primary medical care appears to be accelerating across the world" [2], yet training the current and next generation of psychiatrists continues to be a significant challenge for medical student and residency educators.

There is no gold standard for how to achieve effective integration of psychiatry/behavioral health into primary care. Cultural, economic, and sociopolitical realities will shape the best model for each country and health-care education system (medical schools, residency programs, and postgraduate training). In order to achieve meaningful change from the current specialty-driven paradigm, education on integrated care models must begin with first-year medical students and continue through residency training and beyond, in both primary care and psychiatry. The World Psychiatric Association has done an admirable job in providing a forum for discussion and numerous scholarly activities focused on continuing medical education for psychiatrists from around the globe. This has been achieved through numerous scientific congresses held at various international locations and the work of scientific sections, such as medicine, psychiatry and primary care, and psychiatric education. However, as is the case in all of clinical medicine, the key to a successful outcome is early intervention and appropriate follow-up. The same is true for changing the culture of psychiatric care delivery by integrating it into the primary care setting. As Thompson points out, the clinical and cost benefits of primary health care teams that fuse primary psychiatric care with primary medical care will drive the evolving global health-care system and the future of psychiatry. The authors of this paper believe this can only be accomplished by increasing medical student exposure to this "new" model and providing didactic and clinical experiences for psychiatric and primary care residents. This core training (medical school and residency) needs to be reinforced through CME opportunities for practicing psychiatrists. This continuum of educational experiences is necessary for optimal success and long-term sustainability, as it requires a change in culture from the existing siloed approach to mental health care.

23.2 Medical Student Education in Integrated Care

Students choosing a career in medicine typically do not enter medical school with a preconceived idea on how care is best delivered to their future patients. Many will not have selected a specialty until well into their training, with their final decision being heavily influenced by their preclinical and didactic experiences, combined with attitudes and opinions of their teachers and mentors throughout medical school. Advances in medical science have been dramatic over the past 50 years, resulting in an increase in specialization and a decrease in primary care-focused models of care delivery. Medical students are exposed to specialists providing patient care in a fragmented model, with primary care providers providing triage to the various

medical specialists. In virtually all countries worldwide, specialists receive greater compensation and prestige. This results in medical students choosing a medical/surgical specialist career over primary care. Top performing medical students strive to get accepted into the more competitive specialty training programs, not primary care. Other than a general medicine/primary care rotation, only their psychiatry rotation offers the potential to be trained in an integrated care model. This current situation offers very limited, if any, opportunity for the medical student to experience firsthand the value of an integrated care model. Virtually every medical school utilizes residents as primary educators of students, especially during clinical rotations. In order to effectively change the current specialty-driven model, medical students will need to be exposed to an integrated model beginning with their initial core didactic lectures and continuing through the clinical clerkship years. Changing the specialty-driven culture will require an integration of the content, as well as the process of medical training for all students. Supervisors of students will need to "buy in" to the model and be willing to adapt their current practices. Sharing successful strategies employed by schools who have adopted this integrated approach will be important. There are a number of potentially effective strategies for integrating mental health into primary care education for medical students. A comprehensive approach of formal didactic lectures, case-based discussion groups, and clinical experiences early in their medical training is likely to have the greatest impact on changing the culture of fragmented, specialty-driven, medical care. For example, during the initial lectures given to first-year medical students, a few lectures should be devoted specifically to the topic of integrated behavioral and physical health care. It is best if the lectures were given in both the psychiatry and primary care sections of the curriculum. Having a lecture in each of these disciplines reinforces the concepts of true integration. When the students progress to their clinical rotations, psychiatry residents mentoring the students can be encouraged to provide clinical examples of mental health integration programs. Similarly, medical students may be invited, either as observers or participants, to psychiatry resident training activities focused on integration of mental health services in the primary care setting.

At Kocaeli University Medical School, in Kocaeli, Turkey, during the last 22 years, various applications of such activities have been implemented. Some of them are presented below.

A "learning together" program was established for the primary care physicians. Psychiatry residents and final-year medical students were invited to participate in combined didactic and clinical teaching sessions, with special discussions led by faculty after the sessions. This "learning together" program was organized for 10 days, lasting approximately 2 months, 1 day each week for about six to ten primary care physicians (general practitioners) working at different primary healthcare centers in Kocaeli province. There were theoretical and practical aspects of the activity; some of the sessions were carried out at the Kocaeli University psychiatry department, others at various health centers where the physicians were originally located. At the sessions held in health centers, other health staff (nurses, midwives, and sometimes the auxiliary personnel) were also invited.

The "learning together" concept was based on the reality that the learning process had two faces: for some topics (such as assessment and management aspects of the psychiatric disorders), psychiatrists who had started the training activity were more equipped to provide the service, while for other issues (such as frequently seen mental health problems at the settings where general health-care services were provided and some psychosocial aspects of health problems for which physically oriented diagnosis and management were applied), general practitioners had much more experience. As part of the lectures provided by the faculty of the psychiatry department, general practitioners were asked to present their experiences in the field to all the members of the department, including the students. This approach, during the interactive training period, created an environment where all the participants learned, and taught, simultaneously and interchangeably. The training activities not only covered psychiatric disorders and physical diseases but were able to address "mental health promotion" and "prevention of psychiatric disorders" in the general medical setting as well.

The general practitioners were also invited to the ongoing mental health awareness programs for the public, both in the specific 2 months of their training and after their training program ended. This allowed the students to experience the integrated training from both the psychiatric and general medicine perspective.

The mental health awareness programs for the public started after the Marmara earthquake where more than 17,000 people died and more than twice that number were seriously injured. First psychosocial support was the main target of the meetings organized at the tent cities; later as the time passed, other topics such as interpersonal and intrafamilial issues came to be the topics of interest of the participants. In order to keep the family problems away from being disclosed among other people, short clips from favorite TV serials were used to facilitate discussions on interpersonal topics and to enhance awareness on mental well-being [3]. These mental health promotion activities were implemented at various settings and to most of them, students, residents and other mental health professionals participated as well. This activity allowed the students to experience firsthand the important interplay between physical illness and injury and mental health.

Utilization of multimedia for facilitating discussions without disclosing personal information grew as a model and was implemented for different purposes at different places (at groups for mentally ill patients at inpatient and outpatient services, at different in-service training sessions for various professionals—nurses, teachers, members of armed forces, lawyers, etc.). Most of the medical students, all residents, and the entire clinical faculty providing care joined together for discussions on optimal patient care, usually in small groups at each session. At the conclusion of each session, critical assessments of the interactions were made together with all levels of trainees and instructors.

The goals of these combined teaching sessions were to demonstrate the interaction of social psychiatry, especially focusing on mental health promotion and prevention, and general medical care.

Another series of monthly meetings were organized together with the Provincial Directorate of Health targeting members of "psychosocial crisis and suicide

prevention units" of seven state hospitals of the Kocaeli province. The monthly supervision meetings continued more than 8 years. Physicians, psychologists, social workers, nurses, school counsellors, and students of these disciplines were the participants of the meetings. Most of the time, there were case discussions or discussions on previously assigned films or books. At some meetings, depending on the interest of the participants, popular mental health issues were discussed as well. Role plays, going over alternative approaches, discussing how to manage challenging situations, and working on different emotions were some of the techniques and/or topics employed. After the sessions, the teaching faculty, either immediately after the meeting or the following day, performed critical assessments with residents and the students.

Another clinical experience on teaching mental health integration into primary care has been carried out for the last 3 years. Clerkship students on psychiatry, together with a psychiatry resident, are taken to the only community mental health center of the province. The students spend half a day, out of a 3-week clerkship, working in the clinic. The visits are divided into three parts, first being an introductory discussion on history and current situation of global and national preventive psychiatry. The students' recalled knowledge is searched for (usually not much is seen to be remembered), then some milestones in historical development of prevention and promotion are underlined, and a short history of community mental health centers in Turkey is summarized.

In the second part, common therapeutic activities with the patients are performed, including physical exercises, painting, chess course, psychoeducation session, etc.). The students are encouraged to ask the patients how these activities affect their physical health.

In the last part, a large circle is made together with the patients, with students and patients sitting among one another. Games are played, songs are sang, and discussions are carried out usually in line with the day's topic determined by the center's nurse. Finally patients are requested to give recommendations and feedback to the soon-to-be doctors.

After the visit, each student provides written feedback on his/her observations and thoughts. Most of the notes address the unique experiences they have gone through and how the visit helped them to break their stereotypes about mentally ill people. These visits provide the students an opportunity to observe how seriously ill patients can manage in the community and how thoughtful, kind, and friendly they can be. In addition, the students are able to appreciate the medical illness psychiatric patients' experience and the interplay of physical and mental illness. Even the residents (usually the first-year residents working in the inpatient unit) say they benefit from these visits emphasizing that they are used to seeing acute phases of chronic mentally ill patients at the inpatient unit and get to see how they are able to function in a community setting working with general practice physicians.

All these experiences demonstrate to the students that the majority of mental health services continue out of the walls of the psychiatry wards, making them aware of mental health issues in their future roles on the primary care services or at other medical units, changing the culture of specialty-driven care.

23.3 Psychiatry Resident Education in Integrated Care

The integration of psychiatric care in primary care needs to become the standard of care delivery in the near future. However, training psychiatry residents to deliver integrated care is still in infancy. Traditionally, psychiatry residents are trained in inpatient psychiatry, outpatient psychiatry, and consult-liaison. Consult-liaison psychiatry is typically done in context of inpatient medical and surgical services. Unfortunately, depending on country of training, there may be little or no training in providing psychiatric consultation to primary care physicians. Also, it's not uncommon for psychiatry residents to not receive any didactic and clinical education on integrated care. For example, training in integrated care is not offered to psychiatry residents in South Korea [4].

However, now that integrated models of mental health care are increasingly widespread, residency training in this model is gaining more importance particularly in North America. In fact, training in "shared/collaborative mental health care" has now become mandatory for all psychiatry residents across Canada, and a majority of general psychiatry and child and adolescent psychiatry training programs in the United States offer integrated care rotations, many of which are electives for senior residents [5, 6]. However, there's a disconnect between this drive for resident education in integrated care and scarcity of the subject matter in literature.

Literature on psychiatry residency education in integrated care is lacking. A PubMed search using terms "integrated care" or "collaborative care" and "residency" yields less than 30 relevant results, a few of which are geared toward education of family medicine and pediatric residents. This may reflect the lack of clarity on advantages of training residents in this model, clinical challenges that residents might face, as well as challenges of introducing this training from administrative and educational perspective. This chapter aims to bridge some of this gap by reviewing current literature and by incorporating psychiatry residents' perspective based on their experiences in training in integrated care.

23.3.1 A Resident's Perspective

As a third-year psychiatry resident at University of Southern California, I was first in my residency program to be given the option to participate in integrative outpatient care in the primary care clinic. In truth, I did not know what integrative care would involve, and certainly, without this optional experience, I would still not appreciate all the challenges and rewards with this vehicle of care delivery. None of the other residents seemed to know much about integrated care either as we had not received didactic training on the subject. What sparked my interest was just hearing about it and doing a quick literature search on the topic. After realizing that there's been increased implementation of integrated care, I wanted to be competent in delivering this model. That's why I chose to spend one half day per week in primary care consultation in our third year.

23.4 Training Advantages and Challenges

Residents require exposure to community and primary care settings to understand the community-based services. Training in integrated care offers a great opportunity for residents to increase awareness of the integrated care model [6] and to learn a variety of skills that are unique to this model.

Integrated care focuses on population health and measurement-based care [7, 8]. The model consists of an interdisciplinary team that includes the primary care provider, a behavioral care manager, and a psychiatric consultant. In this interdisciplinary team, psychiatrists are positioned to assume leadership role given their experience and expertise in the treatment of the medically and psychiatrically complex patient [9]. Hence, psychiatry residents have to learn to build trusting relationships with nonpsychiatrists to support shared patient care and education [6]. More specifically, psychiatry residents often have to teach nonpsychiatric providers how to use screening tools to detect psychiatric illnesses, perform mental health assessments, and be ready to answer any psychopharmacological questions [10].

Because only one in eight people in the United States with a mental health disorder consults a psychiatrist [11] while most people who seek mental health care do so in primary care, residents are exposed to a broader patient population. According to [12], topics that are encountered by integrative care team are major depressive disorder, substance use disorder, anxiety, and suicide/violence risk. Some of the less commonly reported topics are somatic symptoms or fatigue, which are even less commonly encountered in psychiatric clinics. Hence, psychiatry residents not only learn how to approach typical psychiatric illness, like bipolar disorder, PTSD, personality disorders, and psychotic disorders [12], they also see patients who wouldn't otherwise be seen in a psychiatric clinic.

Similarly, psychiatry residents in integrated care have the opportunity to act as consultants on behavioral components of health and medical care [10]. For instance, they can improve patient adherence to medication treatment and improve their strategies for treating obesity, nicotine dependence, and unhealthy lifestyles. Psychiatry residents can also help treat substance use disorder by pharmacologic recommendation, referral to higher levels of care, and encouraging motivational interviewing for eliciting change.

Psychiatry residents learn to leverage their proficiency in medical communication in their integrated role. Psychopharmacologic recommendation is a common request for psychiatric consult [13]. To ensure implementation, adherence, and confidence, it is often helpful to discuss rationale of a particular recommendation. For example, a breast cancer survivor on tamoxifen was placed on Prozac. However, a quick discussion on liver metabolism for both medications resulted in immediate response in medication change. Psychiatry residents bring knowledge of the latest evidence-based pharmacologic and non-pharmacologic management of diseases along with understanding of drug-drug interaction to an integrated team. Additionally, through repeated interaction and communication around specific scenarios, these consultations foster the capacity of primary care providers to

confidently and competently manage psychiatric disorders. An advantage of electronic medical records (EMR) is the ability to integrate these communications into workflow and schedule.

23.4.1 Resident's Perspective

An important aspect of collaborative management in our clinic has been the use of systematic research evidence as it applies to individual cases when possible. The discussion has been most successful in our clinic when provided in real time in context to patient care. Having standard guidelines also allows for shared agreement and important "buy-in" amongst stakeholders to improve a collegial atmosphere. In the beginning, overcoming barriers in clinical inertia and treatment hesitation required some finesse in medical communication. However over time, our collaborative team became more efficient at counterbalancing the evidence-based recommendations with the patient-level experience and population-based input of the primary care provider towards better outcome.

I have found the use of EMR messaging to be invaluable in delivering timely recommendations and answers to management questions. These communications allow opportunities for teaching, and I would often include the rationale for diagnosis and explanation of treatment decision. Additionally, primary care providers would frequently send brief communications for "curbside" consultations, which when appropriate increased efficiency and throughput of collaborative management. These personal communications and response also improve team dynamic, garner better support, and demystify management of psychiatric illness, allowing for increasing confidence in the collaborative model over time.

On a more personal level, I have encountered some of the most interesting cases in our integrative clinic, not only with psychopharmacologic decision making, but also in referring patients to therapists for CBT, IPT, and psychodynamic psychotherapy. Additionally, most of these patients would most likely have never sought psychiatric help outside of primary care. One could wonder how much needed care is not delivered to an unidentified population in need.

23.5 Administrative and Training Challenges

Even though there have been more psychiatry training programs that offer integrated care rotations [5], many are either in infancy or yet to be developed. It poses a challenge for program directors and educators to establish this rotation. Identifying a clinical rotation site and psychiatrist faculty member to supervise trainees as well as funding and space may all be barriers [14]. A commonly identified difficulty relates to availability of care managers (CMs) in a collaborative model. The CMs function as the lynchpin connecting the team to the patients, utilizing the telephone and clinical outcome metrics, and alerting the team to any concerns. At the same

time, the CM's contact with patients helps keep patients engaged in their care, improving adherence and defining treatment goals. Often a nurse or a social worker has been preferred in this role. As the program initiates and expands, the need for CM-capable clinicians grows, drawing on an already strained mental health clinician resource pool. The training of CM can also be an ongoing challenge with turnover and scheduling. Recorded training material can be helpful and should cover common population-specific situations. Non-nurse CMs may be an option but would likely require nursing support.

Once these logistical considerations are met, residency programs should offer clear competencies required for the successful practice of integrated care and provide faculty development and valid assessment tools for use in integrated care settings [15]. There will be need to establish clear parameters for assessing patient need, obtain and evaluate outcome metrics (e.g., PHQ9, GAD7), and revise treatment protocol. Care must be taken to prevent "one-way" referrals or transfer of patient care from the primary care provider to the psychiatrist. Often patients with complex psychopathology may require the psychiatrist to take the lead in assessment and management. However, coordination of general medical management, psychopharmacologic treatment, and interventions must be accompanied by continued involvement of all team members. The notion is to promote a systematic, planned approach to care for chronic health conditions, by matching the skills of team members to specific tasks to improve quality and efficiency of care delivery [16].

23.5.1 A Resident's Perspective

I was the first in my residency program to start the integrated care rotation. Two of the twelve psychiatry residents started working with PCPs at a primary care clinic that was in close proximity to the outpatient psychiatric clinic in the university medical center. Our program director, who took on the initiative to start the rotation, became our psychiatric supervisor. Since we hadn't received any didactic training on integrated care, we were asked to review an online training module on collaborative care, developed by the University of Washington AIMS Center. Then, we established screening tools for depression, anxiety, and cognition (PHQ-9, GAD-7, and Mini-Cog). In the beginning of the year, there was no dedicated staff to administer these screens. We also did not have a case manager to track these scores, call patients for follow-up, and schedule appointments. With help of the director at primary care clinic, we were able to find health-care staff for some of these tasks. Although we have yet to find a case manager, we have a psychiatric social worker who provides appropriate resources, referral, and therapy to patients. Soon, we had an interdisciplinary team involving PCPs, psychiatry residents, nursing staff, and psychiatric social worker. PCPs communicated with psychiatry residents and psychiatric social worker via a messaging system on EMR as well as directly via face-to-face. Overall, the psychiatric team was highly appreciated by PCPs. Given positive experiences of psychiatry residents, the integrated care rotation is to be expanded to almost all third-year residents next year. We're also going

to implement didactic training to second-year residents so that they'll be better prepared to start the rotation in third year.

23.6 Discussion

Integrated care is a well-studied model in which integrated psychiatric and primary care can be delivered in a cost-effective manner, with better outcome while reducing stigma relating to mental health [17, 18]. However, despite its recognized importance and international interest, there has been little in terms of literature with integrated training in residency.

The integrated care model focuses on four essential elements. An effective delivery method can be multidisciplinary team driven, local population focused, measurement-guided, and evidence-based [19, 20]. In this team, the roles and tasks are shared with focus and responsibility on health outcome. The manner which the care is delivered is designed with attention to a specific population. Targeted treatment and effective goals are achieved with measurements and evidence-based care.

In traditional residency training, the role of a psychiatrist has more often been that of a consultant, often irrespective of shared responsibility of tasks or goals. To effectively train future psychiatrists to practice in an integrated care model, programs can adapt integrated, collaborative training into their curriculum.

23.6.1 Resident's Perspective

It is abundantly clear that integrative models of care delivery are the emerging direction for efficient, broad-based, population-directed care. I've gained a new perspective and appreciation in our clinic and a willingness to incorporate collaborative care into my future practice. I strongly do not think that would be the case without this experience in training. Without this exposure during training, I fear that the expected pivot to integrated care as imagined at WPA and other organization may not become as widespread as needed. Although there are a few programs who have initiated organized and structured experience in integrative care, we would recommend that all programs consider this experience an accessible part of training. To cultivate interest, the model should be emphasized early in training. Programs should certainly incorporate the essential elements of integrated care with clear competencies to develop. Psychiatric residents should be encouraged to utilize their unique skill sets in medical communication in interaction with our primary care colleagues. Residents with good knowledge of clinical outpatient psychiatry including the most recent developments in psychopharmacology would be most appropriate in this role. The residents should have direct supervision with expressed intent to expand the resident's understanding of system-based care. As more programs invest more effort into developing integrative training, I believe that more residents and near-future psychiatrists much like myself will take on the challenge of making integrated care a main vehicle of care delivery.

23.7 Integrated Care: Postgraduate Educational Issues

Following previous discussions on medical student and residency education in integrated care, what are the issues facing psychiatrists who have finished training and are considering careers in this emerging treatment setting? As systems of care recognize the benefits of integrated care, the need for well-trained clinicians will continue to grow. However, as previously stated, current medical school and residency experiences are highly variable. Most practicing psychiatrists have limited experience in the integrated model, having been trained in the "siloed" consultative role. Research is limited, but recent studies shed some light on the complexity of the problem of training "catching up" with the demand.

National systems have varying capacities to address this issue, which is beyond the scope of this discussion, but evolving US health-care reform may provide psychiatrists with the opportunity to use their unique medical and behavioral health skills in integrated care settings to improve patient outcomes, increase cost-effectiveness, and educate our medical colleagues. To be successful, new competencies will be required. Raney [21] addresses the need for psychiatrists to embrace a team-based culture, become accessible and reliable consultants, and provide support to primary care providers in a culture of communication, education, and leadership. As consultants in collaborative care teams, she comments that psychiatrists must understand liability concerns for consultations provided to patients they have not directly examined. In public mental health settings, in addition to managing problems caused by psychotropic medications, they may be called upon to assume greater oversight of the general medical care of their patients, requiring enhanced primary care skills.

In looking at the perceived educational needs of integrated care psychiatric consultants, Ratzliff et al. [12] surveyed 52 psychiatrists working in various integrated care settings. They identified perceived educational priorities related to their roles as clinical consultant, clinical educator, and clinical team leader. Almost all psychiatrists indicated they provided educational support for primary care providers (PCPs) and behavioral health providers (BHPs), commonly integrating education into clinical consultations. The authors subclassified essential topics and skills relevant to specific groups within the integrated care team, noting the overlap in educational needs according to team role (see Fig. 23.1).

When asked about their preferred method of obtaining training, the psychiatric consultants preferred attending conferences (92%). Other common training methods were online materials (81%), learning on the job (73%), learning from colleagues (65%), and courses on integrated care (50%). Interestingly, only 21% indicated "residency training" to learn about integrated care, suggesting most did not receive education on this during residency. However, it was noted that the development of integrated care rotations may be an ideal way for residency programs to address ACGME milestones on providing collaborative care with other physicians and leading a multidisciplinary team.

Further analysis of these psychiatric consultants' experiences [12] indicated their experiences in working in integrated care were very positive and highlighted four

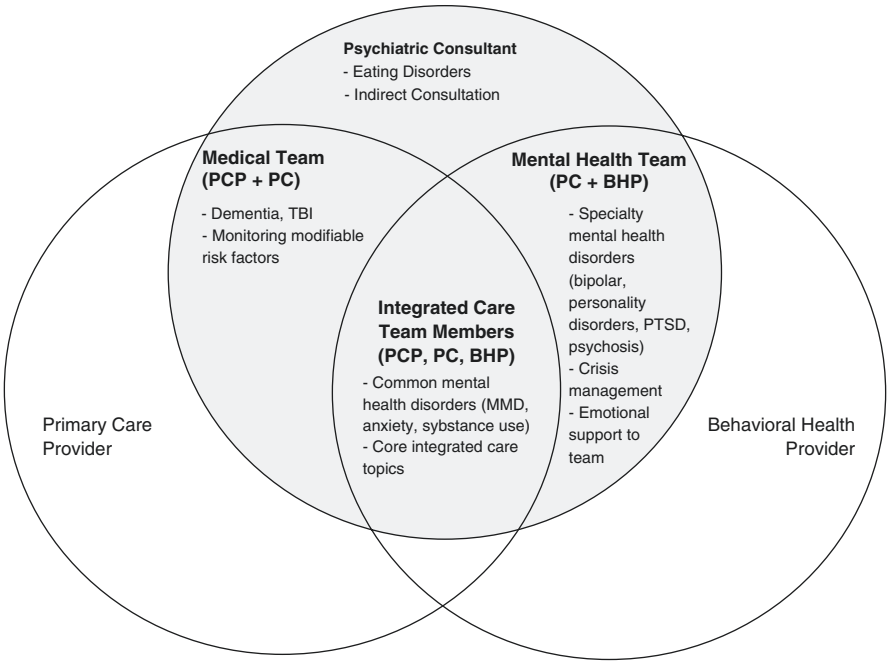

Fig. 23.1 Team member groups and identified educational needs sorted by role on the primary care team. From: Ratzliff A, Norfleet K, Chan YF, Raney L, Unutzer J. Perceived educational needs of the integrated care psychiatric consultant. Academic Psychiatry 39 (2015), page 451. With permission of Springer

themes: working in a patient-centered care model, working with a team, the role of psychiatrist as educator, and opportunities for growth and innovation. Identified challenges were cultural change when training new team members and financial/reimbursement concerns. [Note: since this publication CMS has created CPT codes for coordinated care]. Study limitations include sample size, possible selection bias (convenience sample), and findings based on self-report. However, the study does provide some insights into the range of activities, benefits, and challenges in integrated care practice.

Workforce challenges in integrated care settings are further addressed in a recent report in the family medicine literature. In an observational cross-case comparison study of 19 US practices in the process of integrating behavioral health and primary care, Hall et al. [22] reported that organizations had difficulty finding clinicians with the necessary skills and experience to work in an integrated setting. This included behavioral health clinicians, primary care clinicians, and psychiatrists. Practice leaders often did not know the required skills and underestimated the time and resources required to train new clinicians. Clinicians needed relevant training to work effectively on integrated care teams. Organizational interventions included hiring outside training consultants, sending employees to external training

programs, participating as residency or practicum training sites, or creating their own training programs. The internal programs included the development of training manuals for the "onboarding" of new employees, extensive "shadowing" experiences, and protected time for education, mentoring, and support for new and established clinicians and staff. The authors' conclusion: "Insufficient training capacity and practical experience opportunities continue to be major barriers to supplying the workforce needed for effective behavioral health and primary care integration. Until the training capacity grows to meet the demand, practices must put forth considerable effort and resources to train their own employees."

These examples reflect the complexity of implementing effective integrated care programs. As new physicians are exposed to this model during medical school and residency, their preparation for integrative practice will improve but will depend on adequate training of faculty and clinical supervisors as well. Educational issues go beyond psychiatric training to include primary care physicians, behavioral health clinicians, support staff, and organizational administrators. From a psychiatric perspective, postgraduate courses, online programs, literature, and clinical experience will be required for ongoing training and support in this exciting, evolving field.

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Person Centred Psychiatry and Neuropsychoanalysis: Bridging the Gap Between the Suffering Mind and the Dysfunctioning Brain

Fabian Guenole and Michel Botbol

Abstract

More than other medical disciplines, psychiatry is exposed to the negative effects of a disorder-centred approach. Indeed, a disorder-centred approach neglects key aspects for psychiatric clinical practice and research such as subjectivity and psychodynamic dimensions. The current implicit or explicit tendency is then to apply to psychiatry, the paradigm based on the biomedical classifications used in other medical disciplines. The problem is that, despite all its other merits, this paradigm, and the practices related to it, does not fully allow inclusion of the patients' emotional life and more globally their subjectivity. On the other hand, dynamic psychiatry puts its focus on these emotional and subjective dimensions but does not really take into account biological facts and up-to-date biological knowledge.

Person-centred psychiatry has had the great merit of bringing this dilemma at the forefront of international psychiatry, but it is still struggling to find an adapted approach to overcome it. In contributing to this movement, one of the aims of the WPA Psychoanalysis in Psychiatry Section is to participate to this effort, through the exploration on how psychoanalysis can contribute to develop a more integrative psychiatry in a person-centred perspective. As an advanced branch of psychoanalysis, neuropsychoanalysis is another way to take up this challenge. After introducing this new concept, this chapter will give examples of its application and consider to what extent it can build up a bridge on the gap between the suffering mind and the dysfunctioning brain.

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The main dilemma health professionals have to face when dealing with mental health or psychological issues is the fact that—maybe more than other medical disciplines—psychiatry and mental health are exposed to the negative effects of a disorder-centred approach. Because of the many competing theories about the very nature of one's mental life, a disorder-centred approach risks neglecting many of the non-objective aspects of the person's mental health, including key aspects such as subjectivity and psychodynamic dimensions. The current implicit or explicit tendency of international psychiatry is to mimic the paradigm of the biomedical classifications used in other medical disciplines.

The great achievement of Prof Juan Mezzich during his term as WPA president (2005–2008) [1] is to have brought this dilemma at the forefront of international psychiatry and to have then extended this perspective to medicine at large through the creation of the International College of Person-Centred Medicine. The main stake of this approach is to fight against this abusive reductionism that leaves us "with half a science" [2] and landmarks not well adapted to clinical practice in psychiatry [3].

In this perspective, the modernity and originality of person-centred psychiatry (PCP) resides in the fact that it does not satisfy itself with asserting its principles but strives to define conditions for the effective implementation of this ambition, in each psychiatric situation. What counts the most here is to meet real patients' needs and not those of more or less paradigmatic entities, defined by each medical speciality, induced to adopt a reductionist approach to comply with the requirement of research methodologies.

Strongly involved in this struggle, the WPA Section on Psychoanalysis in Psychiatry explores how psychoanalysis can contribute to develop a more integrative psychiatry in a person-centred way from both a clinical and a neuroscientific perspective.

The starting point here is the observation that, despite all its other merits, biological psychiatry, and related clinical practices, does not fully allow inclusion of the patients' emotional life, and more globally their subjectivity, in its observational field [4, 5]. On the other hand, (psycho)dynamic psychiatry [6] does not really take into account biological facts or hardly deals with up-to-date biological knowledge [7].

The main objective of this paper is to consider to what extent neuropsychoanalysis can contribute to take up the challenge of bridging the gap between the suffering mind and the dysfunctional brain.

24.1 The Neuropsychoanalytic Perspective

The aim of biological psychiatry is to investigate in mentally ill the different kinds of dysfunctions that can be evidenced in their brain, the organ of the mind; they struggle to do it as precisely and as reproducibly as possible. Dynamic psychiatry investigates, as precisely and as intimately as possible, the different kinds of disturbances that can be found in the same patients regarding their mind, the product of the brain. Brain dysfunctions can be evidenced objectively, using, for example, functional neuroimaging, whereas mental disturbances can be understood rather

(inter)subjectively, using empathy and the clinician's introspection: mental suffering is the emergence of brain dysfunctions embodying the suffering mind. Each is just as real as the other, and both together represent two aspects of the basically single psychophysical nature of mental disorders [8].

To illustrate this rather theoretical assumption, we could take the example of a depressed patient who attempts committing suicide: from a biological point of view, the person displays depleted brain monoamines levels that caused severe clinical features of depression; from a psychological point of view, this subject feels extremely painful affects he wants to escape at all costs, even if it means to die. Both views are possibly true and may together reflect the depression complex, from a "double-aspect monistic perspective" [9]. Biological psychiatry and dynamic psychiatry thus study two aspects of the same thing: disorders of human beings, our fellow beings, and bridging the apparent gap between the biological approach of mental disorders and the dynamic one; in the psychiatric field, it is the aim of what has been called "neuro-psychoanalysis" [10].

To some, this term may spontaneously evoke a futuristic brain imaging-guided psychotherapeutic technique; to others, it may sound as an attempt to defend psychoanalysis against accusations of being obsolescent by giving it a fashionable prefix; to some, it may even appear as a hoax, that is to say, the combination of terms that seems an oxymoron. What is meant under the term neuropsychoanalysis is actually more modestly, more honestly, and more seriously, the attempt to open an interdisciplinary field between neuroscience and psychoanalysis which, as original as it may appear, is in fact nothing but natural [10].

It must indeed be stressed that Sigmund Freud himself was originally a neurologist, who made, during his early career, several major contributions to neuroscience [11], and that he moved to a strictly psychological method of exploration by pragmatism only: neurological knowledge was useless at this time for understanding the neurotic cases who formed the main part of his clientele, but he clearly hoped that this renouncement to the neurological point of view would be provisory [11]. The neuropsychoanalytic approach consists in a way of starting again from where Freud stopped more than a century ago, considering that the neuroscientific progresses made since then allow it. It is true that neuropsychology is now no longer confined to the study of perceptive modalities or other narrowly circumscribed mental functions; it is now concerned with emotions, motivation in decision-making and behaviour, imagination, personal aspects of memory and identity, consciousness and even dreams! Moreover, neuroscientists also consider now that the vast majority of mental processes are unconscious. To this broadening of the horizons of neuropsychology corresponds uninterrupted technical advances in brain imaging and other functional explorations, as well as in molecular neurobiology. The question is: why not to add to that the knowledge and the tried and true observation technique that psychoanalysis can offer?

The practical proposals cover two main areas of research. The first one is *clinical neuropsychoanalysis*: the psychoanalytic study of brain-damaged patients [12] or subjects with other types of brain changes (e.g. functional ones, like for psychotropic medications). The second area of research is *psychodynamic neuroscience* [13],

or "psychoanalytically informed neuroscience": the neuroscientific investigation of hypotheses inspired by the psychoanalytic theoretical corpus, allowing to test psychoanalytic hypotheses using neuroscientific methods.

24.2 Early Neuropsychoanalytic Clinical Findings and Concepts

The most significant contribution made by neuropsychoanalysis to date concerns knowledge obtained in brain-damaged patients, with psychoanalytical observations carried out for different lesional localizations and associated neuropsychological syndromes [12, 14, 15].

Among these observations, those inpatients with extensive lesions of the right hemisphere have revealed new understandings of the mysterious clinical syndrome which is associated with such brain damage [12, 14, 15]. Without entering in details into these works, it can be said that psychoanalytical observation of several cases showed that anosognosia or anosodiaphoria, two impressive clinical features of the right hemisphere syndrome, results from psychological defensive mechanisms implying denial and thus that the perisylvian convexity of the right hemisphere has, in conjunction with its role in spatial cognition, a neurophysiological role in the establishment of a mature affective relationship with the environment. Patients with extensive lesions of the right hemisphere are thus manifestations of narcissistic object relations, which makes impossible for him restoring a sound inner world by usual mourning processes of their loss of autonomy. This limitation does not exist in cases of left hemisphere damage because the left brain does not seem to be a critical part of the neuroanatomic substrate underlying maturation of object relations—in this cases, patients actually would mourn normally their loss of autonomy [12].

24.3 An Example of Neuropsychoanalytic Researches in Psychiatry: Depression

In the field of clinical psychiatry, neural correlates of psychodynamic psychotherapy processes in mental disorders in which they have been shown to be efficient [16], are an interesting paradigm of neuropsychoanalytic research; we review here such researches on psychodynamic psychotherapies of depressive disorders.

Pr. J. Lehtonen and his colleagues at the University Hospital of Kuopio (Finland) have conducted during the last 15 years a series of studies investigating serotonin brain transmission during psychodynamic therapy for depression, using single-photon emission computed tomography. Two case studies [17, 18] firstly showed that decreased serotonin transporter (SERT) binding at midbrain level, which is known to be significantly associated with major depression [19], normalized after 1 year of psychodynamic psychotherapy (without antidepressant medication); interestingly, in one of these two cases, alleviation of symptoms occurred only 6 months after SERT normalization, suggesting that serotonin depletion and depressive

symptoms may not be necessarily synchronized. Laasonen-Balk and colleagues [20] then collected a sample of patients with major depression, whose SERT densities were investigated before and after 6 months of psychodynamic psychotherapy: 8/18 patients had a significant alleviation of symptoms at follow-up, and a significantly greater increase in midbrain SERT binding compared to others; here again, an increase in SERT binding without immediate symptom relief was noted, as clinical improvement without SERT changes in some cases. Joensuu et al. [21] subsequently found that an increase of midbrain SERT availability at midbrain during (at least) 1 year of psychodynamic psychotherapy was predicted by the baseline severity of depressive symptoms, and it had been previously found [22] that patients with atypical depressive features (reactive mood and hypersomnia-hyperphagia) where preferentially those whose SERT binding significantly increased during psychodynamic psychotherapy.

Roffman et al. [23] administered resting positron emission tomography brain scans before and after brief dynamic psychotherapy to patients with major depression under stable antidepressant medication. Resting activity within the posterior right insula correlated with depression severity and improvement in depression scores correlated with reduction of insular metabolism in patients who completed treatment. This in turn was associated with improvement of insight, a good indicator of successful psychotherapeutic processes.

Other interesting studies have been conducted by a network of German clinical researchers (the Hanse-Neuropsychoanalysis Study Group), using functional magnetic resonance imagery (fMRI). Buchheim et al. [24] reported about a 42-year-old female with dysthymia who undertook psychoanalytic psychotherapy, monitored with monthly brain fMRI during 1 year; these fMRI sessions compared brain activation during watching pictures tailored to the patient's core conflicts or neutral ones. Clinically, the patient presented narcissistic defences, including periodic self-distancing, which were significantly associated with signal elicited by conflict-targeted material in the posterior cingulate, suggesting this limbic structure is involved in narcissistic defences and resistance during psychodynamic psychotherapy.

Before that, Buchheim et al. [25] had used the same fMRI paradigm before and after 15 months of psychodynamic psychotherapy in a group of unmedicated patients with recurrent-resistant depression. Patients showed at baseline significant activations in the left anterior hippocampus, amygdala, subgenual cingulate, and medial prefrontal cortex in response to conflict-targeted material, which did not persist at follow-up. Reduction of these activations, particularly in the medial prefrontal cortex, was associated with symptom reduction.

More recently, Wiswede et al. [26] investigated changes in fMRI brain reactions to individualized psychic conflict-targeted stimuli in unmedicated patients with recurrent depression before and after 8 months of psychodynamic psychotherapy, compared to healthy controls. Patients showed enhanced activation in several limbic and subcortical regions, including amygdala and basal ganglia at baseline; they significantly improved in depression scores at follow-up, and no significant difference in brain activity persisted between them and controls.

Though results of these diverse studies are difficult to summarise, the following points may serve as a preliminary synthesis:

1. Alleviation of symptoms during psychodynamic therapy for depression seems to be associated with normalization of resting posterior insular hyperactivity [23]—which is known to be associated with human pain [27].
2. It seems to be associated also with normalization of brain hyperactivations during mobilization of psychic conflict [25, 26]. These hyperactivations concern different brain regions, which can be divided into two categories: limbic and paralimbic ones (amygdala, subgenual anterior cingular cortex, insula), which may correspond to emotional manifestations of depression [28, 29], and medial prefrontal cortex and basal ganglia, which may reflect emotional control processes and defensive mechanisms [29, 30].
3. Correction of a brain serotonin depletion seems to often occur during psychotherapy, sometimes before alleviation of symptoms. Here again, a link with modulation of pain signalling could be made, since serotonin has a broad anti-nociceptive effects on the central nervous system [31].

All these preliminary conclusions need to be confirmed and extended in the future with further studies of brain changes within psychodynamic psychotherapy processes. In addition to its interest for a better understanding of psychodynamic processes, such research may contribute to better define case selection, particularly in patients resistant to antidepressant medication.

Bridging the gap between the suffering mind and dysfunctioning brain—without being content with speculation or vague transpositions—such a neuropsychoanalytic approach is serving the epistemological need to model mental disorders as scientifically as possible without having to give up on the ambition to integrate in its focus the subjective and dynamic dimensions, central in a person centered perspective.

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Torture and Sequels to Persecution: A Global Challenge

25

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Abstract

Political persecution, torture, war and civil war are a growing problem, contributing also significantly to the present international refugee crises. The severe long-term impact on social systems, physical and especially psychological health, which can even become transgenerational, has been well documented. Violence in this context can be seen as the probably most significant global risk factor in mental health. Addressing prevention, support, treatment and long-term rehabilitation requires an interdisciplinary effort and close collaboration between health-care, legal and other experts, as well as of international organisations and UN bodies. The increasing importance of transcultural factors is of special relevance in the development of programmes in war areas and for displaced populations. Protection for vulnerable groups and human rights standards must be supported in different settings including asylum procedures.

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25.1 Introduction

Violence can today be seen as probably the most important challenge to mental health. Domestic, criminal and sexual violence are all common problems in most countries, but war, civil war and persecution have also become global challenges [1]. Research of the last decades has uncovered the frequently long-lasting adverse mental health impact of torture and violence [2]. It should be considered that psychological sequels frequently require comprehensive treatment approaches including psychotherapy and pharmacotherapy that are in this form not available to the majority of the most affected populations [3] because of financial limitations but also as trained clinical experts might not be available. In the following chapter of this book, we want to focus on torture and related acts of extreme violence as a special and complex, often interdisciplinary, issue in mental health.

25.2 Torture: A Question of Definitions?

Torture is defined by the UN Convention Against Torture (CAT) in Art. 1 as "any act by which severe pain or suffering, whether physical or mental, is intentionally inflicted on a person for such purposes as obtaining from him or a third person information or a confession, punishing him for an act he or a third person has committed or is suspected of having committed, or intimidating or coercing him or a third person, or for any reason based on discrimination of any kind, when such pain or suffering is inflicted by or at the instigation of or with the consent or acquiescence of a public official or other person acting in an official capacity".

Cruel, inhuman or degrading treatment (IDT) is equally prohibited according to the CAT but characterised by a lack of specific intention.

This definition of torture is narrow to provide a clear legal framework and should in general be used as a point of reference, especially in forensic settings. In a treatment setting, a more flexible interpretation, such as that provided by the WMA in the declaration of Tokyo, might be justified.[1] Special articles in the convention provide for the protection of survivors against forced return (refoulement, art. 3) and for their right to full rehabilitation. This is usually understood to mean not only legal but also medical treatment, social rehabilitation and redress for justice.

Torture might sometimes be limited to psychological torture, especially when a strategy avoiding evidence of torture by physical sequels is intended by the perpetrator, but physical torture must always be seen as a risk factoror for later psychological symptoms [4].

A convention alone does not provide sufficient safeguards against the use of torture or guarantee the implementation of that standard. The use of torture is common and in fact rising in many countries. As a result, the United Nations has implemented a number of additional measures and agencies including the creation of the UN Committee Against Torture (again frequently abbreviated CAT) but also

[1] http://www.wma.net/en/20activities/10ethics/20tokyo/.

the office of the Special Rapporteur on Torture and – of special relevance for the health-care profession – the Istanbul Protocol (IP[2]) [5, 6] that will be discussed later on in this article. The European Committee for the Prevention of Torture and Inhuman or Degrading Treatment and Punishment (CPT) has been established separately and with an extended mandate that, for example, also covers monitoring of psychiatric hospitals and other places where a person might be restricted in his/her liberty [7]. The identification and definition of some specific acts as torture as, for example, in the case of "hooding", is a responsibility especially of human rights and legal bodies like the UN and EU Committees against Torture or the European Court on Human Rights (ECHR). The OPCAT (Optional Protocol to the Convention against Torture and Other Cruel) implements a legal mechanism to realise the provisions of the CAT in a country.

25.3 The Impact of Torture

Considering the impact on victims, it is important to realise that torture in spite of the clear legal definition frequently is not a "simple" event [8]. While in some cases a short instance of violence is experienced, which can potentially be integrated by good coping strategies, torture can be and is frequently part of a lengthy suffering lasting in the worst case over years or life-long and might include traumatic experiences like the murder of friends or the inability to fulfil obligations to support and protect ones family while imprisoned due to exile or due to physical or psychological injuries received. It is further frequently embedded in exposure to other forms of violence and persecution outside of imprisonment including discrimination, bereavement, war or civil war and socio-politico-economic marginalisation. Torture in concentration camps is an example of such extreme settings of torture and can be said to first have been demonstrated to be followed by severe long-term impact even in the second and third generations [9, 10].

Recent data have demonstrated epigenetic alterations evident in both exposed parents and offspring of violence and torture [11]. Thus, extreme life experiences may also interact with the cultural background, for example, when religious or cultural rules are intentionally violated to humiliate the victim, as in the case of Abu Ghraib [12].Torture is used in many countries indiscriminately against any criminal in police stations or prisons, but also against members of the political opposition, and torture can lead to the death of the victim. Consequently it is not possible to speak of "the torture survivor" in the most general terms nor is it possible to describe a homogenous "torture syndrome" [13]. A holistic understanding of the individual and his/her experience is required to reflect the complexity of possible factors.

Posttraumatic stress disorder (PTSD) has been demonstrated to be the most common specific and common mental disorder after torture [4, 8, 14]. PTSD can affect up to nearly all members of highly exposed groups and can affect survivors on a

[2] The protocol is available on the website of the UN High Commissioner for Human Rights http://www.ohchr.org/Documents/Publications/training8Rev1en.pdf accessed 20.12.2016.

long-term basis even decades after torture [15, 16], as also documented in concentration camp survivors as the group with the so far longest follow-up period [17]. PTSD is presently seen in evolutionary psychology [18] as a maladaptive development of an in-principle adaptive pattern, an understanding that can also be used to explain the symptoms experienced to victims in a way that is not stigmatising, the last being a major risk in the psychiatric care of victims in societies where mental health problems are still stigmatised.

The recent changes in DSM-5 now include "complex" symptoms that have been described as frequent in torture survivors, such as dissociative symptoms and shame and survivor guilt feelings [19], which are common problems in torture survivors with a significant impact on long-term symptoms [20]. This should not lead to a too simplified focus in research and treatment. Major depression is nearly as common in victims [21], and chronic pain is an important and often treatment-resistant problem [22, 23]. This can reflect chronic injuries caused by torture with specific sequels including but not limited to chronic pain, such as those resulting from falanga (beatings to the sole of the feet [24]). Psychological and cultural factors like idioms of distress as discussed later on [25, 26] can also affect presentation of torture sequels. Comorbidity can be expected to adversely affect the long-term *course by interaction of specific problems like chronic pain, brain trauma and PTSD* [27, 28], and this in turn can lead to increased risk of complications including suicidal ideation or suicide [29, 30] or substance abuse as self-help strategy [31, 32]. The ICD 10 included the important category "Enduring personality change after catastrophic experiences" (F 62.0) referring to complex torture as in concentration camp experiences [33, 34]. It is to be hoped that this category will be included in ICD 11 in spite of the still limited data and not subsumed in complex PTSD.

In children, who can be direct or indirect victims, a wider range of symptoms have been observed, and DSM-5 has included extended definitions of PTSD for that group, though sequels are again not limited to PTSD. The term developmental trauma disorder (DTD) has been proposed to explain the various PTSD symptoms in children that might reflect the influence of on age, support availability, gender or the repeated nature of the trauma exposure. The term "toxic stress" has also been fronted by researchers to explain complex torture sequels in children.

Disability due to physical and psychological factors can be severe [35, 36], and sexual and family functioning are frequently significantly impaired [37]. Resilience factors and coping strategies can modify outcome [16, 38], but severe torture must be expected to affect all survivors especially under adverse conditions including children.

25.3.1 Brain Trauma

Brain trauma is a common, but under-documented, problem in torture. Beatings and kicks to the head, uncontrolled falls and being pushed against walls or objects are common in torture [39, 40]. The symptoms are similar to or overlap with comorbid depression and PTSD. The spectrum of possible injuries including mild chronic

neurocognitive disorder [41], chronic traumatic encephalopathy (CTE) [42] or sequels to asphyxia [43, 44] must be considered besides changes due to PTSD [45]. Possible blast exposure during war or suicide bombings that can be part of the history of torture survivors can also lead to blunt brain trauma and should be included in diagnostic assessment [46, 47]. Traumatic epilepsy is not uncommon in torture survivors [41].

25.3.2 Culture and Torture

DSM-5 has finally included the culture-sensitive models of illness behaviour and especially culture-based "idioms of distress" already well-established in transcultural psychiatry and cultural anthropology that should be explored as possible key issues in torture in the next years [19]. Such symptoms include the experience of being haunted by spirits such as those allegedly responsible for nightmare death in Hmong survivors [48], the Cen spirits in Acholi groups in Northern Uganda [49] or the presentation of physical symptoms and dissociations that are culture based rather than primarily a part of somatoform disorder [102]. Instruments like the Cultural Formulation Interview (CFI) as also recommended by DSM-5 [50, 51] can offer additional information to established standard instruments like the excellent and frequently locally validated Harvard Trauma Questionnaire (HTQ) [52]. Such cultural models improve understanding of the experience of survivors, which might be of major concern for victims. They should guide intervention models, especially as in traditional cultures where support and healing models can be available to address a person in distress, this interventions answer to their specific idioms. However, culture change and migration can challenge such traditional models of distress and support.

25.4 Treatment and Rehabilitation

Rehabilitation including all treatment efforts for torture survivors should follow a holistic approach that is consequently based on a culture-sensitive, integrative model that makes wherever possible use of positive social support and community factors. Protection of the victim, and in some countries also the helpers, is also a precondition and must be a first priority. It can be supported by medical findings, as discussed separately in regard to refugees, but also by international solidarity.

The already mentioned complex nature of physical and psychological sequels and special vulnerability of the patient group requires collaboration and agreement on a strategic plan for rehabilitation between the psychiatrist, psychologist or psychotherapist, family physician or primary care service, physiotherapist and social services and traditional healers in traditional communities. Due to possible triggering of flashbacks by cues reminding of torture that might include a number of apparently harmless situations like waiting, uniformed security personnel, closed rooms, windows with bars, loud male voices or medical examination and treatment steps, special care must be taken and culture-bound symptoms of distress respected [26].

The experience of helplessness must be avoided, and the patient should be well informed and able to take breaks to control a process.

Standard psychopharmacological treatments for PTSD or more unspecific common sequels are not torture specific in itself but should consider problems common in survivors like high levels of anxiety, presence of brain trauma, integration with analgesic-based regimens and ethnic psychological and biological factors like genetic polymorphisms and cytochrome variations. Improvement of sleep problems might be a first and especially important step in treatment. Side effects must be more carefully explained and considered than in other groups. Family-based interventions, if adequate, can address relationship problems common in trauma survivors.

Standard psychotherapeutic approaches have been successfully used in torture survivors, usually adapted to the high vulnerability and complex trauma factors in torture survivors including short CBT and trauma-focused CBT [53], creative media and psychodynamic models [54]. EMDR is a technique that is also being used in several settings [55]. Testimony therapy has been one of the earliest models developed specifically to adress trauma after exposure to political violence[3]. It takes up the narrative not only completing, integrating and correcting memories but also as giving evidence against a perpetrator when a court case cannot be brought forward to provide justice. *Narrative Exposure Therapy (NET)* has been promoted as a new special approach focusing on but not limited to non-Western cultures, though recent reviews have asked for future careful evaluation [56]. In many situations, community-based approaches that focus on group or social network interventions and support will be the method of choice, not only because trained psychiatrists and psychotherapists might not be available but also as recovery is strongly dependent on the social environment in many cultures. Especially in young adult groups like former child soldiers, special reintegration programmes might be required to address the destruction of social structures in a war or civil war environment [57]. Group support programmes (GSP) have been well-established and include group support therapy in Uganda [58, 59]. Legal aid is important as reparations without justice may impede total recovery/rehabilitation.

In refugees, transcultural aspects but also stressors related to displacement in a different culture, separation from family members and isolation must be addressed by the treatment plan and by special resources.

25.5 Special Aspects

25.5.1 Refugees

Refugee numbers are rising not only in Europe but all over the world. The UNHCR stated in its 2015 report that “an average 24 people were forced to flee each minute in 2015, four times more than a decade earlier, when six people fled every 60 seconds”. They will be either displaced in the country or region or become part of a wave of global forced migration that challenges their coping skills and resources

[3] https://www.freedomfromtorture.org/sites/default/files/documents/Blackwell-Testimony%20.pdf.

with displacement and cultural differences but also challenges the existing support and protection mechanism in host countries. Torture survivors must be expected to be a substantial part of that population, though they are frequently not identified in general health-care settings [60]. Displacement will add a number of additional stressors to the impact of torture that include a foreign cultural environment, insecure stay, lack of access to supportive factors like that of family members, new discrimination, racism, separation [61, 62] and again inability to take care of family members [63].

Early recognition should lead to protection as well as specific support and holistic rehabilitation in the host country, as outlined, for example, in the EU Reception Conditions Directive for Refugees (Directive 2013/33/EU). Besides identification by screening instruments such as the Refugee Health Screener that must be seen as a helpful but limited strategy [64], medical expertise plays a key role to confirm, document and report on torture, especially to offer grounds for special protection against forced return to a country where torture threatens, as demanded by the UN CATs article 3. The so far largely neglected [65, 66] use of medical expertise, which should be based on the Istanbul Protocol [67], provides for a number of important aims besides primary protection. Abuse including torture and inhuman or degrading treatment of refugees has been observed also as being common in some transit and host countries. This indicates a weakening of even "first world" democratic countries in their dedication to respect fundamental human rights as does the increasing use of detention and forced return (refoulement).

Detention of survivors must be avoided under any circumstances and as an unproportional measure due to the high risk of undue stress and retraumatisation in this especially vulnerable group [68, 69]. Extended or incorrect asylum procedures can cause substantial suffering that should be prevented by modified procedures for vulnerable groups. Refoulement of survivors is strictly prohibited by International Human Rights standards including the UN CAT and must be expected to lead to adverse outcomes even in refugees not exposed to torture, as was demonstrated in a recent study with UNICEF in regard to families who returned to Kosovo.[4] Documentation of torture in asylum seekers and refugees is a necessity when dealing with refugees. The Table 25.1 below summarises the aims to be followed.

25.5.2 Gender

Groups at risk for being tortured include female children and women. Gender-based violence (GBV) in general, especially towards women, seems to be growing worldwide.[5] The result of rape and other sexual violence related to torture are a key problem after torture especially in women, and sexual torture is a common component of war crimes. They may result in sexual health problems; pregnancy; difficulty forming, attaching or maintaining relationships; withdrawal; and fear of intimacy and may

[4] https://www.unicef.org/.../SILENT_HARM_Eng_Web.pdf accessed 25.12.2016.

[5] http://www.euro.who.int/__data/assets/pdf_file/0008/298196/Stepping-up-action-on-refugee-migrant-health.pdf accessed 2.2.2017.

Table 25.1 Documenting torture in asylum seekers and refugees

Procedure	Rationale
Preservation of evidence	Medical or psychological assessment can be difficult, impossible or dangerous for both the victim and the medical expert in many countries where torture is common. Preservation of evidence by advanced models of documentation is therefore of special importance in host countries. It can be essential for the criminal and civil law case
Instigation of an investigation	This step can be difficult, as long as no fair process can be expected in the country where torture took place. Newly established tools such as universal jurisdiction might change this situation
Monitoring by international bodies	Monitoring and reporting of human rights violations can be difficult or impossible in countries with ongoing civilian rights violations though international bodies, such as the UN Committee Against Torture (UNCAT), require reliable data
Acknowledgement of suffering	A correct and respectful interview can help the survivor to experience attention and respect for the suffering encountered
Protection	Survivors are entitled to special protection, including protection against detention and refoulement
Preparation and needs assessment for comprehensive rehabilitation	A comprehensive report based on the IP can also identify treatment needs and offer early intervention and secondary prevention
Treatment and rehabilitation needs	It is important to meticulously document all injuries – physical, psychological, material, social and ecological – which will need to be addressed as well summarised in the Istanbul Protocol

increase the vulnerability of women to HIV/AIDS. As a consequence of rape, survivors are frequently stigmatised, not allowed to get married, may become victims of "honour killings" or might become suicidal as demonstrated after the war in former Yugoslavia [37], and special support and protection are required. Women's health literacy varies, and training can be therefore helpful to increase the autonomy and skills of female survivors as refugees [70]. Women often are forced to provide sexual services to secure survival for themselves and their dependents. Their social control by men is often strict since male relatives may feel threatened by the Western lifestyle and autonomy among women [71]. Still there is a lack of conclusive studies explaining why for every traumatised man, three women will develop PTSD over the life span, and PTSD and the different interaction factors in gender and posttraumatic stress should be explored in more detail and in an interdisciplinary perspective [72, 73]. The question of gender-based persecution and sexual torture is not limited to women in spite of the especially severe impact on that group. Gender-based persecution in many countries also affects homosexuals and transsexuals, and torture can also make use of gender factors [74].

25.5.3 Africa as a Special Case: Torture, PTSD, Stigma and Appetitive Aggression in Africa

Africa, as a continent, has suffered torture for decades. This has taken such forms as slavery, colonisation, wars for independence and today's post-independence

wars and tortures including dictatorships; political repression; insurgences; ideological, race and ethnic wars; as well as fundamentalisms. The whole African region is experiencing the psychological distress aftermath of continuous warfare, political turmoil and dictatorial repressions such as posttraumatic stress disorder (PTSD), depression, anxiety and substance abuse, among others, and the accompanying population displacements both within and outside the countries' borders. Generally, people with mental illness, such as those due to torture, face many challenges in their lives including both enacted and internalised stigma, the latter often referred to as self-stigma; and stigma is most harmful when individuals internalise it [75].

Internalised or self-stigma is defined as "a state in which an individual accepts and agrees with societal prejudices about a particular condition (e.g. mental disorders) and applies them to oneself" [75]. Internalised stigma has been found to be associated with lowered self-esteem and hope and may carry on for generations as is seen in marginalised indigenous native communities all over the world. Self-stigma may also negatively influence treatment-seeking behaviour [76]. Lastly, the increasing levels of poverty in post conflict Africa has had severe deleterious effects on its people and worsened the felt stigma and negatively impacted the African peoples' quality of life [77].

From the mental health perspective, this is worrying because of an association between poverty and mental illnesses, such as PTSD, depression, anxiety, substance abuse as well as increasing levels of stigma and aggression. Trauma exposure often leads to mental disorders and violence in communities. The type of violence that is often experienced by individuals exposed to trauma or among its perpetrators of violence is termed as "appetitive aggression" defined as the "perpetration of violence and/or the infliction of harm to a victim for the purpose of violence-related relief/lessening of anxiety/enjoyment" [78].

People who suffer from PTSD and other trauma spectrum disorders feel easily threatened and out-casted and have low self-esteem (self-stigma) due to dysregulation of their emotions (including startle response, hypervigilance), thus making them more likely to turn to aggression as self-defence, hence the term "appetitive aggression". Traumatic experiences lead to emotional dysregulation which in turn leads to easy irritability and ultimately to aggression. The resultant violence results from a form of reactive aggression and the need to revenge for relief of the inner tension/anxiety, hence creating "appetitive" aggression. Trauma exposure, especially if repeated, leads to appetitive aggression and PTSD and as noted to "toxic stress" is often seen in former child soldiers. Appetitive aggression is thus similar to an adaptation to earlier experiences of violence. This is because such affected people often have PTSD with startled responses as they feel vulnerable and are easily threatened. They are often out-casted and have low self-esteem and self-stigma. Treatment as provided in the form of *Narrative Exposure Therapy (NET)* helps them in reconstructing an autobiography of themselves and a memory of their past experiences (see earlier in this chapter). This provides them an understanding of why they feel and behave the way they do ("appetitive" aggression), reduces their inner fears and tensions and may thus reduce their violent tendencies.

Phenomenologically, appetitive aggression reduces the risk of trauma-related distress among the perpetrators and therefore could be adaptive for survival in a violent environment [79, 80]. The powerful social and psychological rewards gained from it reduce the vulnerability to the trauma-related psychological distress hence its seeming protective effect [42]. However, this "protective" effect diminishes with high levels of traumatisation and creates a permanent paranoia and hypervigilance which drives the appetitive aggression [46]. This may explain why some people who were exposed to trauma or who perpetrated trauma continue to torture others, as is often seen in militarisms and also the diverse types of violence reported in post conflict communities in Africa such as the political violence by the security agencies (police, army, rebels, prison officers) or even in the common people as in riots, mob/vigilante violence, domestic violence, gender-based violence, intimate partner violence and child abuse [47, 81]. There seems to be an intricate relationship between trauma, psychological distress (e.g. PTSD), stigma and aggression. African countries are often led by former warlords, turned politicians, and Africa is a continent which is experiencing significant social violence. It is therefore imperative to recognise the relationship between trauma/torture, psychological distress (PTSD), self-stigma and appetitive aggression among African populations and how it is perpetrated. This may be of help in the post-war reintegration and rehabilitation plans of individuals who have experienced trauma and in peace-building and conflict resolution in Africa.

25.5.4 The Particpiation of Medical Doctors and Psychiatrists in Human Rights Violations

The professional umbrella organisations including the World Medical Association and the World Psychiatric Association have taken a clear position underlining the special role of health professionals that does not permit any participation in torture.[6] The recent discussion in the American Psychological Association [44] has drawn attention to the fact that there is always a risk that mental health officials can be enlisted in the effort to participate actively in torture and other severe human rights violations. Continuous effort is necessary to monitor ongoing activities for such violations of ethics and international humanitarian law. Participation in torture must be broadly defined and includes also collaboration in the development of torture techniques, in the insufficient documentation and reporting on torture and inhuman or degrading treatment or in forced feeding of mentally competent hunger strikers (WMA Declaration of Malta[7]). Doctors are "at risk" to violate their ethics especially in dual obligation situations that might include working in prisons in a totalitarian state, where non-compliance with pressure might be followed by physical danger but also less obvious situations. The use of hospitalisation in psychiatric hospitals as part of political abuse of the profession might include treatment that is in fact torture

[6] See, for example, the Declaration of Tokyo and the WMA Handbook of Ethics. www.wma.net/en/30publications/30ethicsmanual/pdf/ethics_manual_en.pdf, accessed 25.12.2016.

[7] http://www.wma.net/en/30publications/10policies/h31/.

and against the will and interest of the "patient" [82] though it can be seen as a more rare problem today compared to before as, for example, during the cold war. Places of detention of refugees or for those waiting for progressing in the asylum process in general have been identified as such situations for easy and implicit violation of these ethics as was the example in the case of Australia [50, 51].

Appropriate sanctioning mechanisms have not yet been implemented in most countries, and the professional international umbrella organisations like the World Psychiatric Association have a decisive role in drawing attention and putting pressure on member organisations to take active steps against abuses. Another challenge is the protection of those doctors who speak up against torture, who refuse to participate or who do document and report torture. It is again an important task for the national and international umbrella organisations to speak up for and support these members as in the recent case of Professor Korur,[8] a leading expert in the documentation of torture and a renowned collaborator of United Nations human rights activities.

25.6 Documentation and Assessment

25.6.1 The Istanbul Protocol (IP): Key Aspects of the Protocol and the Interdisciplinary Framework of Assessment

Due to the potentially complex and interdisciplinary nature of torture sequels, but also the legally and politically sensitive situation in which survivors are examined, there is always the risk of pressure on the physician conducting the examination. An objective international framework is thus required to guide this process. The standard for assessment of torture survivors has been established by an UN General Assembly Decision,[9] in the form of the Istanbul Protocol, as the "Manual on the Effective Investigation and Documentation of Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment" (IP) [40, 63]. It has been developed by an international expert group, is supported by the World Medical Association and the World Psychiatric Association and gives a comprehensive interdisciplinary framework for documentation, reporting and independent investigation of allegation to be applied in any examination of victims of alleged torture including asylum procedure. Psychological aspects are mentioned or elaborated in most of the chapters, as they can influence reporting, but also because they may possibly lead to secondary victimisation (retraumatisation). An important task in the implementation is the improved collaboration between the medical field and legal field which might involve challenges in mutual understanding, for example, in the presentation of specific psychiatric concepts such as countertransference to legal professionals.

Implementation of the Istanbul Protocol especially in asylum cases is still an ongoing issue [64, 65]. This has inspired a number of specific implementation

[8] See statement at http://www.wma.net/en/40news/20archives/2016/2016_14/ accessed 20.12.2016.

[9] 4.12.2000 as part of Resolution A/RES/55/89.

projects that include large multi-country collaborations efforts like the International Rehabilitation Council for Torture Survivors (IRCT) IPIP and FEAT projects[10] and the also EU-funded ARTIP realised in collaboration with our section.[11] The IP should, according to the WMA, be globally a part of pre- and postgraduate training of physicians. Due to the complex and interdisciplinary-oriented text and framework provided by the protocol, that addresses health-care and legal professionals summaries, including guidelines and short supportive training materials like those provided by the ARTIP project[12] have been developed to ease learning and everyday use of the protocol but are not intended to replace the protocol.

25.7 Prevention

Sequels to violence such as acts of torture can be seen as taking a special place in psychiatry not only because of their severe nature but also because the main aetiological factors for long-term mental health impact can, at least theoretically, be prevented. Possible interventions are again based on an interdisciplinary approach and need mental health professionals to support individual and policy-based interventions.

25.7.1 Primary Prevention

Though it appears to be unrealistic to expect a "world without violence", possible steps should be taken to reduce any relevant factors as much as possible. In the case of torture, an international system of humanitarian laws and mechanisms is of crucial importance in order to provide monitoring and carry out sanctions related to the actual implementation. In order to be effective, such a system should be mirrored by local and national laws, but also by new approaches such as that of Universal Jurisdiction models. A number of international declarations and treaties refer to the prohibition of torture that is to be seen as absolute. At the core is the already mentioned UN Convention Against Torture as well as measures such as criminal law in local legislation, the persecution of perpetrators and access to justice for victims. Training measures are also an important aspect of prevention. Such measures could be directed to officials who provide professional knowledge in alternatives to torture in order to get information as part of an investigation. The IP as a teaching framework also addresses the relevant basic international legal and ethical framework and can be used as a tool. Teaching of human rights at all levels of the country's education and law enforcement systems should be mandatory for all nations. Cultural and/or religious practices that allow torture should be outlawed.

[10] See www.irct.org accessed 20.10.2016.

[11] http://www.istanbulprotocol.info/index.php/de/ accessed 20.10.2016.

[12] See www.istanbulprotocol.info.

25.8 Secondary and Tertiary Prevention and the Role of Social Factors in Recovery

These aspects of prevention play a very important role in the further development and fate of survivors of torture and can be seen as complimentary parts in rehabilitation. Again, an interdisciplinary approach including an improved collaboration between psychiatrists, medical doctors and other professionals and society at large is required. In a holistic setting, supportive and protective factors play a key role that can be at least at times equally important as psychiatric treatment and psychotherapy [83, 84]. As a first step, any threat of further persecution or torture must be addressed as early as possible, as outlined in the paragraph on refugees. Documentation and reporting by the health-care professional should be followed by a "prompt and effective" investigation that would not only identify and sanction the perpetrator to avoid impunity and reconfirm rule of law but also lead to preventing future torture in the same institution or country. The already discussed Istanbul Protocol [85, 86] is an important tool in this part of the process. Redress and reparations should also be a consequence of this process. They might not be limited to material reparations, but also to social and public acts like, for example, the decision of the Inter-American Court on Human Rights in the "Castro-Castro" case in Peru, providing for a monument to a group of citizens killed under torture that confirms that dignity and their role as innocent victims of a state-sponsored crime.[13] Costs of treatment or loss of capacity or professional development should also be compensated.

The prevention of torture or other forms of extreme violence and persecution and support of victims and their families should, on a broader scale, mobilise and involve society as a whole, as in the case, for example, of national Truth and Reconciliation Committees. Experience of the last decades has demonstrated that this type of intervention requires careful consideration to be efficient and might not always work easily in a long-term perspective [87]. Existing cultural models especially in traditional societies should be carefully examined to serve as models or to be integrated, as they can be highly efficient in more every day acts of violence as in the Mato-Oput ritual of the Acholi in Uganda [88]. However, these could be overwhelmed in a complex and extensive use of violence-based setting like the Rwanda genocide [89]. Vamik Volkan, a Turkish American group psychoanalyst, developed and successfully tested models to reduce intergroup tensions and contribute to prevention of developments that could lead to civil war [90].

The positive reaction of the social environment in the broadest sense should be emphasised as social support has been identified as an important factor in the recovery of victims of violence in general but especially in survivors of torture [91]. This should always be seen as an equally necessary part to be considered in holistic and community-based rehabilitation [92] as noted earlier also in secondary and tertiary prevention.

[13] www.corteidh.or.cr/docs/casos/articulos/seriec_160_ing.pdf accessed 1.2.2017.

25.9 Indirect Victims

The psychological impact of extreme violence can be expected to affect others apart from the direct victim. In most cases, family members and persons in the close social network including neighbours and workmates should be considered as further strong arguments against the use of torture as it affects these third parties and negatively affects society as a whole [93]. Conditions of arrest that can be violent and might even lead to traumatic stress in others present, their unclear fate and unknown outcome of arrest but also the psychological changes in the survivor after he/she returns home can lead to significant relationship problems and secondary trauma in family members. The mechanisms of transgenerational transmission including epigenetic mechanisms as mentioned in regard to Holocaust survivor families are presently under research and must be expected to be part of the long-term impact of torture. This is presently the focus of ongoing research [32–34]. Indirect or vicarious trauma has also been observed in helpers and even mental health professionals who work with victims of torture or similar acts of violence on long-term basis [94, 95]. This includes court clerks, translators and other aids in such complex cases as even in the International Court of Justice. Care must be taken in their treatment to provide sufficient support and supervision or intervision for all team members [96].

Special consideration should also be given to the often lifelong suffering of those indirect victims where torture victims do not survive their ordeal and never return to their families and friends [97] as in the case of "desaparecidos" in the Latin American dictatorships. This has been acknowledged in a recent finding of the European Court on Human Rights that pledged a significant material recompensation to the families of persons killed in the 1974 Turkish invasion in Cyprus. The argument was that the lack of an efficient investigation into the unclear fate of the family members caused secondary victims to be exposed to significant emotional suffering (Application no. 25781/94).

Conclusions

Torture and similar acts of extreme violence are severe human rights violations. They have been demonstrated to lead to long-term sequels affecting not only the victim but also family members, helpers and society at large. They perpetuate war, political unrest and suffering in countries in a process which may span generations. Interdisciplinary collaboration with a special role for psychiatrists and other mental health professionals is required to provide for efficient prevention, protection and treatment as a background to holistic rehabilitation. More research is required to develop new and more culture-sensitive, efficient models to offer treatment for survivors that can also be provided in situations where resources are low. At present special issues of concern are the protection and support of torture survivors displaced as refugees and the maintenance of basic human rights standards not only in war zones like Syria but also in apparently peaceful and industrial "developed" countries as in the European Union, the USA and Australia.

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The Concept of the Disruptive Events and Reconstructive Relational Experience as a Model of Crises and Disasters Interventions

26

José T. Thomé

Abstract

We live in the twenty-first century with the frequent presence of the violent discontinuity in the mankind's daily life. We call Disruptive this violent event that promotes experiences by placing it against disorganizing extreme situations.

We live in the twenty-first century with the frequent presence of the violent discontinuity in the mankind's daily life. We call Disruptive this violent event that promotes experiences by placing it against disorganizing extreme situations.

These experiences are caused, for example, by wars, by politics, by political corruption, by the economy, by religion, by ideological fanaticism, by the urban violence, by terrorism practiced by radical groups or by the state, by natural or anthropogenic disasters and/or, as a consequence, the catastrophes.

26.1 The Concept of the Disruptive

The Disruptive Concept proposed by Moty Benyakar [6] makes it possible to differentiate what "goes on outside" of what goes on "in the mind or in the psyche." Not every event is destabilizing or traumatic to the psyche, and when it is, it will not be the same for all individuals it harms. We differentiate the phatic universe from the psychic universe, each of which has its own specificities. The phatic universe is related to the external or the "surrounding" of the psyche and has its own dynamic process.

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These situations establish emotional experiences generated from real facts, provoking, in most of the cases, threatening perceptions of reality. So the society is exposed to all great human fears simultaneously. Healthy people individuals and/or communities plagued by such disruptive violence face a type of emotional stress, which may evolve into a potentially traumatic disturb and may present psychic maladjustment and illness.

His Disruptive Concept is an alternative to a "traumatic situation," which has restricted and distorted research and clinical approach based in the Post Traumatic Stress Disorder—PTSD. The situation *will never be traumatic*, but it's *traumatogenic*. The trauma may occur only in the psyche. The Psyche is the result of the interaction between the internal facts versus the eternal facts, creating a mental or intrapsychic reality through the experiences.

The Benyakar model establishes a differential: the diagnosis of the post-traumatic stress disorder may not be a diagnosis for all disruptive situations. We can understand the illness caused by the disruptive as the "Pathologies by Disruption," which include the PTSD. We cannot forget that if the PTSD presents a 70/80% of comorbidity.

According to Benyakar: crises and natural/or social disasters, provoked or not by human beings, are challenges that force us to rethink the way the environment erupts in people's psyche, and should be analyzed in terms of the personal reactions of the people affected and their psychological impact.

These facts affect physical and mental health. The disruption generated by the natural events and human violence demonstrated the power of nature and man, the proximity of death exposed the fragility of social contact rules (New Orleans—Katrina) and man's destructive reaction in his natural state.

The violence of the emotional impact caused by these causes in the psyche of the people involved may destabilize or disorganize them, temporarily or definitely. However we are not prepared to live disruptive events or disruptive environment that will produce anguish. The uncertainty caused by Disruption is permanently present (Altman 2017).

It considers the pathogenic quality of a factual situation that erupts in the psyche, producing the disorder.

The disruptive model is not based on the classical psychological trauma theory of psychoanalysis, but rather on Piera Aulagnier's model of psychic apparatus modified by him.

A disruptive event destabilizes the emotional balance, generating feelings of insecurity, disbelief, helplessness, and hopelessness. In this time we live with/in uncertainty. These feelings, when experienced, are felt through the *sensations* (not emotions and feelings) that are present in our psychic primitivism. Therefore they are not verbal.

Studies and researches have been conducted since the second half of the twentieth century, in order to diagnose symptoms, illness patterns and to develop intervention actions in this new field.

26.2 What is the Reconstructive Relational Experience?

We need for the disruptive situation an assistance intervention. This assistance model is based on the encounter of psyches that is in a relation of intersubjectivities.

This model of assistance interventions (Thome 2013) considers human subjectivity as a starting point. We need a contemporary model for assistance and treatment in this disruption time including Human's Factors or, again, the human subjectivity.

They should be directed to the communities hit by the disruptive, meeting their specific needs and characteristics.

The Reconstructive Relational Experience is as methodological tool as a way of including human factors in the intervention as well as the capabilities of the resilience of the subjects.

The approach of *Reconstructive Relational Experience*—RRE—(Thomé 2013) presents the central value of the intervention, its reconstructive effect on the subject and multiplier effect in the community. The RRE is applied in an intervention as an experiential intervention in crises, which creates a transitory space with transitional qualities for containment and sustainability.

The use of the word Reconstructive is specific. We are NOT CORRECTING but LOOKING FOR NEW MEANINGS by attempting to articulate affection and representation of the disruptive event nowadays.

This can only happen in an encounter that promotes the psychic processing of the imbalances that the anguish provoked. This will only occur within a relationship involving positive affections, or affective, to process the feelings of helplessness and impotence that the disruptive generated. The RRE used in an assistance intervention will lead to a resignification of the conflict.

This model of intervention is created according to each individual or population's specific needs and, at the same time, with the need of systematizing the assistance to this healthy population damaged by the confrontation of a disruptive event.

It is your commitment to the clinician. The clinical function in the assistance interventions is what we are looking for. It allows considering the impact of the disruptive as an opportunity of change for the strengthening of the psychic immunity and resilience.

In ideal terms, models of approach in crisis and disasters should justify their results in three levels: theory, technique, and field. They should be theoretically consolidated with a coherent perspective about the addressee subject, a conception on mental health and its consequent psychopathology, a theoretical basis consensual and accepted in the conditions of the psychic process, the trauma and the elaboration of what is disturbing for the mental and physical health of the involved.

On the other hand, they should include a group of techniques of coherent approaches derived from the support theory. Finally, they should be evaluated by the success in the field experiences where they have been set up.

The bibliography shows that the published interventions in the field of assistance generally comply with any of these conditions, but not with all, and not necessarily can articulate their different levels.

In this article I'm presenting the systematization and integration of an intervention in crisis and catastrophes put to proof and of the multiple field experiences made during 40 years in clinical attention and therapeutic groups' coordination, supervisions, and assistance interventions at the institutions in which I take part.

26.3 Protocol of the Program of Emergency Intervention and Support of the Mental Health Developed to the Population Hit by Floods and Landslides in Santa Catarina-2008/2011

First of all we made the presentation of the protocols and concepts to be reflected and identified by the group to unfold the work of the task force through technical awareness with activity which seeks the formation of a network to deal with the feeling of guilt and helplessness.

To rescue the feeling of self-esteem could start the outline of an organization of a network of support to each other, which will enable the expression of new demands to be discussed at the next meeting.

Establish the need to give continuity to this action through sustainability that the institution will provide for other meetings.

26.4 Reconstructive Relational Experience as a Model of Crisis or Disasters Interventions Based on Human Factors

1. All instances that interact in disruptive situations are perceived as groups of caregivers. The situations caused by disruptive events or actions and/or organized interventions resulting from the training achieved by: professionals of civil defense, health/mental health, educators, lawyers, public ministry, engineers, economists, political and religious leaders, volunteers and the authorities of the State in accordance with their specified complexity.
2. They are transdisciplinary projects (Morin E.) that depend on human factors, therefore, in the observation of qualitative indicators for the evaluation.
3. These actions/interventions are addressed in the amount of points possible in the areas of human knowledge (complexity). Keep the focus on the crisis, not on the reactions to it.
4. *The model is based on the training of key people contributing to the reconstruction by developing of their psychic immunity and resilience and to consequently make the development of the affected ones through the RRE. Its action/intervention is an approach to inter-, multi-, and transdisciplinary both for who cares and to those who are affected or damaged.*

5. The proposed program does not provide medical-psychiatric attendances. Important: do not "medicalization," "psychologizing" or "socializing" the actions.
6. Train to identify/move through listening and recognition of the symptoms as caregivers/affected may submit cases that must be attended and/or aimed for specialized treatment.
7. Most important: do not VICTIMIZE those who were directly or indirectly affected by disruptive events.
8. The dynamics of the interventions are built based on submitted claims by caregivers at each meeting, i.e., by presence in its different stages. Interventions should be carried out by presence to consider human factors differentiated from interventions by demand, which involved quantitative protocol actions.
9. It is in the plot of COMPLEXITY (E. Morin) that applies the dynamics of disasters and their multiple perspectives in evaluation.
10. The intervention should not make part of a Government management as a mortise. It should be understood as a situation of permanent exception because its sequels will appear in various segments of society. (education, health, housing, urban development, labor, economy, security, etc.) for the following years.
11. In the early stages of the impact it should be developed the assistance program which could include clinical treatment for caregivers and affected ones.
12. Having the awareness that we are dealing not with patients, but with healthy people who suddenly, triggered by the disruptive fact face a situation, highly Mental Health Programs should be directed to what we call functional leadership: The care approach is transdisciplinary, including the individual, family, collective, environmental, and institutional, therefore the complexity.
13. Creating a collegiate of managers as a propitious time for knowledge of the problems and referrals to a joint transdisciplinary.
14. Sensitize people to achieve their goals: The goal will always be to offer an early sense of meaning for emotional representation of disruption/destabilization that was experimented on a group of awareness.

26.5 Results and Conclusions

As a work of support network, the value of each person was rescued, therefore minimizing the feeling of natural impotence in such traumatic circumstances.

In the work of awareness-raising with the group, it was possible to note the need to develop actions seeking integration and inter-relationship of the various sectors which attended those affected.

From a complexity perspective (Morin E.), the enlargement of the look and the distribution of the focus tie up the parties facilitating and making the process of individual and collective reconstruction through related experiences (Thomé).

Our intervention project was created and organized from various views and experiences applied in work wrapped in the last decade, joined with current concepts previously expressed in this presentation.

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Neurobiology of Schizophrenia: Electrophysiological Indices

27

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Abstract

The objective of the WPA section on Psychoneurobiology is the promotion of the integration of findings from research fields such as neurophysiology, psychology, neuropsychology and psychiatry. This chapter focuses on the importance of electroencephalographic (EEG) studies for the section's objectives and especially for (a) the study of functional brain abnormalities related to liability to psychosis and schizophrenia pathophysiology and (b) characterization of schizophrenia psychopathological dimensions. The introduction will highlight the

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importance of EEG investigations in psychiatry, outlining a model of brain function, based on the notion of state-dependent information processing, and providing examples relevant to schizophrenia research. The second paragraph will summarize the current state of knowledge about resting state EEG connectivity in subjects with schizophrenia (SCZ) and draw some tentative conclusions about the possible links to the range of cognitive and behavioural abnormalities observed in these patients. The third paragraph will illustrate findings from event-related potential (ERP) studies of subjects at risk for psychosis who later develop schizophrenia-spectrum disorders. Some of the ERP parameters are proposed as biomarkers of the transition to psychosis and, if further validated, can be used to identify subjects for early interventions. The final paragraph of the chapter will summarize findings relevant to the characterization of the psychopathological dimensions of schizophrenia.

27.1 Introduction: The Importance of EEG Studies for the WPA Section on Psychoneurobiology

Martha Koukkou

27.1.1 Why Use the EEG?

In neurophysiological studies, the EEG was used in order to investigate intra-individual variance in the brain's functional state in relationship with the characteristics of the momentary subjective experiences (thoughts, emotions) or behaviours in different populations and experimental settings.

The findings suggested that the brain electrical activity (as manifested in the scalp EEG):

- Is an observable property of large populations of neurons that are engaged in cortical information processing
- Enables functional neuroimaging that attains the high time resolution of human information processing
- Provides information of the level of excitability of the cortical networks

Research in psychoneurobiology showed that there are well established correlations between manifested behavioural development and systematic changes of cortical functioning as manifested in the developmental changes of the awake EEG. In particular, the EEG amplitude and mean frequency, as well as the coordinated patterns of functional connectivity, expressed in the brain electrical microstates, undergo significant developmental changes. Further, EEG coherence between

regions increases with age, differing between hemispheres, and between anterior and posterior areas [1, 2] as well as the "chaotic dynamics" of EEG, i.e. its complexity increases systematically from newborns to adults [3, 4]. Systematic changes of cortical neuroanatomy during development are manifested in the increase of the cortico-cortical connectivity between hemispheres and cortical regions. These changes are the product of the experience-dependent plasticity, with changes related to individual experiences inducing cortico-cortical synaptic complexity.

During Human Development:

- Experience-dependent synaptogenesis results in increased quantity and complexity of the cortical neuronal networks.
- These neuroanatomical developmental changes are accompanied by changes of the scalp EEG and by changes of higher cognitive-emotional functions which characterize the ontogenetic course from childhood to adolescence and adulthood.

The organization and dynamics of neuronal networks represent the product of the development, regulated by multiple factors (genetic and environmental variance) and including the impact of the individual experiences, and lead to the creation of well- or maladapted coping and reality-controlling strategies (the contents of autobiographical memory). For an extended review, see Koukkou and Lehmann [5]. The brain's functional state (which is multifactorially defined), during resting, represents the level of attained complexity of the neural networks during the ontogenetic development, while during information processing, it is a function of memory-driven, dynamic interplay and state-dependent momentary excitability of the same networks.

27.1.2 An Integrative, Complex Living Systems-Oriented Model of the Brain Functions that Create Autobiography

A given degree of coherent coordination among the determinants of the brain's functional state (age, metabolic-hormonal equilibrium, neurotransmitter state) is the prerequisite for a state-adequate level of excitability of the neural network and corresponds to the EEG states. State-dependent, memory-driven processes form the individual's momentary thoughts, emotions and behaviours as well as their conscious perceptions.

In schizophrenia, cognitive-emotional and behavioural changes are caused by the altered excitability of the neuronal networks and disconnection among their main nodes, with altered accessibility of memory contents and "forced" use of state- and/or age-inadequate knowledge in order to cope with usual or excessive stress.

EEG methods are appropriate to investigate the neurophysiology of both normal and psychotic experience and behaviour, based on an integrative, complex living systems-oriented model of brain function outlined above [5, 6].

27.1.3 Electrophysiological Indices and Schizophrenia: Dissociated Brain's Functional States in First-Episode, Neuroleptic-Naïve Productive Patients with Schizophrenia

For our EEG studies in schizophrenia, 19-channel EEG was recorded during resting and after the presentation of short sentences in first-episode, neuroleptic-naïve patients. Based on EEG measurements, we tested the following hypotheses:

- The scalp EEG provides indices of state-dependent, memory-driven information processing.
- SCZ is characterized by deviations in all determinants of the brain's functional state and thus by deviant EEG activity and reactivity.

I will present the results of three studies in which two different EEG analysis methods were used in order to test the above hypotheses.

27.1.3.1 EEG Spectral Analysis

A total of 70 subjects participated: 3 groups of adolescents, 11-, 13- and 14-year-olds, SCZ and age-, gender- and education-matched controls (also called "adults"). The final diagnosis at discharge was DSM-IV schizophrenia or schizophreniform disorder. EEG was recorded from 19 leads during resting and after the verbal presentation of four short sentences.

The EEG was spectral analysed. For each of the 19 recording leads, the spectrum was divided in 3 frequency bands, 2–7.5 (theta), 8–13 (alpha) and 13.5–26 Hz (beta). For each frequency band, the centroid frequency was extracted. The centroid assesses the shape of the power distribution within the band by one number, independent of the total power in the band. It is the centre of gravity along the frequency axis of the band. It is lower when slower frequencies predominate within the band; it is higher when higher frequencies prevail. The centroid is a sensitive measure of developmental EEG changes.

Figure 27.1 presents a summary of the results. SCZ had lower theta centroids than all four normal groups, in resting and in the average of the four activation conditions. SCZ showed the highest values of all groups in alpha and beta, in resting as well as activation EEG states.

The majority of the expected normal age-dependent differences were found between adults and 11-year-olds in the alpha and beta centroids.

The comparisons of the SCZ with the adolescents showed:

- SCZ had the lowest theta centroids compared with all three groups of adolescents and this mainly over anterior leads.
- SCZ had higher alpha centroids as compared with 11- and 14-year-olds.
- SCZ had higher beta centroids in comparison with all three groups of adolescents with differences in the number of leads with significant results.

Given that the differences between the adolescents and the controls correspond to the normal age-dependent differences, the results of the comparisons between

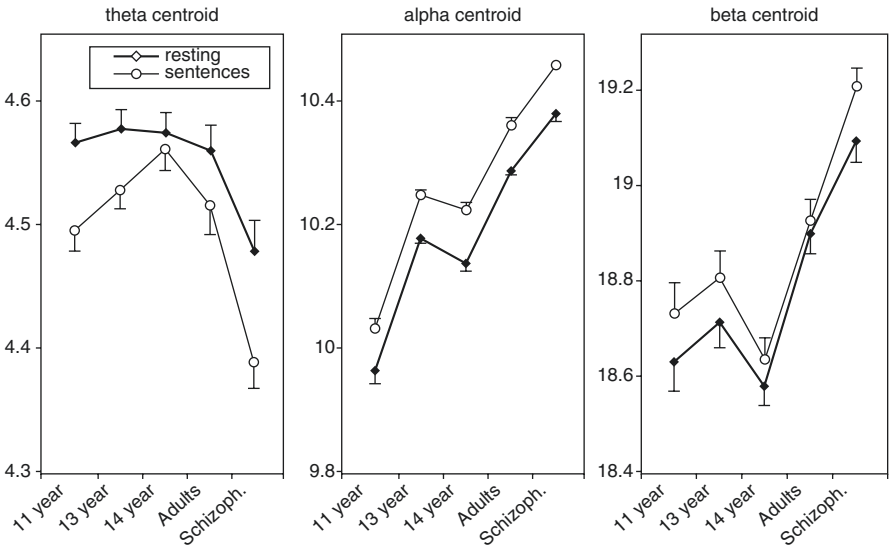

Fig. 27.1 The mean centroids (±1 S.E.) across the 19 leads for resting EEG and for the average of the 4 information-induced states (short sentences) in the theta, alpha and beta frequency bands in the 5 groups (3 adolescent groups, a schizophrenic group and adult normal controls). Reprinted from Journal of Psychiatric Research, Vol 34, M. Koukkou, A. Federspiel, E. Bräker, C. Hug, H. Kleinlogel, M.C.G.Merlo, D. Lehmann. An EEG approach to the neurodevelopmental hypothesis of schizophrenia studying schizophrenics, normal controls and adolescents, 57–73, Copyright (2000), with permission from Elsevier

SCZ and adolescents indicate dissociated, i.e. partially regressed and partially over-activated EEG states. In other words, SCZ show dissociated levels of excitability of neuronal networks, i.e. dissociated levels of the activated and/or inhibited networks [7, 8].

27.1.3.2 EEG Microstate Analysis

In further studies, using new methods for resting EEG analysis, differences were found between neuroleptic-naïve SCZ and age- and gender-matched healthy controls (HC).

In such studies [9] the 19-electrode EEG was recorded in resting, and the momentary electric field configurations were estimated as sequences of momentary maps. The map series were assigned to four microstate classes and tested for differences between SCZ and HC.

One microstate class displayed significantly different field configurations and shorter durations in patients as compared to the matched HC.

In a multicentre study in acute, first-episode, medication-naïve SCZ [8], EEG microstates differed in duration and syntax (i.e. the sequence of transition from one to another microstate class over time) from matched HC.

27.1.4 Discussion

It was the psychiatrist Hans Berger who, in 1929, first provided published evidence of EEG in man [10]. Shagass [11] published in *Biological Psychiatry*, an electrophysiological view of schizophrenia.

What is the relevance of our results for further understanding of the pathogenesis of schizophrenia? We concentrate on what the finding of dissociated EEG states may suggest as to the pathogenesis of the frequent first manifestation of schizophrenia during late adolescence in individuals who earlier had functioned normally.

In adolescence, distinct changes occur (reorganizations) of all determinants of the brain's functional state (the most obvious is the hormonal reorganization), suggesting reorganization in the level of excitability of the neuronal networks. The adolescent is also confronted with expectations and/or demands for social adaptation to the adult ways of life. It has been proposed that adolescence and early adulthood may be experienced as existential and/or environmental stress and that the efficiency to cope with stressful events depends on the quality of the adaptations worked out during development in order to cope with comparable events.

In schizophrenia, heterogeneous and non-specific deviations of all determinants of the brain's functional states have been described to precede the manifestation of the symptoms (including sleep disturbances and behavioural changes indicating stress), as well as to accompany the symptoms, suggesting deviant levels of excitability of the neural networks.

The results suggest that the frequent onset of schizophrenia during late adolescence may be due to imbalances in the coordination of the determinants of the brain's functional states. These imbalances may have multifactorial origins rather than be due to an abnormal function at a single location or due to a fixed brain lesion acquired early or late in life. They lead to the cognitive-emotional and behavioural changes (seen at schizophrenia onset) through an altered excitability of neuronal networks and thus altered accessibility of memory contents which "forces" the individual to use state- and/or age-inadequate knowledge in order to cope with usual or excessive stress.

27.2 EEG Indices of Resting State Connectivity in Schizophrenia

Thomas Koenig, Anja Bänninger, Kathryn Rieger, and Laura Diaz Hernandez

Patients with a diagnosis of schizophrenia respond, in the average, in an often blunted and less accurate and efficient form in a very broad range of tasks. In fact, this range is so heterogeneous that it is difficult to conceive a particular deficit that could commonly explain these observations. One possible solution to this problem may be that we take into account that environmental input does not meet a brain that is essentially inactive but interacts with its momentary baseline activity. Brain and

behavioural responses to a specific stimulus thus vary depending both on the baseline state and on the content of the input. If we assume that there may be systematic alterations of baseline activity in SCZ, the notion of state dependency of brain information processing may explain the broad range of abnormal responses based on a potentially much smaller set of abnormalities of the brain baseline states. In addition, baseline states precede stimulus responses in time and may therefore also causally precede alterations in task response.

Resting state brain activity displays a remarkable amount of organization in space and time that has allowed to characterize in particular the so-called resting state networks. Interestingly, schizophrenia has for a long time been characterized as a disconnection syndrome [12] and has therefore become a domain where the analysis of resting state networks has steadily gained attention. In the study of resting state networks and brain functional connectivity, EEG and magnetoencephalography (MEG) data have a unique place because their excellent time resolution is compatible with the speed of human brain information processing. The aim of the following brief review is to summarize the current state of knowledge about resting state EEG connectivity in SCZ and draw some tentative conclusions about the possible links to the abnormal responses seen in so many domains.

EEG analyses of brain functional connectivity need to take into account the confounding effects of volume conduction [13]. Volume conduction in EEG and MEG refers to the fact that even a single source in the brain produces a field on the scalp that is potentially widely distributed and that the scalp fields of several such sources are additive. A similarity of two signals recorded on the scalp may thus potentially be caused by the same source that simultaneously affects both recording sites. Based on how this problem is addressed, analyses of resting state EEG and MEG connectivity can be divided into two main classes of approaches, namely, measures that assess non-lagged connectivity, such as factorization and microstate analysis, and measures that quantify lagged connectivity, such as lagged coherence and the phase locking index.

This choice of methodology implies very different understandings of what constitutes connectivity: non-lagged connectivity implies the simultaneous co-activation of network elements and disregards delayed interactions, whereas lagged connectivity implies sequential activation and excludes simultaneity. The approaches are therefore mutually exclusive in terms of what mathematically defines “being connected”. We will structure our brief review on EEG resting state connectivity in schizophrenia along this division and later try to integrate the findings.

It is also important to note here that none of these measures allow to directly translate connectivity patterns among sensors into anatomically corresponding brain connectivity patterns [14]. Our overview is therefore limited to studies that have either used inverse solutions to explicitly estimate the activity of particular regions of interest, and then quantify the amount of similarity among these estimates using lagged indices of connectivity, or that make global statements about connectivity patterns that explicitly accommodate volume conduction. Unfortunately, the number of such studies is yet small.

27.2.1 Lagged Measures of EEG Resting State Connectivity in Schizophrenia

The first study comparing lagged coherence in inverse space among SCZ and HC was an MEG study published by Hinkley et al. [15]. For each voxel, the authors computed the mean lagged alpha band connectivity with all remaining voxels (global connectivity). They found increased global connectivity in SCZ in the right inferior frontal gyrus and the left occipital gyrus, whereas decreased global connectivity was found in the right superior temporal gyrus and the left middle frontal gyrus and the precentral gyrus.

A later study by Lehmann et al. [16] investigated only medication-naïve patients. Lagged connectivity was computed between inverse solutions estimated for regions of interest (ROI) and in different frequency bands. The authors reported patients to have decreased connectivity between anterior and posterior ROIs in the lower alpha band and right-lateralized increased connectivity between anterior and posterior ROIs in the delta band.

Di Lorenzo et al. [17] found increased lagged connectivity in medicated SCZ in the delta, theta and beta bands, and the affected connections again were those predominantly linking anterior and posterior regions. In the alpha band, there was a decrease of lagged connectivity, mostly affecting connections among frontal regions but also including parietal parts of the brain. A theta band increase in lagged connectivity in patients was also reported by Andreou et al. [18], but found to be predominantly left lateralized, whereas another study by Shreekantiah Umesh et al. [19] that reported theta band lagged connectivity increases in remitted patients found increases between bilateral parietal and frontal regions.

The consensus among these studies seems difficult to name in terms of the involved regions, which may partially be explained by quite different analysis methods employed, differences in the statistical power and thresholds used and differences in the patients' clinical state and medication. Interestingly, these studies, however, converge well on the affected frequency bands and in the direction of the changes of differences in frequency bands. Delta, theta and beta lagged connectivity seems to be increased in patients, whereas alpha lagged connectivity tended to decrease. This pattern is reminiscent of the pattern of abnormalities that results when comparing spectral power between SCZ and HC, where delta, theta and beta power consistently tended to be increased and alpha power was (not as consistently) found to be decreased [20].

27.2.2 Non-lagged Measures of EEG Resting State Connectivity in Schizophrenia

Within the non-lagged measures of EEG connectivity that take volume conduction into account, there are a few studies that used a very global approach to compare SCZ and controls. These studies merely quantified how well the entire multichannel data recorded during an EEG epoch can be accounted for by the activity of

network activity defined by simultaneous, non-lagged oscillations of neuronal activity. One of these measures, the so-called omega-complexity, estimates the number of independent processes [21] that account for the measured EEG, whereas each of these processes can be considered to result from the activity of a network consisting of simultaneously oscillating regions. Another such measure is global field synchronization (GFS) that estimates, in the frequency domain, how much of the total variance of the signal can be explained by the activity of a single network of this type [22].

Papers using such global measures found differences between SCZ and HC that correspond to the results of the studies on lagged connectivity in an interesting way. Studies based on omega-complexity, which is a broad-band measure, found increased complexity in SCZ as compared to HC [23–26], which was taken as evidence for a "loosened cooperativity… of the active brain processes" [26]. This disconnection could mostly be accounted for by activity recorded at frontal electrodes. On the other side, the two existing studies on GFS in schizophrenia found that non-lagged type of connectivity explained less variance of theta band activity in patients, yielding lower GFS values [22, 24].

Despite all the differences in patient characteristics and methodological choices, the overall pattern that seems to emerge is that there is a shift from a non-lagged type of connectivity in HC, which is accounted for by low omega-complexity and high GFS values, towards interactions with a time delay in SCZ, which increases measures of lagged connectivity. Within this overall pattern, it seems that processes appearing in the theta band were most consistently affected by this shift.

The hypothesis that there may be an increased variance in the timing of neuronal connectivity in SCZ is interesting from several perspectives. Firstly, non-lagged type of neuronal co-activation is a candidate mechanism to account for the fact that multifaceted representations of environmental and mental information can apparently be perceived as something unitary, like seeing eyes and a nose and a mouth results in the unitary percept of a face. This "binding phenomenon" may be explained by time-locked activity of all local mechanisms that encode partial aspects of the mental representation, and the unity of the experience is encoded by the simultaneity of activation across the local processes [27]. If this apparent loosening of synchronicity indeed entails less unity on the level of the mental phenomenology, the hypothesis may help to account for the nature of some of the prominent positive symptoms, such as thought disorders, experiences of derealization and ego disturbances. Secondly, ERP responses to a broad range of stimuli are typically blunted in SCZ, which may be a result of increased variance in the timing of the activation of task-relevant processing resources, leading, as others have also suggested, to an increased cancellation of ERP signals by averaging. Finally, the fact that such a hypothesis makes statements about the organization of activity among network elements rather than the functioning of particular elements is supported by the limited success of trying to tie the diagnosis of schizophrenia to a localized structural or functional brain abnormality.

Despite this explanatory potential, the proposal that there may be an increased variance in the timing of neuronal co-activation in SCZ remains very global and is

uninformative about the kind of networks that may be primarily affected. In order to come to more specific conclusions, it is necessary and feasible to parse the measurements of brain activity into subcomponents that are defined by sufficiently similar dynamics of the involved processes. While several solutions to this problem exist, a coherent body of evidence on resting state EEG in schizophrenia has so far relied on the identification of so-called microstates [28]. EEG microstates represent subsecond time periods that can largely be accounted for by the activity of synchronous but potentially distributed activity in the brain. EEG microstates were found to cluster into a small set of highly replicable spatial configurations that have well-defined temporal parameters, such as their mean duration, their occurrence and the total time covered by each type of configuration.

The first report that a specific type of microstates was altered in schizophrenia was related to a microstate class labelled "D" that was later related to fronto-parietal executive control network functions [29]. This type of microstates was found to be shortened in medication-naïve acute SCZ as compared to HC [9]. This shortening was also correlated with the presence of paranoid-hallucinatory symptoms. The authors suggested that microstates of class D may have a protective role against psychotic experiences that is impaired when these states are shortened. A later study that compared EEG microstates in frequently hallucinating patients in time periods with vs without hallucinations could confirm the link of the shorting of this class D with the presence of hallucinations [30]. Microstate class D was also found to increase in patients that responded well to antipsychotic treatment, whereas no shortening of microstate class D before treatment and no increase of microstate class D duration were found in patients with a poor drug response [31].

Several studies found an increased count and an increased overall time spent in another type of microstates, the so-called class C, as recently summarized by a meta-analysis on microstate studies in schizophrenia [32]. This microstate class C appears to be related to salience processing [29]. Interestingly, the increase of microstate class C has also been found in adolescents with the 22q11 deletion syndrome, who have a 30 times higher risk to develop psychosis. The authors of this study suggested that this deviant microstate pattern may be related to aberrant salience mapping or to processes that are activated to compensate such deficits [33], which correspond well with the fact that antipsychotic medication typically interferes with neurotransmitter systems strongly involved in salience processing.

The pattern of alterations in EEG resting state microstates in SCZ reported so far and the patterns of EEG resting state microstate changes observed in studies investigating HC under different conditions allow us to draw a series of tentative explanations of these alterations. Firstly, in a large developmental study including subjects between 6 and 80 years of age, late adolescence was the time when microstate class C was found to be most frequent, and microstate class D least frequent [34]. This coincides with the typical age of onset of schizophrenia and supports the view that schizophrenia may be related to late neurodevelopmental problems. The other interesting aspect in the overall picture is that there seems to be a balance between microstates of classes C and D that is not only shifted in the favour of C during schizophrenia but also relates to particular state changes in HC in certain conditions. An overview of these observations can be found in the meta-analysis by

Rieger et al. [32]. In summary, the authors showed that this balance between microstates of classes C and D was consistently shifted towards C in HC when these subjects entered states that are characterized by reduced reality testing and monitoring of the self within its physical environment. The states found to be related to such shifts from D to C were, namely, hypnosis and sleep. These are states where attention-related updating of mental content from external-reality-close information, as assumingly observable through the presence of microstates of class D, is reduced, whereas the experiences reported by subjects often are characterized to be particularly salient, which are assumingly observable by the presence of microstate class C.

27.2.3 Future Directions

The present state of knowledge indicates that there are consistent abnormalities in EEG connectivity measures related to schizophrenia and that these findings can to some degree be interpreted within a common framework. The picture we have so far requires however further clarification in two aspects. Firstly, there is a broad variety of methodological approaches to EEG that use terms like "connectivity" but refer to mathematically very different and even incompatible concepts. This needs, on the long run, an overarching theoretical and empirical framework that permits us to differentiate patient groups not only in terms of more or less connectivity of a particular type but also in terms of changes of the type of connectivity that is observed and to draw conclusions about what type of connectivity is beneficial or detrimental for a healthy functioning. The second shortcoming of the current state of knowledge about EEG connectivity differences related to abnormalities in schizophrenia is that across the studies presented so far, there is a considerable heterogeneity of symptoms among the patients, which is yet to be insufficiently taken into account but must be expected to systematically relate to specific networks [35]. The current body of evidence gives hope that with EEG models of brain connectivity that can simultaneously account for non-lagged and lagged connectivity, combined with patient assessment approaches that are oriented towards biologically meaningful diagnostic entities, we may substantially increase our understanding of this disorder in the future.

27.3 Electrophysiological Markers of Transition to Psychosis

Yuko Higuchi and Tomiki Sumiyoshi

27.3.1 Introduction

Schizophrenia usually develops around the adolescence period, with the whole life risk of about 0.85%. It disturbs patients not only by positive symptoms (hallucinations, delusions, etc.) but also causing deterioration of daily/social functions and

seriously affecting patients' life. Early intervention into psychosis is a comprehensive and evidence-based approach aiming at detection and treatment of psychotic symptoms in their early stages, reducing the long-term adverse impact of psychosis and preventing relapses [36]. Shorter duration of untreated psychosis (DUP) has been associated with a greater response to antipsychotic drugs in terms of symptoms and quality of life. Contrary, prolonged DUP is associated with decreased levels of social functions, for example, work function and communication skills, as well as longer hospitalization [37, 38]. In this context, efforts have been directed to detect and immediately treat patients who are in early stage of psychosis. Recently, the importance of intervention to "prodromal stage" of schizophrenia has been also recognized. Operationalized criteria to detect putative prodromal symptoms of psychosis have been largely tested and used worldwide. These criteria are known as ultrahigh risk (UHR), clinical high risk (CHR) and at-risk mental states (ARMS) and allow the identification of subjects with about 30% risk of developing psychosis over a 2-year period [39], mostly schizophrenia-spectrum disorders. For early diagnosis, objective biomarkers, particularly those based on brain morphology, neurophysiology and neuropsychology, have been proposed to provide information [40–42]. However, reliable measurement tools are not confirmed. Therefore, much effort is going on to detect biological markers for diagnosing psychotic disease. In this section, we describe neurophysiological findings, particularly event-related potentials.

27.3.2 Event-Related Potentials (ERPs)

ERP is one of the methods to assess the brain function using EEG. It occurs in response to an internal or external event. We can get quantitatively information about some aspects of cognitive disturbance, by measuring parameters such as amplitude or the latency of ERPs. The ERPs are recorded using an electroencephalograph and a stimulator (e.g. auditory or visual). It is a simple and noninvasive procedure, and efforts on patients are minimum. Recently, some ERPs are thought to be useful as trait markers of schizophrenia. Especially, P300 and mismatch negativity (MMN) have been widely used for this purpose.

P300 recordings are performed usually as follows: EEG is recorded in electrical and sound shield room, and low-probability (around 10–20%) target stimuli are presented intermixed with frequent standard stimuli. Target stimuli differ from standard ones in physical characteristics (tones of different frequencies, e.g. 1000 vs 2000 Hz, or durations, e.g. 50 vs 100 ms, different pictures and so on). For P300, subjects are requested to pay attention to the target stimuli carefully and perform a task, (e.g. to press a button promptly in response to infrequent target stimuli), while for MMN subjects have to ignore the stimuli. Thus, while P300 indexes task-related attentional and categorization processes, MMN is a sensory memory-based brain response to any discriminable change occurring in a stream of stimuli, in the absence of attention [43], indexing pre-attentive change detection. In patients with psychosis, both ERP components are altered. Furthermore, using the MMN recording

paradigm, a further component can be elicited: the P3a, a component indexing the automatic allocation of attention to changes in the environment.

Light et al. [44] in their large consortium study (about 1000 SCZ) obtained reliable MMN/P3a measurements by using a simple two-channel recording system, in relatively modest recording conditions (e.g. usually lacking sound proofing and/or electrical shielding of recording rooms with often little local expertise in electrophysiology). They concluded that MMN/P3a recording can be added as biomarkers to multisite clinical studies without specialized EEG research centres. For this reason, widely clinical application is expected in the future.

27.3.3 P300 in Psychotic Disorders

SCZ show smaller amplitudes of P300 than HC. Meta-analysis showed that the effect size for the P300 amplitude reduction in schizophrenia was 0.85 and for the P300 latency augmentation was −0.57 [45]. Further, Ozgurdal et al. [46] indicated that reduction of P300 amplitudes has been also noted in subjects with ARMS. Frommann et al. [47] also report that smaller P300 amplitudes are present prior to a putative onset of psychosis in high-risk individuals, and the abnormalities of late initial prodromal state (LIPS) were more severe than early initial prodromal state (EIPS) for psychosis. Thus, some evidences indicate that P300 is useful as biomarker of psychotic disorders.

However, several confounds should be taken into account when using P300 as a biomarker. It requires vigilance and motivation might influence the results. For example, if a patient is in an acute catatonic stupor state, or has severe symptoms, which prevent collaboration, P300 cannot be recorded. Furthermore, some studies have reported that P300 amplitude is affected by various factors, including medication, e.g. olanzapine, clozapine and perospirone [48–50]. Bramon et al. [45] also described in their meta-analysis (1) the P300 amplitude was significantly more abnormal in drug-free than in medicated patients and (2) on the contrary, the presence/absence of antipsychotic treatment did not have a significant effect on the P300 latency. Other studies and a meta-analysis did not report any effect of medication status on P300 amplitude [51].

27.3.4 P300 in Subjects at Risk for Psychosis

There are few studies about P300 for electrophysiological marker of transition to psychosis. van Tricht et al. [52] found that P300 amplitudes at Pz were significantly smaller in UHR-T (who later made the transition to overt psychosis) patients compared to UHR-NT (who did not make the transition) subjects. On the other hand, Bramon et al. [53] described that compared to the cases remaining at risk, the individuals making a transition to psychosis did not significantly differ in their P300 or N100 amplitudes and latencies. We also measured P300 in HC, ARMS subjects and SCZ. The mean amplitudes were smaller in schizophrenia group compared to other

groups. There were no significant differences in latency. Both P300 parameters were not statistically different between ARMS converter and non-converter.

27.3.5 MMN in Schizophrenia Patients

As for P300, abnormalities of MMN in SCZ were repeatedly reported. There are about 200 articles in peer-reviewed international journals reporting a MMN amplitude reduction in SCZ, and the effect size is over 0.95 [54]. Several other psychiatric disorders (i.e. bipolar disorder with psychotic features, major depressive disorder, borderline personality disorder, Alzheimer's disease) show none or smaller reductions in MMN than schizophrenia [55–57] even when cognitive impairment or psychotic symptoms were more severe than in the schizophrenia group [55]. Recent meta-analysis, including affective disorders, indicates high specificity of schizophrenia [54].

Unlike P300, MMN has several advantages: (1) no or minimal collaboration is required from subjects, so the influence of their motivation and ability is small, (2) drowsiness (even at stage REM) does not impede the recording of MMN, and (3) the influence of psychotropic drugs commonly used for schizophrenia is little (e.g. dopamine antagonists, benzodiazepines) [58, 59].

There are several types of MMNs, such as duration MMN (dMMN) and frequency MMN (fMMN), based on the mode of presentation of target stimuli. The impairment of dMMN for schizophrenia is greater than that of fMMN [60], with the latter emerging only in the chronic, but not early stage of schizophrenia [61]. Thus, dMMN can be a more sensitive marker than fMMN, in the context of early psychosis. Haigh et al. [61] demonstrated in their meta-analysis that in subjects at disease onset, no reduction of fMMN was found compared to HC (Cohen's $d < 0.04$), whereas small-to-medium reduction of dMMN was found (Cohen's $d = 0.47$) [61]. Generally, dMMN appears to mainly index the trait aspect of schizophrenia, whereas fMMN may be more closely related to the state aspect of the pathological process [62]. Several studies also showed that the dMMN amplitude of chronic schizophrenia was lower than in first-episode schizophrenia [63, 64]. Thus, dMMN amplitude also is gradually reduced by the progress of clinical stage.

27.3.6 MMN in Clinical High-Risk Subjects

Recently, several studies reported dMMN amplitude reduction already in the prodromal stage of schizophrenia. We measured dMMN/P3a/reorienting negativity complex in ARMS subjects, first-episode schizophrenia (FES) and 19 HC participants [63]. During the follow-up period (2.2 years), 4 out of the 19 ARMS subjects transitioned to schizophrenia (converters), while 15 did not (non-converters). Figure 27.2 indicates that dMMN amplitudes of converters were significantly smaller than those of non-converters before onset of the illness. dMMN amplitudes of non-converters did not differ from those of HC, while converters showed significantly smaller dMMN amplitudes compared to HC. Our data confirm that

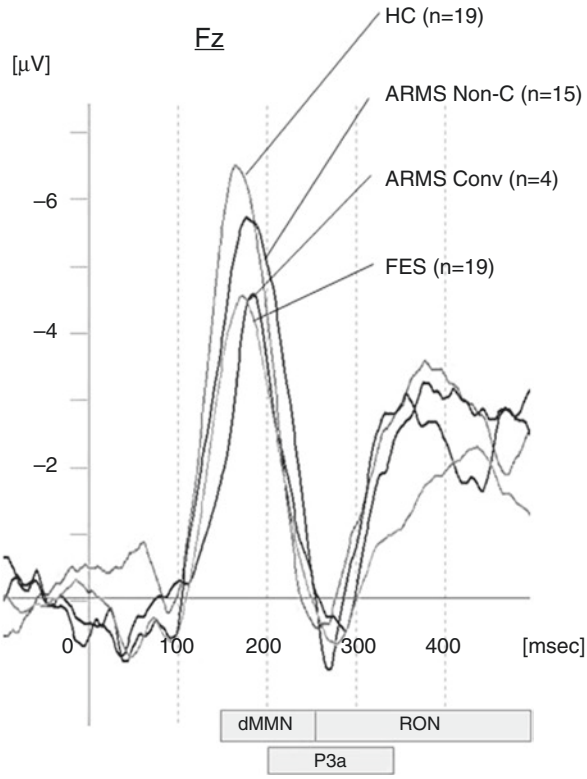

Fig. 27.2 Duration mismatch negativity (dMMN)/P3a/reorienting negativity (RON) complex waveforms at the Fz lead. Waveforms are represented for healthy controls (HC), ARMS converters (Conv) and non-converters (Non-C) and first-episode schizophrenia (FES). MMN, P3a and RON peaks were identified within the 150–250 ms, 200–350 ms and 250–500 ms search windows, respectively

diminished dMMN amplitudes provide a biomarker, which is present before and after the development of psychosis. There are some meta-analysis and review articles, which discussed this issue. Nagai et al. [65] reviewed MMN in schizophrenia and ARMS patients, considering both dMMN and fMMN. They concluded that dMMN amplitude reduces before the onset of psychosis and may be a significant predictor of the conversion to psychosis. Erickson et al. [54] showed, in their meta-analysis, that the CHR participants exhibited a modest effect size of 0.40 for differences with respect to HC. They also calculate a separate effect size for converters and non-converters that was 0.79 and 0.17, respectively, with converter showing significantly higher effect size.

As described above, several evidences about low dMMN amplitude of high-risk subjects accumulated. However, the question of whether we use dMMN as a biomarker of schizophrenia is still open. For example, Naatanen et al. [62] report that the transition may indicate a quantitative change on an illness dimension rather than categorical change from "healthy" to "ill", so a single time point recording of MMN to predict transition is unlikely to be an optimal approach. Moreover, MMN has some "interindividual" difference but is surprisingly stable "intra-individual", in longitudinal dMMN measurements. It was reported that MMN amplitude shows a reduction with aging [66]. If a subject does not have any trait of schizophrenia, MMN decline is not found across repeated measurements, except for the age-appropriate

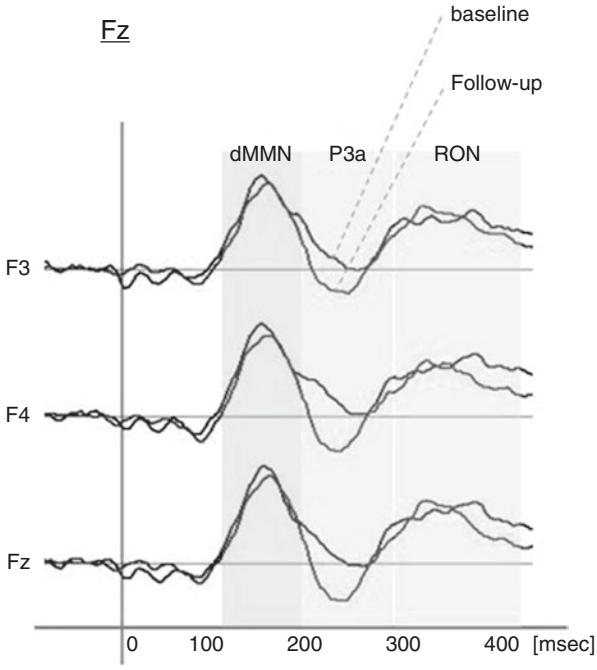

Fig. 27.3 Duration mismatch negativity (dMMN)/P3a complex grand-average waveforms (n = 15) at the Fz lead. Waveforms are represented for ARMS non-converter at baseline and follow-up [2.4 (±1.6) years later]

decline. The key information is coming from the potential change of MMN versus the individual baseline, thus giving an index of a trajectory of individual illness progression [62]. We measured dMMN longitudinally in ARMS subjects (preliminary data, Fig. 27.3). All subjects received interventions, including CBT and/or antipsychotic drugs. All subjects did not convert to overt psychosis including schizophrenia during the observation period (2.4 ± 1.6 years). dMMN reduced little and didn't reach significance. On the other hand, P3a amplitudes were increased at frontal leads.

In summary, ARMS subjects without reductions of dMMN amplitudes are unlikely to develop psychosis, indicating usefulness as a trait marker. On the other hand, P3a amplitudes are subject to change according to clinical status. Further investigation is needed to examine the role for MMN/P3a/RON complex in the prediction of transition to psychosis.

27.3.7 Conclusions

P300 amplitude is reduced and its latency is prolonged in schizophrenia. P300 amplitude might be affected by medication and patients' condition, so caution is needed when using P300 as biomarker of schizophrenia risk. On the other hand, MMN is considered to be relatively free from these confounding factors. Reduction of MMN amplitude in schizophrenia is robust, and evidence for diminished dMMN amplitude

in ARMS has accumulated. Thus, reduction in dMMN amplitudes before the onset of psychosis may provide a more robust marker of the conversion to psychosis.

27.4 Electrophysiological Alterations and Psychopathological Dimensions in Schizophrenia

Annarita Vignapiano, Giulia Maria Giordano, Antonella Amodio, and Armida Mucci

27.4.1 Introduction

Reflecting the progress in the conceptualization of schizophrenia as heterogeneous syndrome, DSM-V places emphasis on its psychopathological dimensions. Many factor-analytic studies of psychopathological ratings allowed to identify negative, positive, disorganization dimensions that do not appear to be affected by age, severity of symptoms and chronicity of the illness.

Numerous studies revealed abnormalities of ERPs in subjects with schizophrenia that might be related to different symptom dimensions and presumably contribute to the psychopathology of the disease [67, 68].

ERPs are indices of the physiological underpinning of different functions such as early perception and attention (P50, N100, P200), automatic allocation of attention (P3a), task-related effortful processes (P3b; Fig. 27.4), automatic or preconscious processes (MMN), semantic memory (N400) and anticipation [contingent negative variation (CNV), stimulus-preceding negativity (SPN)] or evaluation [feedback-related negativity (FRN)] of reward.

Several studies have used ERPs to investigate the neurobiological basis of symptom dimensions in schizophrenia, particularly the positive, negative and disorganized dimensions, but the findings are inconsistent.

In the next sections of this paragraph, we will overview the electrophysiological correlates of the different symptom dimensions and review the pathophysiological hypotheses related to these correlates.

27.4.2 Electrophysiological Alterations and Positive Dimension

Delusions and hallucinations are considered hallmark symptoms of schizophrenia. These symptoms can become chronic, causing an impaired quality of life. Current treatments, including antipsychotics, exhibit variable effectiveness against them.

P50, N100, P300, MMN and N400 are ERP components more frequently investigated in association with positive symptoms.

According to the hypothesis that positive symptoms in schizophrenia might be underpinned by information overload due to sensory gating deficits, several ERP components related to gating and early attentive processes, such as P50 and N100, were investigated.

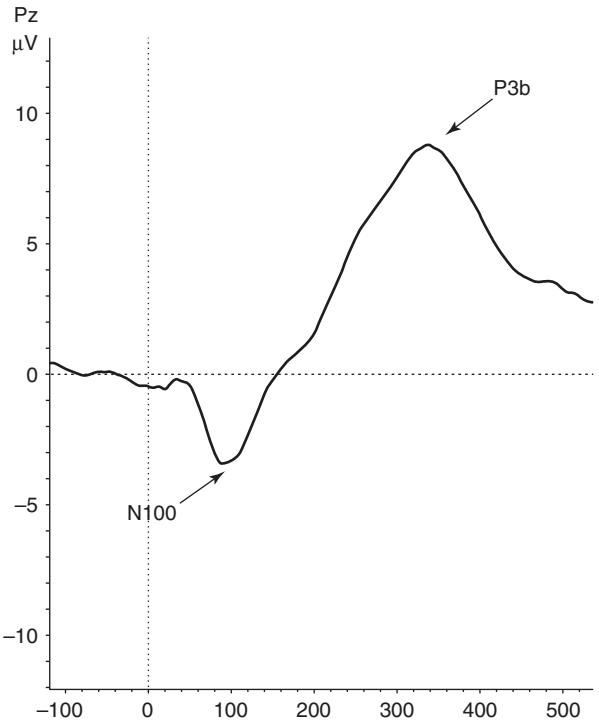

Fig. 27.4 Example of N100-P3b like waveform time-locked to the target stimulus at the Pz lead in healthy controls

P50 appears approximately 50 ms after the presentation of auditory stimuli; its amplitude reduction with stimuli repetition is thought to index sensory gating, known to be impaired in SCZ [68].

An association of P50 abnormalities with auditory hallucinations and delusional thoughts was reported in some but not all studies [69, 70].

N100 is a negative component that appears about 100 ms following an auditory stimulus (Fig. 27.4), generated from primary and secondary auditory cortical areas. Some studies revealed that N100 amplitude reduction in SCZ was related to the severity and experience of hallucinations [71, 72], suggesting a top-down stimulation of auditory cortex, which reduced the reactivity to external stimuli. N100 abnormalities might be related to abnormalities of the so-called corollary discharge, a neural signal involved in the recognition of self-generated signals [73, 74].

Pre-attentive sensory processing, as indexed by MMN abnormalities, is also impaired in SCZ (see the third paragraph of this chapter for information on the MMN). The reduction of MMN amplitude was related to the presence and severity of positive symptoms [75], particularly to auditory hallucinations [76]. These data suggest that impairment of early integration of information might subtend positive symptomatology.

P300 subcomponents abnormalities were consistently reported in schizophrenia [51] (see the third paragraph of this chapter for information on P300) and were

differently related to positive symptoms [77]. P3a amplitude was associated with the predisposition to auditory hallucination and their severity, while P3b was related to the presence and severity of hallucinations and delusions [74]. However, several studies failed to find any association between P3b amplitude and positive symptoms [68].

In addition to difficulties in early processes, SCZ showed an impairment of information integration and semantic memory as revealed by abnormalities of N400, a negativity peaking at approximately 400 ms, after presentation of any potentially meaningful stimulus [78]. According to some authors, this impairment might explain the persistence of the delusions despite the awareness of contradictory information [79].

In conclusion, the current literature suggests that positive symptoms might be related to an aberrant intrinsic organization of functional brain networks, leading to alterations of sensory gating, an incorrect perception of the environment due to reduced integration of information [80] and a failure in corollary discharge [74].

27.4.3 Electrophysiological Alterations and Negative Dimension

Negative symptoms have long been recognized as a core dimension of schizophrenia, have a strong impact on quality of life and social functioning and do not respond to pharmacological treatment. They can be grouped into two domains: a motivation-related domain, referred to as avolition, including apathy, anhedonia and asociality, and an expression-related domain, referred to as diminished expression, including alogia and blunted affect [81]. Negative symptoms represent a heterogeneous clinical construct, including primary symptoms and secondary symptoms caused by other factors, such as positive symptoms, depression, social deprivation, substance abuse and antipsychotic medications [82, 83]. Primary and enduring negative symptoms, with distinct neurobiological and clinical correlates, characterize a schizophrenia subtype named deficit schizophrenia (DS) [83].

The findings concerning the associations of ERP abnormalities with negative symptoms have been controversial, in particular for P50-N100 sensory gating abnormalities and P300 or MMN amplitude reduction [67, 84].

Recent research was devoted to the study of negative symptom domains. Avolition is related to a deficit of motivation, and several aspects of this complex construct were found impaired in SCZ, with the exception of the hedonic experience [85]. In particular, SCZ seem to have difficulties in the anticipation and evaluation of reward [86] that were partially reflected by abnormalities in CNV, SPN and FRN [87, 88]. The CNV is a slow negative wave, related to preparatory attention, motivation and anticipation of salient stimuli. Two independent studies did not find any relationship between early and late components of CNV and anhedonia or negative symptoms [88, 89]. Moreover, in the latter study, during a monetary incentive delay task, the authors found an association of early P300 abnormalities with social anhedonia but not with the negative symptom domains. These findings suggested that negative symptoms might have multiple pathophysiological mechanisms and that motivation and anhedonia might be partially independent constructs.

SPN is a negative ERP component involved in anticipation of feedback, and it has been found to be correlated with trait anhedonia [88].

FRN is related to the brain activity in the anterior cingulate cortex; it is sensitive to the expectedness of the feedback as well as to feedback valence [87]. Horan et al. [90] reported that FRN amplitude difference between positive and negative feedback correlated with positive symptoms, a result probably due to the use of the Brief Psychiatric Rating Scale (BPRS) that does not evaluate the motivation-related domain of negative symptoms.

Few studies investigated ERPs in patients with deficit schizophrenia [91–93]. An amplitude reduction of P300 was found over the left temporal region in patients with NDS and in both this region and the right parietal region in patients with DS [93]. Mucci et al. [92] revealed a double dissociation of ERP abnormalities: patients with NDS showed a left-side reduction of the P300 component, while patients with DS showed a reduced amplitude of the N100 over the scalp central leads. In the study conducted by Li et al. [91], the authors found that NDS showed delayed latency of P3b and DS showed delayed point A in CNV that correlated with global functioning but not with individual negative symptoms. Furthermore, both DS and NDS showed similar abnormalities in N100, MMN, P3a, CNV amplitude and P50 gating. In conclusion, it is difficult to identify electrophysiological abnormalities associated with negative symptoms, probably due to their heterogeneity or to the tendency of different authors to examine one specific ERP component, rather than several components.

27.4.4 Electrophysiological Alterations and Disorganization Dimension

Disorganization has been recognized as a longitudinally stable symptom domain that is present since the earliest manifestation of the illness [94]. A variety of studies have reported different definitions, including heterogeneous symptoms, such as inappropriate affect, poverty of content of speech, positive and negative aspects of thought disorder, attentional deficits and sometimes bizarre behaviour [95].

Few neurophysiological studies have analysed ERP components, such as P50, N100, P200, P300 and N400, related to disorganization dimension, reporting inconsistent findings.

P50 sensory gating abnormalities have been associated with vigilance and sustained attention [96]. In SCZ and in schizotypal individuals, a significant relationship between disorganization and P50 suppression deficits was observed [97], suggesting that disorganization might be underpinned by difficulties in inhibiting information at early pre-attentive stage.

As regard to other ERP components, Williams et al. [98] found an association of disorganization with increased latency of N100, P200, P300 and decreased P200 amplitude, that might suggest a widespread disturbance in the control of information processing.

Moreover, an association of disorganization with a reduction of posterior P300 amplitude was found in young recent-onset SCZ [99]. Since the posterior P300

indicates the subsequent updating of memory of the current situation, these observations suggested that disorganization was related to an impairment in memory function, which occurred in the early stage of the disease [100].

Some studies focused on specific aspects of disorganization, such as disorganized speech, which was found related to an impairment in how concepts are elaborated in semantic memory, as indexed by abnormalities in N400 [78]. Some N400 studies observed that SCZ had deficits in the use of semantic context and hyperactivity of the semantic network, the last more prominent in presence of a formal thought disorder that might be described as a more general "conceptual disorganization" [78, 101]. These findings were not corroborated by other studies [102, 103].

Current literature is unable to clarify ERP abnormalities associated with disorganization probably due to the extremely heterogeneous aspects included in this dimension and the failure of instruments to detect its core aspects.

Conclusions

In this paragraph, we provided an overview of electrophysiological correlates of schizophrenia dimensions. The findings suggest that SCZ have ERP deficits from the early phase of sensory processing (i.e. P50, N100, N400) to the relatively late phase (i.e. P300, N400) and in the anticipation and evaluation of salient stimuli (CNV, SPN, FRN). These abnormalities have been found to correlate with different psychopathological symptom domains; however, no conclusion can be drawn as findings were inconsistent and conflicting [67, 68, 77]. Discrepancy in literature findings was partly due to heterogeneity in the definition and assessment of psychopathological dimensions, which represents a major obstacle to progress in schizophrenia research. Another possible reason for inconsistencies might be related to poor control of confounding variables, such as cognitive dysfunctions, often observed in SCZ and rarely assessed by the reviewed studies, which might contribute to different ERP abnormalities. Finally, the most recent pathophysiological models of schizophrenia indicate a diffuse disconnectivity and lack of coordination among neural networks, which might lead to different cognitive and behavioural manifestations and multiple ERP abnormalities. According to these models, schizophrenia involves substantial inter- and intra-individual variability. Future studies should better characterize symptom dimensions, systematically assess cognitive dysfunctions and study multiple components of the ERPs, as well as resting state dysfunctions and the relationships among them.

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Psychoneuroendocrinology of Resilience: An Overview

28

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Abstract

Resilience is defined as the ability to bounce back from trauma and stressful situations. Resilience has many psychosocial and biological variables that play a role in its genesis and development. The present chapter looks at the psychoneuroendocrinological basis of resilience and looks at various hormones that play a role in the genesis, development and maintenance of resilience.

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28.1 Introduction

Resilience is the capacity people have to adapt swiftly and successfully to stressful/traumatic events while not reverting back to the original state [1]. Various studies have illustrated the importance of resilience on the individuals' capacity to form a healthy response while enduring trauma, and this has been noted across all ages [2]. Resilience is a construct which is likely to be involved in the diathesis for psychiatric disorders [3] and has biological, social and psychological determinants [4]. The present chapter provides the reader a brief overview of the psychoneuroendocrinological processes that contribute to resilience.

28.2 The Relationship Between Allostasis and Resilience

The term 'allostasis' describes the dynamic regulation of nonessential set points in response to stress in order to preserve critical variables and in the defence of homeostasis [5]. Homeostasis has been defined in physiology as the maintenance of states that are essential to the survival of the organism [6]. Allostatic load is a term coined by researchers to define the physiological cost of adaptation to stress. The severity of allostatic load affects the brain's ability to resume its pre-allostatic state and is inversely proportional to the degree of resilience; resilience is the capacity to minimize allostatic load [7]. Thus allostasis, homeostasis and allostatic load are physiological variables that determine one's relative capacity to be resilient and 'bounce back' in the face of trauma. Various psychoneuroendocrinological factors have been incriminated in allostasis and homeostasis, and they in turn affect the ability of a person to be resilient (Fig. 28.1).

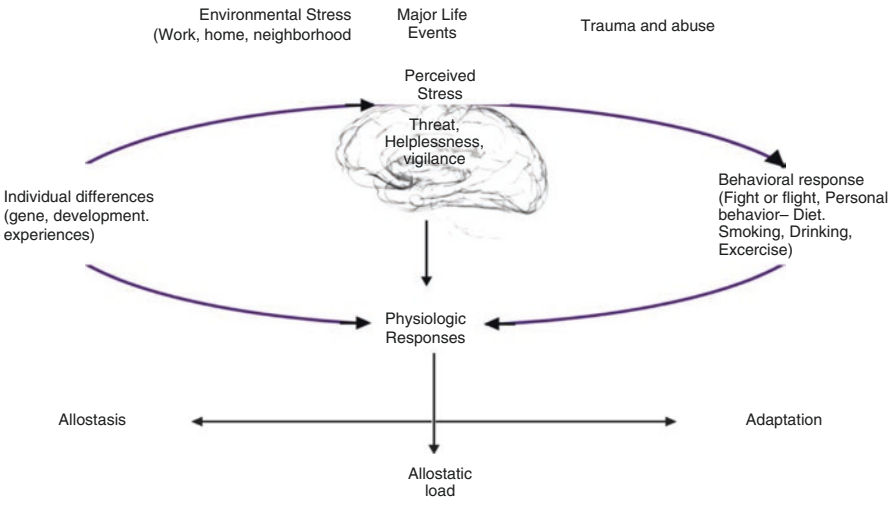

Fig. 28.1 The relationship between resilience, allostasis and allostatic load

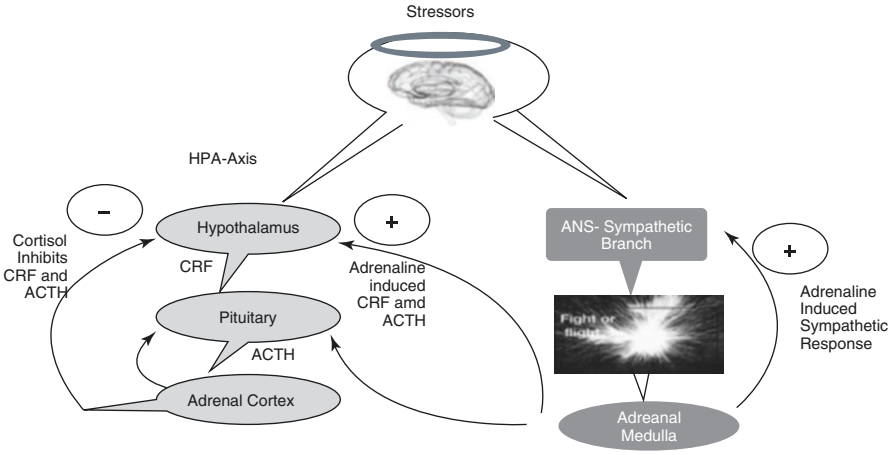

Fig. 28.2 The role of cortisol in the HPA axis response to stress

28.3 Psychoneuroendocrinological Factors in Resilience

28.3.1 Cortisol

The hypothalamic-pituitary-adrenal (HPA) axis is the main physiological system of the body that is implicated in the management of the organism's response to stress. Whenever stress is perceived, the neurons in the paraventricular nucleus of the hypothalamus secrete corticotrophin-releasing hormone (CRH) that acts upon the anterior pituitary to release adrenocorticotrophic hormone (ACTH) which in turn releases cortisol from the adrenal cortex—the main stress management hormone (Fig. 28.2) [8]. These hormones exert effects on various systems of the body that in turn lead to the classic physiological stress response [9]. Cortisol has also been implicated along with its derivatives in maintaining attention, vigilance, arousal and memory formation. Cortisol hypersecretion may play a role in hippocampal neurotoxicity and excitotoxicity in response to stress [10]. Cortisol also modulates NMDA receptors and therefore is implicated in learning and memory and in the registration of emotional memory in relation to trauma [11].

Individuals with both single trauma exposure as well as those with multiple trauma exposure such as child abuse and neglect display abnormal patterns of cortisol secretion both at baseline and in response to stress [12]. Moreover 40–50% of adults exposed to repeated trauma also display an abnormal cortisol response in the dexamethasone suppression test [13]. Chronic hypersecretion of cortisol also sensitizes to increased vulnerability to various physical illnesses including diabetes and hypertension as well as cardiovascular disorders that may ensue in patients with repeated trauma [14]. The ratio of cortisol to dehydroepiandrosterone (DHEA) has been used as predictive biomarker to stress [15]. This ratio has been positively correlated with survival and resilience in response to trauma. In contrast, the ratio has been linked negatively across both genders in patients with depression, anxiety disorders and posttraumatic stress disorder (PTSD). Further research is underway to

investigate the role of this ratio and the viability of treatments to address the underlying biology in trauma and related disorders [16, 17].

28.3.2 Corticotrophin-Releasing Hormone (CRH)

In addition to its role in the release of cortisol and ACTH, CRH has been implicated in the modulation of the central nervous system (CNS) stress response in relation to trauma [18]. CRH receptors are heterogeneously distributed in the brain and with high density in regions like the hippocampus, amygdala, prefrontal and cingulate cortex along with the insular cortex and the anterior pituitary glands [19]. There are two main types of CRH receptors in the brain, viz. CRHR-1 and CRHR-2 which are G-protein-coupled receptors. CRHR-1 has been found to be associated with the release of norepinephrine from the locus coeruleus, the thalamus and the striatum [20]. CRHR-1 antagonists have been used in clinical trials for the management of anxiety disorders and stress-related conditions, but the results have been disappointing [21]. Increased CRH concentrations in cerebrospinal fluid (CSF) have been reported in patients with depression, panic disorder and PTSD [22]. Stress in early life has been reported to result in abnormally high CSF concentrations of CRH. Environmental and genetic factors contribute to the CRH response to trauma at an early age [23]. Whether CRH receptor antagonists may yet have a role in the treatment of mood and anxiety disorders is unclear [24].

28.3.3 Neuropeptide Y

Neuropeptide Y (NPY) is one of the most abundant neuropeptides in the CNS and has been implicated in a variety of physiological functions like appetitive behaviour, sexuality, circadian regulation, stress responses and cardiovascular function [25]. There are multiple types of NPY receptors in the brain ranging from NPY-1 to NPY-4 [26]. NPY is known to act in opposition to CRH on certain passages; it counteracts the anxiety-producing effects of CRH via various receptors in the hippocampus, thalamus, amygdala and hypothalamus [27]. It also helps in reduction of the physical symptoms that may develop in response to stress and trauma. NPY levels have been linked to the development of resilience, though discordant findings have appeared [28]. Increased NPY levels have been linked to reduction in anxiety and stress as well as the development of resilience in relation to trauma. Higher NPY levels have been noted in resilient individuals such as military and police personnel and in patients with PTSD [29]. Decreased levels of NPY have been reported in depression related to trauma and in maladaptive anxiety responses to stress [30].

28.3.4 Galanin

Galanin is one of the recently implicated neuropeptides in allostasis and resilience. Galanin containing neurons and receptors is abundant in the amygdala and has been implicated in the anxiety response [31]. Galanin has two main receptor subtypes,

GAL-1 and GAL-2, which are both anxiolytic when activated. Galanin agonists are being posited as anxiolytics as they blunt the stress response [32]. The recent discovery of GAL-3 receptors has led to the development of GAL-3 antagonists in the management of anxiety disorders [33].

28.3.5 Testosterone

Testosterone is the male sexual hormone produced by the Leydig cells of the testes and essential for the sexuality function in the male, aggressive behaviour, development of secondary sexual characteristics and bone density [34]. High testosterone levels have been linked to aggressive behaviour [35], success in sports [35], social status and social stature [36] and psychopathic behaviour [37]. Stress has been reported to result in low testosterone levels, and testosterone has been implicated as a treatment for mood and anxiety disorders [38]. Men and women with lower basal levels of testosterone have been linked to vulnerability for depression as well reduced resilience in the wake of stress and trauma [39]. Testosterone has been reported to reduce the cortisol response to stress [40].

28.3.6 Oestrogen

Oestrogen is a steroid hormone that is produced by the enzymatic conversion of androgens. It acts via well-characterized peripheral and CNS receptors. Oestrogen is the major gonadal steroid in women. It regulates the menstrual cycle and the development of secondary sexual characteristics [41]. Oestrogens play a role in modulating the stress response system. Oestrogen reduces the stress-induced excitability of neurons in various parts of the brain and inhibits the cortisol response to stress [42]. Pregnancy is a state in which oestrogen levels are high and cortisol responses are decreased. Premenstrual and postpartum periods and perimenopausal states are associated with reduced oestrogen levels and are states in which depression and anxiety prevalence rates are high and resilience to trauma may be reduced [43]. Oestrogen has also been implicated in increasing the release of NPY and galanin as well as their gene expression in the CNS [44, 45]. Oestrogen-related drugs are being investigated in the treatment of psychiatric disorders including Alzheimer's disease and schizophrenia [46, 47].

28.3.7 Allopregnanolone

Allopregnanolone (ALLP) is a cholesterol-derived neuroactive steroid synthesized from progesterone. It modulates the ϒ-aminobutyric acid (GABA-A) receptor, the major inhibitory neurotransmitter in the CNS [48]. Stress increases ALLP concentrations in the brain, and ALLP has been documented to possess potent anxiolytic activity partly due to its modulation of GABA. The anxiolytic properties of ALLP may also be in part due to HPA axis modulation by inhibiting the cortisol response cycle to stress [49].

Studies investigating the chronic stress response highlight a significant reduction in ALLP concentrations in the presence of stress; maybe repeated trauma and chronic stress may alter ALLP levels. ALLP may be an important factor in resilience [50].

28.4 Developmental Cascades and Resilience

Mild to moderately stressful experiences that are challenging promote the development of arousal regulation and resilience. Coping with early life stress enhances cortisol arousal regulation and resilience. This is supported by longitudinal laboratory animal studies of development [51]. Exposure to mild early life stress inoculates against subsequent stressful experiences, increases exploration of novel situations and decreases stress levels of cortisol [52]. Stress inoculation also enhances prefrontal-dependent cognitive control of behaviour and increases ventromedial prefrontal cortical volumes [53]. Early life stress inoculation triggers developmental cascades across multiple domains of adaptive functioning, and these have profound biological and neuroendocrine implications [54]. It is well known that adverse psychosocial environments trigger biological and endocrinologic cascades that may persistently modulate the stress response and generate lifelong patterns of adaptation to stress and trauma. This clearly affects the development of resilience to trauma [55].

28.5 Future Research Needs

Although we have made huge strides in understanding the neuroendocrine contributions to stress and resilience, there is much work to be still done. There is a need for intensive research to convert the existing biological findings, identifying at risk populations and novel therapeutic targets and interventions to improve resilience. There is also a need to study what genetic and epigenetic factors affect the neuroendocrine responses and what may be done to conserve appropriate responses from an early age to facilitate the positive development of resilience. Developmental traumatology, an emerging field in trauma and resilience, needs to focus on these factors along with the internal interplay of various hormones and their effects on one another so that hormones working in a similar manner towards development of resilience are to be enhanced while thwarting the effects of hormones that reduce resilience.

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Common Factors in Psychotherapy

29

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Abstract

Many meta-analyses and research study reviews affirm the comparable effectiveness of psychotherapies in adult patients. This points to common (or core) factors in diverse schools of psychotherapy.

In this chapter, we review the core factors that we believe are fundamentally responsible for transformative change in psychotherapy processes.

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These core factors include the therapeutic alliance, empathy, goal consensus and collaboration, positive regard and affirmation, mastery, congruence/genuineness, mentalization and emotional experience. Evidence-based research on common factors has shown that relationship factors in a therapeutic dyad or group setting predict the outcome of psychotherapy, which is related to some of these common factors, and is also found to correlate with improved levels of functioning (Fisher et al. Psychotherapy 53:105–116, 2016). The effectiveness of psychotherapies may rely more on commonalities rather than on differences of theory and technique.

29.1 Introduction

For most of the twentieth century, psychoanalysis provided a substrate for integrating psychological theory with the delivery of psychotherapy clinical services. Over the last decades, psychotherapy education worldwide has moved away from the complexity of the psychoanalytic model and focused on developing competency and expertise in the practice of what have been called acronym therapies, such as cognitive behavioral therapy (CBT), dialectic behavior therapy (DBT), and interpersonal therapy (IPT), to mention just a few. Many of the newer psychotherapies are manualized, short-term, and easier to integrate in educational curricula in academic medical centers that serve a large number of patients. Much debate exists on the superiority of some of these treatment modalities over the others. The authors take the position that effectiveness may largely correspond to core commonalities of therapies, if these are provided with expertise. In this chapter we review core factors that we believe are fundamentally responsible for transformative change in psychotherapy processes.

An editorial published in *JAMA Psychiatry* [1] indicates that short-term psychodynamic psychotherapy for depressive disorders is as effective as cognitive behavioral therapy. Many meta-analyses and research study reviews affirm the comparable effectiveness of psychotherapies in adult patients [2, 3]. In another multicenter trial, cognitive behavioral therapy was not found superior to short-term psychoanalytic therapy in adolescents [4]. In complex conditions with coexisting comorbidity such as borderline personality disorder, multiple psychotherapy treatments have been found to be effective [5]. To try to explain these findings, researchers have described active therapeutic factors considered common or overlapping that appear to account for the lion's share of treatment outcome in over 400 forms of psychotherapy theoretical models [6]. These therapeutic or curative factors are referred to as common factors not only because they are found in different forms of therapy but also because they are applicable and effective in the treatment of various psychiatric conditions [7].

Evidence-based research on common factors has shown that relationship factors in a therapeutic dyad or group setting predict the outcome of psychotherapy. The common factors include *the therapeutic alliance, empathy, goal consensus and*

collaboration, positive regard and affirmation, mastery, congruence/genuineness, and mentalization. *Emotional experience*, which is related to some of these common factors, is also found to correlate with improved levels of functioning [8]. The effectiveness of psychotherapies may rely more on commonalities rather than on differences of theory and technique.

Psychotherapy treatment outcomes can be conceptualized in different ways. The authors encourage a multidimensional view of outcomes that includes symptomatic reduction, improvement in level of functioning and quality of life (in areas including marital-romantic, sexual, occupational, academic, family-interpersonal, prosocial-community involvement, spiritual, and religious), achievement of therapeutic goals that are collaboratively determined, a mature shift in defensive functioning, attaining age and culturally appropriate developmental milestones, and personal growth (including personality integration, efficiency, serenity, generativity, development of individuation, harmonious interdependence, affiliative behaviors, and altruism). This chapter will explore the common factors in psychotherapy treatments that determine improved outcomes.

29.2 Therapeutic Alliance

Therapeutic alliance may be defined as the working relationship between patient and therapist. It is by far the most investigated common factor with a highly acknowledged curative role in psychotherapy. A strong therapeutic alliance is regarded as a significant predictor of psychotherapy outcome, increasing mutuality and involvement and investment of the patient and therapist in the treatment. The therapeutic alliance is essentially an object relationship where the therapist is experienced in a trusting way as providing a sense of security. In addition, the therapeutic alliance allows patients to deal with frustrations tolerating the tension that results from the controlled exploration of conflicts, which is an integral part of therapy. Accepting this state of necessary tension builds resilience and tolerance of distressing affects, encourages creative problem-solving skills, and helps prevent premature termination.

Neutrality and abstinence are two essential components of the therapeutic alliance. Neutrality is a mindset that allows the therapist to maintain a therapeutic perspective with whatever reaction, response, or intervention chosen with respect to therapeutic advantage or usefulness. Psychotherapists are neutral to the data presented by the patients, not to the patients themselves, as affective resonance is important and needs not be confused with neutrality. The patient perceives neutrality to the data they present as a nonjudgmental stance where the therapist engages the patient to consider the meaningfulness of all behavior and communications. Abstinence prescribes a form of action (doing or enacting vs. abstaining) by which an intermediate course of action can be determined in the space between undue gratification and undue frustration. Abstinence requires comfort with thoughtful silences, evenly suspended attention and judicious sharing of the therapist's reciprocal emotions not to deflect from the therapeutic process.

Keeping within bounds of neutrality and abstinence allows for the participation and partnership of the therapist with the patient as a real person, encouraging the development of a secure therapeutic alliance. Psychometric instruments, such as the Working Alliance Inventory (WAI), have been validated to measure progress in treatment with regard to this important aspect of psychotherapy process [9]. The WAI may be collaboratively self-administered at different points during treatment by patient and therapist to evaluate strength or deficits of the therapeutic alliance. Patient ratings of the WAI tend to be more predictive of outcomes than therapist ratings. Factors correlating with treatment impasses include over structuring or failure to structure therapy, inappropriate self-disclosure, excessive silence, and categorical transference interpretations. Positive alliance factors include affirmations, exploratory interventions, accurate interpretations, and facilitating the expression of affect [10].

29.3 Therapeutic Alliance and Transference

Transference refers to how relationships in the present can be influenced by relationships in the past, and some of these influences are unknowingly transferred to our present day-to-day interactions with others. Clinical examination of these interactions can be meaningful. Transference is defined as the projection of feelings and perceptions related to the patient's past object relations onto the person of the therapist. This often takes place at preconscious or unconscious levels and distorts the patient's perceptions of the therapist. Exploring the transference neurosis is a powerful psychotherapeutic tool and, in some instances if left unexplored, can result in either disruption of the therapeutic process or premature termination of treatment.

The therapeutic alliance involves both aspects of a mature ego with intact reality testing and a reenactment of the early caregiver-child relationships. A therapeutic alliance based on an "objective reality" needs to exist, or be established, between patient and therapist in order to experience symptomatic relief and explore transferential distortions. The capacity to form relationships arises during very early preoedipal development. Attachment theorists locate the critical period of attachment in the first 6 months of life. Patients with successful preoedipal developmental trajectories, nevertheless, may manifest conflicts that affect the therapeutic alliance during stressful periods of treatment. The less successful the outcome of initial preverbal attachments, the greater, in later conflict situations, will be a tendency toward regression and poorly demarcated ego boundaries. We now turn our attention to the relationship between the therapeutic alliance and ego development.

29.4 Therapeutic Alliance and Ego Development

Difficulties in the parent-child relationship such as caregiver rigidity, withdrawal, ambivalence, or neglect would tend to disrupt ego development and result in the formation of unstable ego identity, unsatisfactory self-esteem, and impaired basic

trust. Transference neuroses and the therapeutic alliance tend to merge, and lose their differentiation, if early life disruptions, traumas, and conflicts (involving reality testing and the development of object relations) move into the foreground of the psychotherapeutic process. In order not to disturb the integrity of the therapeutic alliance, there is a need for reintegration of these "basic ego capabilities" [11] in psychotherapy treatments. Safeguarding the therapeutic alliance serves as a barrier to unnecessary, perhaps counter-therapeutic, ego regression. This is especially important in the treatment of persons with borderline and narcissistic personality disorders.

Much emphasis was placed in classical psychoanalysis to the analysis of the transference as an essential important psychotherapeutic intervention. Høoglend et al. [12] at the University of Oslo decided to test conventional wisdom and designed an experiment randomizing patients to two groups, each receiving once a week sessions of psychodynamic psychotherapy with therapists who had 15–20 years of clinical experience. In one group treatment was conducted as usual, where transference interpretations occurred, and in the other group, therapists were instructed not to make transference interpretations. In general, there were no detectable differences in overall outcome suggesting that transference interpretations are perhaps superfluous. However, upon close examination, the investigators concluded that while patients with high-quality object relations do not benefit from transference interpretations, patients with low-quality object relations (including persons with borderline and narcissistic personality structure) benefit from transference interpretations.

29.5 Developmental Issues and Affective Bonding

Patients who begin a psychotherapy treatment usually present with complex transdiagnostic themes that can be sorted into four broad categories [11]. These include:

1. *Failure of establishing affective bonds,* which results from the failure to establish a viable affective bond between parent and child in the first months of infancy. Consequences of failure of secure attachments and affective bonds include difficulties with basic tension control and inability to titrate affective input and prevent under- or overstimulation. These persons are easily angered, show mistrust, are unable to compromise or delay gratification, and show total disregard for the needs of others. In an extreme form, these behaviors constitute distinctive features of borderline personality disorder. They manifest difficulties sustaining interpersonal relationships, and the therapeutic alliance often takes a long time to establish. An ego-supportive approach that emphasizes developing emphatic relationships based on an understanding of the developmental issues is helpful.
2. *Alexithymia,* which stems in part from understimulation during infancy and/or parental intolerance of the infant's affective expressions. These patients as adults have difficulty understanding and labeling their emotions, withdraw from affective situations, and have difficulty relating to others in a meaningful way. Health and illness anxiety, or using somatization as a defense mechanism, often result

from being confronted with situations which demand nuanced emotional flexibility. Helping these patients overcome their shame and fear of affective responsiveness involves helping them experience and articulate their emotions by connecting narrative with affect in a coordinated way. This process benefits and strengthens the therapeutic alliance.

3. *Problems related to affective attunement:* Between the ages of 7 and 18 months, a child starts to become aware of the interpersonal aspects of relationships and to develop a sense of self. Affective attunement involves the mother or caregiver showing that he or she is interested in sharing affective experiences, demonstrating that the child's needs are acknowledged, and validating that what he/she is doing makes a difference. The determinants of secure attachments are paramount in setting the stage for a healthy developmental trajectory. Failure to receive appropriate responses (failure of empathic responses) during this stage of development may lead to a sense of shame and denial of such needs. Adults with narcissistic personality disorders suffer the consequences having experienced inadequately modulated affective exchanges earlier in life. Emphatic immersion in the psychotherapeutic process is the cornerstone of treatment with these patients.
4. *Emphatic failure during the oedipal phase-preschool years:* Patients who have a healthy development during infancy usually develop a sound character structure through adulthood and secure attachments. However, if exposed to emphatic failures around ages of 3–5, patients later in life may encounter psychoneurotic issues related to competitive strivings or have difficulty negotiating loving emotions and affection when interpersonal tension coexists.

29.6 Empathy

Empathy, a common factor in all therapies, is ubiquitous, an inherent quality of all relationships, and both constitutionally determined and learned. Therapists in training might be less precise in assessing their own emphatic capacities, yet empathy can be learned like any other psychotherapeutic skill.

Learning this skill is aided by close supervision, preferably observing the therapy sessions or viewing video excerpts with a supervisor so that every nuance of therapy can be observed, encouraging self-assessment of therapist to help observe, reflect, and understand emotional processes and decode the steps involved in therapeutic empathic responses to patients.

The concept of countertransference is relevant to understand empathy as a curative factor in all therapies. The contemporary definition of countertransference is all-inclusive, meaning that it is the entirety of emotions that clinicians experience toward patients. In a therapeutic process, there is a bidirectional interplay of emotional reactions, creating a state of resonance and harmony if emotions are correctly aligned or an impasse or empathic failure if there is lack of awareness or validation, with unconscious motivations or displacements contaminating the coordination of emotional resonance.

Countertransference could be further subdivided as concordant or complementary. Concordant countertransference is akin to an empathic link, where the therapist identifies with a self-representation of the patient. Concordant countertransferences reflect the intrinsic valence and type of emotions expressed by the patient. A complementary countertransference occurs when the therapist's conflicts are activated by the patient's expression of emotion. A therapist may unconsciously associate the emotions present in the therapeutic exchange with other past experiences, amplifying the emotional state, distorting it, or creating emotional avoidance. Although complementary countertransferences are usually rooted in memories associated with the therapist's personal experiences, clinicians need to remember that this also includes memories and unconscious associations to previous patients and other treatment experiences.

Empathy is a complex phenomenon that can be further subdivided into several key factors [13]. These include mimicry, when engaging in motor and sensory synchronization and mirroring processes; emotional contagion, meaning that emotions are usually shared, and affective sharing is often times effortless; sympathy, or the expression of concern for the sorrow of the other; and compassion, which literally means experiencing the suffering of others. In psychotherapy, in addition to mimicry, affective sharing, and showing concern for and experiencing the suffering of others, there is another factor that becomes the key curative element. Maintaining in perspective boundaries between self and other is crucial, and composure when facing adversity, while validating emotions, is what patients seem to appreciate the most in a psychotherapeutic holding environment. The therapist's seemingly natural ability to distinguish the source of emotions when in a dyadic state of resonance, to determine how much is self-centered or triggered by the other, in addition to reflecting on the actual emotions expressed by the patient, while containing affects that are overwhelming to the patient, creates ego strength through validation, reliance, and cooperation.

Several steps involved in the process of developing and expressing empathy:

1. Becoming aware of the affect awakened in the therapist by the patient: Our initial response to our patients is not under cortical control, and conscious effort needs to occur to become aware of the emotions that patients elicit in us. This emphasizes the importance of being in the moment, and able to experience and acknowledge the feelings in us, both positive and negative, evoked by the patient. It is not unusual for a therapist to guard against patients' emotions as a result of the therapist's own unresolved issues. This is one area in which personal therapy is very helpful.
2. Decentering the therapist's emotional experience is to step back from what one is feeling to think about it dispassionately. This allows the therapist to think about what the patient is feeling and not what the therapist is feeling about the patient.
3. Comparing the content of the patient's verbal message to the feelings related to this message, discovered through the empathic steps described above, helps

therapist understand the real message as well as possibly psychological defenses if there is incongruity between the verbal communication and feelings.
4. Establishing the significance of what is communicated as it relates to the patient's present mental state but also in relation to overall conflicts helps guide our therapeutic responses.

29.7 Emotional Experience

The therapist's openness and empathic responses to the emotions expressed by patients allow and facilitate the expression of emotions, which has been identified as a common factor correlating with symptomatic and overall improvement in psychotherapy [8]. Most patients appreciate using psychotherapy as a forum for emotional expression and anticipate that expression of emotions is an integral part of treatment. Within the safe environment of the therapeutic interaction, negative or painful emotional experiences may be processed toward a new and more positive end result. Empathy, compassion, and encouragement are reported to be key elements facilitating the process of emotional expression [14].

In a meta-analysis of 10 studies of short-term psychodynamic psychotherapy, Diener et al. [15] found that therapists' facilitation of affect independently correlates with 30% improvement in treatment success rate. The effect is more robust when cases are videotaped, audiotaped, and supervised. Examples of therapist actions designed to facilitate a patient's emotional experience and expression include interventions such as "I noticed that your voice changed a bit when we were talking about your relationship, and I wonder what you are feeling right now"; "In order to make these feelings more clear, it might help to try and focus in on exactly what you're experiencing right now, at this moment"; "you are silent now and seem immersed in thoughts, it may help us if you put your feelings into words"; and "you seem to be experiencing distress, please share what you are thinking and feeling." Encouraging emotional expression can be accomplished through a narrative anamnesis, as Sullivan proposed with the technique of "detailed inquiry," basically a process of facilitation of expression of affect through guided free association [16].

In a psychotherapy process, experiencing and tolerating affects in sessions and in other interpersonal relations become a treatment objective. The achievement of therapeutic objectives scale (ATOS) examines dimensions of treatment process that include insight (defined as the concordance of patient's and therapist's goals), motivation to change, building capacity for self-regard and caring for others, and affective regulation [17]. Affective regulation and expression are measured in the following domains in the ATOS:

- Affective arousal/exposure: How much bodily arousal of feeling is experienced in the session?
- Adaptive expression of affect: How effectively is the patient able to express these feelings interpersonally in session and outside the session?
- Degree of inhibition: How much anxiety, guilt, shame, or emotional pain is elicited in sessions, interfering with experiencing affects?

The psychotherapist examines both the concordant expression of thoughts and feelings and also the observable nonverbal expression corresponding to sadness, anxiety, guilt, shame, and anger, including nonverbal expressions such as shakiness, hesitancy, vigilance, trembling, crying, grimacing, and others.

29.8 Goal Consensus/Collaboration

Sometimes recognized as part of the therapeutic alliance, goal consensus can be defined as a mutual agreement between the patient and the therapist on the tasks and goals of and expectations of treatment [18]. The different components of goal consensus include understanding:

1. The chief complaint is the patient's initial statement as to what is bothering him, for instance, "I am depressed."
2. The goal is what the patient would like to accomplish or how he would like to feel, for instance, "I would like to feel well enough to return to work."
3. The request is how the patient would like the clinician to respond, to help him/her achieve the desired goal. He/she might request clarification: "Help me understand the reasons why." He/she might request social intervention: "Tell my family to stop degrading me." He/she might request medical intervention: "Give me something for my nerves."

In initial interviews, the complaint is invariably elicited, goals are usually elicited, and the requests are often not elicited. Eliciting and using patient's requests to negotiate a treatment plan correlate positively and substantially with outcomes [19].

29.9 Mastery

Evidence supports the positive effects of a sense of control or mastery. Most forms of therapy find it valuable, but some deem it more important than others. Psychodynamic psychotherapists believe that insight into desires, fears, and inhibitions can lead to the beginnings of the experience of mastery. True mastery requires successfully applying insights over the patterns patients seek to change.

Cognitive therapy provides patients with structured tasks having well-defined goals. Recommends dividing tasks into small, progressively more difficult steps. The first few steps are conducted in the treatment room. When they prove successful, the remainder is assigned as homework. This is termed "graded task assignment." To track the patient's subjective sense of mastery and make it salient, designed what they termed the "mastery and pleasure technique."

29.10 Congruence/Genuineness

For a therapist to be experienced as genuine, she/he needs to be self-aware of the multiplicity and totality of emotional experiences. Genuineness is not related to self-revelations or sharing of countertransferences, as it relates more to spontaneity and transparency than to self-disclosure. Neutrality coexists with activity, as the genuine therapist actively relates to the patient in treatment and is emotionally present in the therapeutic process [20].

Congruence refers to the acknowledgment of the patient and therapist each as autonomous but synchronized, referred to by Carl Rogers [21] as the "we-perspective" in treatment. Congruence in psychotherapy helps establish trust, as one perceives the other as real in the moment, as the ethical principle of beneficence guides the process [22].

29.11 Positive Regard/Affirmation

Rogerian and CBT constructs make use of the therapeutic factor of positive regard and affirmation. Affirmations require abstractive effort, condensation, and symbolization and are powerful ways to reinforce positive adaptive behaviors and correct cognitive distortions.

29.12 Mentalization

Mentalization can be described as an "imaginative mental activity, namely, perceiving and interpreting human behavior in terms of intentional mental states (e.g., needs, desires, feelings, beliefs, goals, and reasons)" [23]. It allows to attribute a cause of behavior to a subjective state or find meaning in the actions of others.

Mentalization as the awareness of mental states in self and others could be conscious (explicit) or automatic (implicit). The accepting, patient, and curious approach of therapist and the active collaboration between them create a ground where the patient can explore the outer world as well as his/her inner world and can become open and adaptive. The relationship enhances the capacity of the patient to mentalize.

Conclusion

The common factors described in this chapter are operative in many different forms of psychotherapy although different forms of treatment make differential use of them and therefore may not be as effective. Active awareness of these factors and their integration into therapeutic practice improve outcome in psychotherapy. Moreover, focusing on common factors can facilitate the development of common recommendations for psychotherapists in training.

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The Practice of Freedom: Human Rights and the Global Mental Health Agenda

30

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Abstract

In the long history of human rights advocacy in psychiatry, the Convention on the Rights of Persons with Disabilities (CRPD) sets an important balancing point between the right to adequate care and all human rights and fundamental freedoms and draws on cross-cutting themes including empowerment, citizenship, recovery and community living as a viable alternative to institutional living. Coercion in care, such as restraints, seclusion, forced medications, locked inpatient units, warehousing and forensic institutions, must be curtailed. The optimal attainment of liberty and freedom in care processes entails change, substitution and systematization of availability of practical alternatives: open doors, open communities, open dialogues, free access, community engagement, advance directives, joint decision-making and co-production of policy with

Dedication
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stakeholders and recovery orientation of all services. Absolutist and idealistic insistence on the abandonment of all forms of involuntary treatments straight away will not work, but CRPD has undoubtedly opened a new debate and is definitely setting a new horizon for psychiatry to approach. Deinstitutionalization is a necessary step, by substituting community for hospital care and voluntary for involuntary care wherever possible and changing legislations accordingly. Widening the new frontier involves creating a convergence of clinical and support services with strong advocacy for rights. There is an emerging evidence base for the proposition that optimizing human rights is inherently therapeutic and contributes to healing. In this framework, the WHO has launched The QualityRights Programme for improving quality of care and implementation of core articles of CRPD. An effective action includes challenging social exclusion and inequality, by acting on social determinants of health like quality and stability of home, work, income, supports, relationships and social participation. Political, legal and social action has to be combined with our own emancipation from institutional thinking and practices in mental health and social care, to vastly improve the prospects of a whole life and full citizenship and rights for persons with psychosocial disabilities.

30.1 Introduction: Enabling of Human Rights (HR) Is the Overriding Priority for Mental Health

30.1.1 Entrapment in the Treatment and Care Domain

Despite many efforts, the task of providing more humane and effective care for, and upholding the rights of the huge population with complex and severe mental health problems, is still far from being adequately addressed by international health and disability agendas. The Global Mental Health movement is constructively focussed on correction of the gaps in treatment and in access to social care and social inclusion for people with mental health issues [1].

The abandonment of many of those in need is still the reality worldwide, from the lack of a welfare state 'safety net' and therefore of affordable services in low- and medium-income countries to the many facets of social exclusion and discrimination for people with mental health problems, as well as inequities of access to adequate care in high-income countries. Even when accessing care, there is often poor care quality with persistent risk of stigmatization, social exclusion and loss of rights.

There are still many thousands of people in psychiatric hospitals (or chained or caged) in low- to middle-income countries and still too many institutionalized in richer countries. They need more opportunities to improve their human rights, mental health and wellbeing while they are in these hospitals. In many countries, the development of a comprehensive community mental health system, including supportive community-based residential alternatives, has been and will continue to be

a patchy and slow process. This is due to many factors, economic, political, environmental, social, educational and ideological.

Despite the widely acknowledged contribution of upholding human rights of people living with mental health disorders to improving recovery outcomes, attention to the human rights of these individuals is lagging way behind considerations of their treatment and care.

30.1.2 The Human Rights Movement and Mental Health

30.1.2.1 The Origins of the Human Rights Movement Within Mental Health Services

Historically the mental health human rights movement derived human rights for people with mental illnesses from other rights movements. The disability rights movement co-opted techniques from women's rights and black rights movements, and in turn the mental health consumer movement took many cues from the broader disability movement [2].

People with mental illness were relative latecomers to civil and disability rights activism. They were left out of these movements because they were still institutionalized when this movement was gathering steam and partly because of the stigmatized views from within the movement that individuals with psychotic disorders were too violent, volatile or irrational and unable to meaningfully participate in empowerment [3].

There is now a clearly defined advocacy sector that is overt in trying to define disability rights. Various nations have enacted disability legislation, culminating in international disability rights conventions 'in an attempt to articulate what social justice means for people with disabilities in receipt of government funded services' (Robin Banks—PIAC, personal communication).

Whereas the old paradigm for disability viewed a disabled person as one who cannot function because of a particular impairment, the current paradigm assumes that, whether the disability is physical or psychiatric, the person needs some specific aid or accommodation in order to function. In this 'social model', disability is socially constructed, essentially in social and/or environmental terms [2].

30.1.2.2 Mental Health Advocacy Movements

Barry [4] identifies three distinct mental health advocacy movements that emerged from these origins in North America: Dorothy Dix's campaign for 'the humane treatment of the mentally ill' through the building of state hospitals (i.e. institutionalization as a reform), Clifford Beers' influence in establishing the mental hygiene movement leading to community mental health services, and the grass-roots emergence of the mental health family and consumer empowerment movement (partly exemplified in the development of the National Alliance on Mental Illness, NAMI). Tucker [5] traces the origin of the consumer empowerment movement in the UK to the flattening of the authority structure inherent in the development of the then clinical therapeutic community movement, though arguably this was not so pervasive

nor as long lasting as the movements just mentioned. However, it was influential in making the walls around psychiatric institutions more permeable in countries where therapeutic communities did operate. It also may have partly responsible for a shift towards community healthcare and service user voices and needs beginning to be heard by service providers [2].

The human rights movement in health has been enshrined in instruments such as the UN Universal Declaration of Human Rights, which endowed every person with a claim to basic healthcare [6]. In mental health this has led to professional and family advocacy for the right to psychiatric treatment, which they insist should be enforceable if necessary. Mental health consumers challenge this however, denying that they need compulsory treatment, whether due to their claim to having made an adequate recovery in their own terms or to a lack of insight or appreciation of the perception of others. Tucker [5] argues that "full consumer participation" with greater service user–provider equity is inherent in all high-quality mental healthcare systems, such as therapeutic communities, and that 'add-on' consumer participation is artificial and should be unnecessary. Unfortunately, not all service systems recognize the value of such integrated participation as yet and may need to mandate service user participation for some time to achieve satisfactory acceptance by services [2].

30.1.2.3 Mental Health Human Rights and Politics: Deinstitutionalization

Political climates, legal changes and judicial activism have both impacted and frustrated rights advocacy for people with mental illness. From the consumer viewpoint, the rights to both obtain treatment and to refuse treatment ideally should together constitute the right to mental healthcare [7]. This balance of rights was upheld judicially in parts of the USA from the 1960s. In the USA and other Western countries, attempts by conservative politicians, such as Reagan and Thatcher, to rescind the rights of and retrench services for individuals with mental illness [8] have been tempered by grass-roots local and national advocacy [7]. In Italy, the emancipation of individuals living with severe and persistent mental illnesses (SPMI) from the mental hospitals, their closure and replacement with largely community-based services and facilities and the insistence on the rights of people with SPMI to full citizenship and valued membership of the community were enshrined in the national laws of 1978 [9]. Hospital-based patients and staff were empowered at the same time to stand up for system-wide reforms to improve the quality of their lives and working relationships [2].

The deinstitutionalization movement worldwide has taken the closure of large mental hospitals and other institutions as the principal mainstream task with the ostensible aim of regaining a condition of full rights and citizenship for people with mental health problems who suffered long-term internment. Legislation seldom accompanied those changes, which never were fully achieved in countries other than Italy (and substantially in the UK). Human rights violations are still the reality, even if not generally recognized even by organizations that are engaged in human rights work [10]. The World Health Organization has declared it as 'an unresolved

global crisis' as documented by views, expertise and experience of people with mental and psychosocial disabilities from many countries despite the recent international declarations [2, 11]. For WHO:

> The care available in mental health facilities around the world is not only of poor quality but in many instances actually hinders recovery. It is common for people to be locked away in small, prison-like cells with no human contact or to be chained to their beds, unable to move. Violations are not restricted to inpatient and residential facilities however; many people seeking care from outpatient and community care services are disempowered and also experience extensive restrictions to their basic human rights [12].

30.2 Declaring Human Rights: The Significance of UN-CRPD

There are nine core human rights treaties within the United Nations human rights framework, each of which has established a committee of experts to monitor the implementation by States parties the introduction of the United Nations Convention on the Rights of Persons with Disabilities [13] is of especially huge significance for the human rights of persons with mental health problems, particularly if they are institutionalized.

In a new move for the UN, the CRPD was drafted with full and active participation of people with disabilities, including psychosocial disabilities, and their organizations. The Convention reaffirms a number of substantive rights for persons with disabilities, including persons with mental health problems. It represents an important paradigm shift recognizing that persons with disabilities should not be seen merely as recipients of charity or medical attention, but as holders of rights who have 'inherent human dignity worthy of protection equal to that of other human beings'.

The CRPD is the first high-level international legally binding standard which aims to promote, protect and ensure the full and equal enjoyment of all human rights and fundamental freedoms by all persons with disabilities, including those with mental health conditions, and to promote respect for their inherent dignity. They are capable of claiming those rights and making decisions for their lives based on their free and informed consent as well as being active members of society [14].

The Convention promotes a social model of disability, in which disability is seen as the result of the interaction between people living with impairments and an environment that has many physical, attitudinal, communication and social barriers. Thus disability can be overcome by changing the physical, attitudinal, communication and social environment (barriers) to enable people to fully participate in society [15].

The CRPD includes an agreement that countries will not permit discrimination against people with psychosocial disabilities, meant as the practice of unfairly treating a person or group of people based on prejudice towards their certain characteristics. It provides a clear path towards full and effective participation and inclusion in society, respect for difference and acceptance of persons with disabilities as part of human diversity and humanity, equality of opportunity and accessibility [16].

CRPD is also historically important as it is the first time that the MH community has been considered to be, and has been included as, part of the disability community. In another historical first, it is also the first time that people with MH disability have been consulted directly and have been included in the negotiations and writing process [17]. An international team encompassing organizations like the World Network of Users and Survivors of Psychiatry (WNUSP), MindFreedom/Support Coalition International (MF/SCI) and others from 17 countries, participated actively in the negotiations at the United Nations in New York from August 2002 to December 2006, when it was adopted (it entered into force in May 2008).

The general principles that guide the Convention are inspired by the Universal Declaration of Human Rights (UDHR). Article 3 of CRPD declares:

(a) Respect for inherent dignity, individual autonomy including the freedom to make one's own choices and independence of persons
(b) Non-discrimination
(c) Full and effective participation and inclusion in society
(d) Respect for difference and acceptance of persons with disabilities as part of human diversity and humanity
(e) Equality of opportunity
(f) Accessibility
(g) Equality between men and women
(h) Respect for the evolving capacities of children with disabilities and respect for the right of children with disabilities to preserve their identities

In the following articles of the Convention, particular relevance to those with lived experience of mental illness are the right to liberty and security of the person; the right to equal recognition before the law; the right to enjoy the highest attainable standard of health; and the right to respect for physical and mental integrity [18].

Some of the core implications of CRPD in mental health are outlined in Table 30.1.

States which have signed the CRPD have an obligation to respect, protect and fulfil the internationally agreed upon set of standards guaranteed to all people included in the Convention.

Moreover, on 1 July 2016, the UN Human Rights Council adopted a resolution on mental health and human rights, led by Portugal and Brazil and cosponsored by 61 countries, with more countries still joining. It highlighted that 'persons with mental health conditions or psychosocial disabilities, in particular persons using mental health services, may be subject to, inter alia, widespread discrimination, stigma, prejudice, violence, social exclusion and segregation, unlawful or arbitrary institutionalization, over-medicalization and treatment practices that fail to respect their autonomy, will and preferences' and thus 'the need for States to take active steps to fully integrate a human rights perspective into mental health and community services, particularly with a view to eliminating all forms of violence and discrimination within that context, and to promote the right of everyone to full inclusion and effective participation in society'.

Table 30.1 Some implications of CRPD for people with psychosocial disabilities

CRPD	Right	Main content
Art 9	Accessibility	To be able to access and participate in all areas of life as would a person without disabilities
Art 10	Right to life	To have the same chance as anyone else to live their lives
Art 12	Equal recognition before the law	To be treated equally by the law and to have equal access to legal representation as well To make decisions and choices for themselves To identify people that they know and trust who can support them to make decisions
Art 14	Liberty and security of person	To be free and safe, not be locked up just because their disability or prejudice about dangerousness
Art 15	Freedom from torture or cruel, inhuman or degrading treatment or punishment	To be free from neglect and abuse, e.g. in institutions, as well as from restraint practices
Art 16	Exploitation, violence and abuse	To ensure people with disabilities are protected from violence and abuse in the home and in the community
Art 19	Living independently and being included in the community	To make the same decisions about where they live, just like everyone else, and they should be part of their communities To they must access the full range of supports and services to enable them to lead independent lives in the community
Art 21	Freedom of expression	To have the right to say what they want To have their voices listened to
Art 23	Home and family	To lead normal family and sexual lives and to have personal relationships
Art 24	Education	To have the opportunity to go to mainstream schools and have their learning and educational needs met in those schools
Art 25	Health	To access health services on an equal basis with everyone else and get the same standard of service as others, with their informed consent to treatment Services must be close to where people live to make it easier for them to access and make them more effective
Art 26	Habilitation/rehabilitation	To lead an independent and healthy a life as possible and to receive services and supports in health, work, education and social services to help that happen To have access to peer support services
Art 27	Work and employment	To have the right to work on an equal basis as others
Art 28	Standard of living and social protection	To have an equal right to the same standard of living and social protection as everyone else, e.g. to housing

The Human Rights agenda seems to be nowadays one of the top priorities in the international policies about mental health. For instance, the vision of WHO Mental Health Action Plan 2013–2020 [19] is:

> A world in which mental health is valued, promoted, and protected, mental disorders are prevented and persons affected by these disorders are able to exercise the full range of human rights and to access high-quality, culturally appropriate health and social care in a timely way to promote recovery, all in order to attain the highest possible level of health and participate fully in society and at work free from stigmatization and discrimination.

Therefore the WHO Action Plan puts HR among its cross-cutting principles:

> Mental health strategies, actions and interventions for treatment, prevention and promotion must be compliant with the Convention on the Rights of Persons with Disabilities and other international and regional human rights instruments. In the light of widespread human rights violations and discrimination experienced by people with mental disorders, a human rights perspective is essential in responding to the global burden of mental disorders.

This is another important connection and balancing point, between the right to adequate care and the right to all fundamental human rights. It is not a matter of 'this or that' but of the rights to both.

30.3 The Debate Around CRPD and Mental Health

Service-user organizations like the WNUSP (World Network of Users and Survivors of Psychiatry) proclaimed the CRPD as a 'major victory for users and survivors of psychiatry all around the world' [20], especially for the paradigm shift from paternalism. The UN-CRPD promises a great change in the entitlement of rights for people with mental health problems, but there is a huge gap or discrepancy with the reality of psychiatry everywhere in the world. Full CRPD implementation is widely considered to be idealized but unrealistic in current circumstances. It is either an unachievable ideal or an essential point of arrival, depending on your viewpoint. At the moment, no country is yet ready to fully implement CRPD. However, mental health services such as Trieste's in Italy have demonstrated that is possible to avoid most compulsory treatments in a proactive and mobile community mental health centre practice, while suicidal and forensic incidents remain very low [2].

The United Nations has a designated Committee to oversee the CRPD, to whom States must periodically report. Ratification of the optional protocol by the States means that individuals can complain directly to the Committee.

The Committee also periodically may make interpretations of the meaning of particular articles of the Convention, even if they are not legally binding.

An initial point of departure is the definition of disability itself: people with long-term mental illness are included; whether those with short-term illnesses are included is still debated [18]. 'Mental illness is not necessarily associated with disability; however, a clear distinction is not required since the UN-CRPD phrases principles which should be valid for all human beings, disabled or not' [21].

Anyway, for service-user organizations, 'disability is an evolving concept'. While they recognize the diversity of persons with disabilities, specifically including those who require more intensive support, also they declare:

> The word psychosocial refers to the interaction between psychological and social/cultural components of our disability. The psychological component refers to ways of thinking and processing our experiences and our perception of the world around us. The social/cultural component refers to societal and cultural limits for behavior that interact with those psychological differences/madness as well as the stigma that the society attaches to labeling us as disabled. However, in using the term psychosocial, we have no in intention of associating ourselves with the psychosocial rehabilitation movement [20].

This distancing itself from identification with the psychosocial rehabilitation movement may alienate the service-user movement from the psychiatric professional networks ultimately most likely to be allies in advocating for most of these rights.

A harsh debate has been prompted by the report of Juan Mendez to the UN Human Rights Council (2013) [22]. The UN Special Rapporteur on torture and other cruel, inhuman or degrading treatment—an independent expert appointed by the UN Human Rights Council—voiced serious concerns about discrimination against people with psychosocial disabilities and about the domestic legislations and practices in many parts of the world. He claimed to abolish all kinds of coercive treatment as well as substituted decision-making legislations such as guardianship.

The Committee's General Comment No. 1 (2014) on Article 12 (equal recognition before the law) [23] was widely contested as was the report [24]. This article does not contain any restrictions due to reduced mental capacity. The General Comment defines mental capacity as 'the decision-making skills of a person' and rejects prevailing medical conceptions of mental capacity, stating that it is 'highly controversial' and that mental capacity 'is not, as is commonly presented, an objective, scientific and naturally occurring phenomenon'. The Committee argues that mental capacity and legal capacity should not be 'conflated', and that impaired decision-making skills should not be justification for suspension of legal capacity according to the reaffirmed principle of informed consent. Therefore it concludes that substituted decision-making, compulsory treatment, involuntary admissions and diversion into psychiatric care from the criminal system process on the grounds of mental disability are no longer acceptable. Service-user organizations like WNUSP maintained the same position about the prospect of the abolition of mental health commitment laws, guardianship and the insanity defence, with the simultaneous creation of a wide range of healing support, and the liberation from institutions. 'Deciding whether to accept medical treatment or go into a hospital is an exercise of legal capacity. If someone else, whether a doctor, court, or imposed guardian, is authorized by law to substitute their will for your own, this deprives you of the right to exercise legal capacity on an equal basis with others. Mental health commitment laws violate Article 12' [20]. Also the whole system of guardianship is held to violate Article 12, especially when it implies to be put into a psychiatric institution and be forced to ECT and drugs.

These positions caused considerable concern among psychiatric organizations and stimulated ongoing controversies with client organizations [16]. Several States submitted statements, supporting substituted decision-making in limited circumstances, to be considered by the Committee (Norway, Germany, Denmark and France), as well as mental health user organizations in Northern Europe and Africa. The position expressed by an authoritative international group of psychiatrists [25] looks drastic, when foreseeing 'unintended consequences'. 'The Committee's interpretation conflates the notions of disability, a long-term state, and mental capacity, which is based on a time-limited assessment'. They argued it can be paradoxical in its implications for several fundamental rights, such as the right to enjoyment of the highest attainable standard of health, access to justice (e.g. to be jailed if convicted of a crime instead of being diverted to mental health treatment), the right to liberty and even the right to life that might instead be violated and subject to unintended consequences. This can eventually lead to an increase of persons with severe mental illness untreated in the community, to the violation of human rights of others, such as family members and members of the public, and to an increase of stigma and discrimination.

Interpretations of the General Comment are accepted without modification. Different conclusions could have been reached with wider involvement of stakeholders such as clinicians, professional organizations and a broad range of user groups.

Recent Guidelines on Article 14 of the Convention (the right to liberty and security of persons with disabilities) adopted during the Committee's 14th session, held in September 2015 [26], confirmed and developed the above key issues:

1. The absolute prohibition of detention on the basis of impairment.
2. Includes also when persons with disabilities are deemed dangerous to themselves or others.
3. Involuntary commitment of persons with disabilities on healthcare grounds contradicts the absolute ban on deprivation of liberty on the basis of impairments. The Committee has expressed its concern about the institutionalization of persons with disabilities and the lack of support services in the community.
4. The use of forced treatment, seclusion and various methods of restraint in medical facilities, including physical, chemical and mechanical restraints, are not consistent with the prohibition of torture and other cruel, inhumane or degrading treatment or punishment against persons with disabilities (Article 15).
5. Deprivation of liberty on the basis of perceived dangerousness of persons with disabilities, or the alleged need for care or treatment, is connected with being diverted to a separate track of law, including mental health laws, with a lower standard in terms of human rights protection, particularly of the right to due process and fair trial.
6. All persons with disabilities who have been accused of crimes and detained in jails and institutions, without trial, are allowed to defend themselves against criminal charges in a court of law, and are provided with required support and accommodation to facilitate their effective participation.

7. Concerns have been expressed for the poor living conditions in places of detention, particularly prisons, asking for reasonable accommodation that preserves the dignity of persons with disabilities. They must participate fully in all aspects of daily life in their place of detention, including ensuring their access, on an equal basis with others, to the various areas and services.
8. Security measures, including those which involve forced medical and psychiatric treatment in institutions, must be eliminated. Access to medications and assistance in withdrawing from medications should be made available for those who so decide.
9. About free and informed consent in emergency and crisis situations.
10. States have to ensure that persons with disabilities are not denied the right to exercise their legal capacity on the basis of a third party's analysis of their 'best interests'. It should be replaced by the standard of 'best interpretation of the will and preferences' of the person.
11. Individuals who are currently detained in a psychiatric hospital or similar institution and/or subjected to forced treatment must be informed about ways in which they can effectively and promptly secure their release. This entails systemic measures such as requiring mental health facilities to unlock their doors and inform persons of their right to leave, and establishing a public authority to provide for access to housing, means of subsistence and other forms of economic and social support in order to facilitate deinstitutionalization and the right to live independently and be included in the community.

30.4 Subsets and Implications of Human Rights in Mental Health

Taking into account all these observations, the application of these principles should have a great impact on the lives of persons with psychosocial disabilities.

Freedom from coercion and involuntary status care requires a systematization of strategies regarding:

– Supported and joint decision-making
– Advance directives
– Forming a therapeutic alliance
– Individual care recovery and wellness plans
– Application of supported and joint decision-making methods and software
– Alternatives to seclusion and restraint

This entails retraining health professionals, including mental health professionals, not to keep on habitually telling or implying to our clientele: 'we know what's best for you'. This is known as the colonizing presumption of asserting 'vocational ownership' over a stakeholder group (e.g. service users) by another more dominant stakeholder group (e.g. clinician providers) [27].

Article 12, which refers to equal and full human rights before the law, is the most innovative provision in the Convention for service users and 'survivors' of psychiatry. Assistance has to be offered during time of crisis, confusion or distress. Guardianship and incapacity laws, and provisions throughout the legal system should be developed, linked to recognizing responsibility in the person with the disability.

A practice of critical expertise related to life stories, the complex meaning of crimes, not just assuming positivistic causal mechanisms between the person's illness and behaviour or actions, needed to be further developed. Disability-neutral standards for adjudicating criminal responsibility (e.g. actual criminal intent, taking account of the circumstances of the crime, motivation, etc.) are invoked. It implies the avoiding of a 'separate route' for forensic purposes that is being diverted to special institutions, instead of being able to exercise your rights to continue to have a fair trial and, when sentenced to jail, to include consideration of reasonable community accommodations as alternatives to prison.

Participation in decision-making is meant as being part of negotiation and active two-way consultation, not just a passive and gestural notification. Great importance is given to 'supported' and not 'substitute' decision-making. Basically 'in supported decision-making, the judgment and will of the person are not contested, unlike in guardianship and substituted decision-making' [20]. Mechanisms to provide support in making decisions for a wide range of people with disabilities with diverse needs are needed in order to exercise legal capacity. Support measures should be offered even by the same agencies (banks, notaries, judges, medical personnel) who today require several forms of guardianships.

While self-determination is an important component of the current aspirations of the recovery movement involving individuals with mental illness, claims for total self-determination seem over-idealized and unrealistic. Practical conceptions of self-determination and autonomy must allow for a balance with interdependence, social connectedness and the social aspirations or will of real communities [3]. Consequently autonomous living with a disability becomes a dynamic interaction between the characteristics of the individual and the features of their social, cultural, natural and built environment [3].

To maximize self-determination of those involved, we need to consult with individuals with psychiatric disabilities, their families and other stakeholders, regarding what this would take for each person or group.

Article 12 of the CRPD also indicates that people with lived experience of mental impairment should be engaged in planning and implementing their own treatment, and peer workers should be included wherever possible to help promote empathetic services and improve health outcomes. Article 17 of the CRPD ('Every person with disabilities has a right to respect for his or her physical and mental integrity on an equal basis with others') declares that restrictive practices such as seclusion and restraint and unbeneficial and overly intrusive treatment need to be curtailed and eliminated wherever possible. The term 'seclusion' generally refers to the deliberate confinement of a person, alone, in a room or area that the person cannot freely exit, while the term 'restraint' is meant as physical (bodily force to control freedom of movement), chemical (medication given primarily to control

behaviour), mechanical (device used to control freedom of movement) and even emotional restraint (loss of confidence in being able to express their views openly and honestly for fear of the consequences) [28].

Article 25 of the CRPD indicates that there needs to be a shift away from the current focus on emergency-driven hospital care towards providing access to voluntary, community-based services with an emphasis on early identification and intervention.

As regards to Article 19, living independently in the community is related to deinstitutionalization and community living. This is connected with the choice of living place 'on your own turf and terms', so that treatment, care and support comes to you and goes where and when you want it to go. It emphasizes the importance of developing good quality and sustainable alternatives to institutional care and requires 'the shift of government policies away from institutions towards in-home, residential and other community support services'.

Choice in treatment and treatment setting and parity of access to both general health and mental healthcare are other requirements.

30.5 Cross-Cutting Themes

It has to be considered that human rights have implications with other aspects of care and entitlements. The basic issue is empowerment that has been recognized, together with the human rights approach, by the WHO Action Plan 2013–2020 among its cross-cutting themes, which encompass also multisectoral approach and other aspects of a wider concept of mental healthcare [19].

30.5.1 Empowerment and Partnership

Even in official documents [29], empowerment is depicted as a multidimensional social process that determines changes in the lives of individuals and in the circumstances of their health.

For the individual, empowerment is an active process that means overcoming a state of powerlessness and gaining control of one's life. The process starts with individually defined needs and ambitions and focuses on the development of capacities and resources that support it. Empowerment of individuals [29] is intended to help service users make more treatment and care choices for themselves, adopt self-determination and autonomy, exert more influence on social and political decision-making processes and gain increased self-esteem. An empowerment approach promotes the recognition and development of the service user's strengths, resources and skills that involves decision-making power, access to information and resources and having a range of options from which to choose. It is needed in order to exercise freedom of choice among treatment options and alternatives at each phase of the process of care, from crisis to rehabilitation, housing, job and social inclusion. A low threshold for access (informal, self-referring,

walk-in, no waiting lists, no selection) should be complemented by having an assured way out of the service network, thus avoiding to become stuck in a patients' role—e.g. Australian National Mental Health Service Standards, including a set of Exit and Re-entry Standards [30]. 'Empowering' services must be accountable and offer affordable, community-based, comprehensive and effective treatment and care, must respect people' s right to refuse treatment and be sensitive to different groups' needs, and, are provided on a basis of non-discrimination, ensuring that independent review bodies are in place.

Service-user involvement in services is part of the empowerment process when it offers people who use services the chance to be partners or to be involved in all stages and levels of running, planning, delivering and evaluating services; to choose their key mental health caregivers; to draw up care plans and plan their treatment (encouraging fully informed decision-making, which includes a discussion of risks linked to medication and the importance of health promoting lifestyles); to develop shared crisis plans, advance directives and recovery plans; and to ensure staff are trained in human rights. This entails codesign, co-production and co-implementation at every level of service [27].

At the collective level, empowerment implies including representative, resource-independent service-user advocacy organizations that are involved at the international, national, regional and local levels and also specific attention to the participation of peer workers in the mental health workforce and enhancement of social capital of social networks of individuals and families receiving MH care. In order to reduce stigma and discrimination, it is necessary to engage the public through meeting personally with people with living experience of mental illnesses, awareness campaigns, educating the media to be more sensitive and eventually via mental health promotion and prevention. In that respect, rehabilitation is linked to social participation and challenging social exclusion [29].

World Psychiatric Association's (WPA's) recommendations for the international mental health community on best practices in working with service users and carers while supporting collaborative work between mental health practitioners, service users and family/carers underline as the first of the ten recommendations the notion that 'Respecting human rights is the basis of successful partnerships for mental health' [24]. Partnership implies and entails respect as equal and power sharing [27].

Stemming from the recognition of 'power asymmetries', e.g. the imbalance in power relationships is now an official issue, also the UN Special Rapporteur recommends full participation of service users' representatives at the population level and in mental health services [31].

30.5.2 Multisectoral Approach and Social Determinants

Empowerment needs options and opportunities to be implemented. Outside institutions, in the wider community, 'many people with mental disabilities are still denied many basic rights that most people take for granted. For example, they are denied opportunities to live where they choose, marry, have families, attend school

and seek employment' [16]. This point is strictly connected to a policy for human development addressing the social determinants of health, defined as 'the circumstances in which people are born, grow up, live, work and age', and the systems put in place to deal with illness. These circumstances are in turn shaped by a wider set of forces, such as economics, social policies and politics [32–34]. As maintained in the Report of the Special Rapporteur to the UN Human Rights Council on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health [31]:

> The crisis in mental health should be managed not as a crisis of individual conditions, but as a crisis of social obstacles which hinders individual rights … The urgent need for a shift in approach should prioritize policy innovation at the population level, targeting social determinants and abandon the predominant medical model that seeks to cure individuals by targeting "disorders".

The right to health is also included in the promotion and protection of all human rights, civil, political, economic, social and cultural rights, including the right to personal, social, economic, cultural and political development:

> The right to health is an inclusive right to both health care and the underlying and social determinants of health. Public health has individual and collective dimensions, which are essential in securing the right to the enjoyment of the underlying and social determinants of health. Given the deep connections between mental health and the physical, psychosocial, political and economic environment, the right to determinants of health is a precondition for securing the right to mental health [31].

To achieve social inclusion, we must engage all-of-community and whole-of-life strategies and opportunities. The person in the social context calls into action a whole life (in all domains), a whole system and a whole community [35]. Human rights refer to a whole person and therefore on shared basic values of humanity. A new epistemology of a mental health should be based on a person-centred paradigm valuing the personal and social experience of individuals as human beings and social actors and not on a paradigm of disease [36].

If rehabilitation can be conceived as a programme of restitution and reconstruction of full rights (political, civil, social) and a status of citizenship for individuals disabled by mental illness, the material construction of these rights [37] involves not only the legal recognition of civil and social rights, but also actions in order to acquire resources (houses, jobs, goods, services and related relationships). This can start with deinstitutionalization as a process which reconverts total institutions—and their 'frozen' resources—to community services and provisions for the individuals.

30.5.3 Rights to Care and Human Rights

Despite the above considerations, 'the need for treatment was considered to precede human rights considerations' [38].

One of the key points recognized is the nexus between the right to health and care and the whole array of HR's, safeguarded, e.g. by the Italian law 180.

Even if there are guidelines, protocols, recommendations, monitoring systems in order to control forced treatments and restrictive practices, we should move towards a no-restraint general framework, e.g. an open door policy at all levels of the system, recognizing dignity and rights of individuals, not treated as an 'object of the institution' [39]. The contradictions of power end up being played out in confined places, without any possibility of opening up towards the external world, in a different frame of space and time and with a project that pertains to real life. If I (as doctor, nurse, in any case guardian) have the key, or keys, I decide what is best for you without any possibility of negotiation. If instead, I have to hear your arguments, convince you and persuade you to agree, I must enter into dialogue with you in order to negotiate a solution.

In Italy, deinstitutionalization has been completed by pursuing it until the complete closure of all psychiatric hospitals over two decades (1978–1999). The legislation of 1978 was based on rights (free communication, right to appeal, no prolonged involuntary treatments, no detention during those treatments) and fostered the lowest rate of involuntary treatment in Europe (17/100,000) and the shortest average duration of hospital admission (10 days), avoiding institutional 'careers'. The forensic hospital sector has been included now in a further deinstitutionalization, with the closure of all remaining (6) forensic hospitals, replaced by small (less than 20 beds) regional units linked to MH departments. There was a reduction of individuals detained from 1500 long-term patients to less than 600 usually for a much shorter time. The legal prospect is the right to be found guilty of a crime and the right to trial, and expectation of other developments in penal codes consistent with HR's. The judgement whether guilty implies to be equal in front of law; on the other hand, there is a right to mental health assessment and then a right to mental health services in prison [9, 40].

Other laws supported those changes in terms of citizenship rights, e.g. the law on social co-operatives in 1992, promoting forms of social enterprises with person with psychosocial disabilities as equal members, and on the integration of welfare and health systems in 2000, with the inclusion of mental health in a wider social inclusion planning.

Independent living is no longer regimented in a communal dormitory or group home, nor secluded in special places, but is located in the service user own shared or single occupancy dwelling in a normal street of suburban housing, with appropriate support [41].

30.5.4 Linking Recovery and Citizenship

To strengthen a condition of actual citizenship, persons with psychosocial disabilities should move to a wider field of human individual and social rights (e.g. right to vote, to the highest level of health, to be able to deal with the inequities of social determinants of health).

We can conceive of a fully 'lived citizenship' as the unveiling of the intimate social nature of even the most personal recovery [42–44]. Social integration, intended as adaptation to reality, seems rather linked to a sort of pedagogy of the social game, where it is essential to learn the ability to decode it and grasp the complexity of its multiple levels. The conceptual frameworks most frequently used in guidance documents on the topic of recovery [45] ultimately entail the promotion of citizenship. This principle is intended to support the reintegration of people in the society as full citizens—i.e. rights, responsibilities, inclusion, community residency, communal role, employment—but not instead of a reform or positive or global change in the services (i.e. a 'whole system change').

That is why we prefer mentioning recovery and 'emancipation', because we want to emphasize the aspect of non-freedom that is related to the disease condition as personal and social misery, to the loss of rights or prevention of the access to socially usable resources and therefore to the effort that must be made to re-claim one's life.

Regarding the former classical definition of recovery by Bill Anthony [46]: '… a deeply personal, unique process of changing one's attitudes, values, feelings, goals, skills and roles. It is a way of living a satisfying, hopeful, and contributing life even with limitations caused by the illness. Recovery involves the development of new meaning and purpose in one's life as one grows beyond the catastrophic effects of mental illness', Jan Wallcraft, researcher with a lived experience of recovery, reminds us of the often forgotten second part of this prominent recovery definition:

> Recovery from mental illness involves much more than recovery from the illness itself. People with mental illness may have to recover from the stigma they have incorporated into their very being; from the iatrogenic effects of treatment settings; from lack of recent opportunities for self-determination; from the negative side effects of unemployment; and from crushed dreams. Recovery is often a complex, time-consuming process. Recovery is what people with disabilities do. Treatment, case-management and rehabilitation are what helpers do to facilitate recovery [47].

Wallcraft stresses the fact that 'the ownership of the process of recovery [must reside] firmly with the person recovering'. For mental health workers, this brings about new responsibilities for facilitating recovery and working together with users of services and their families and friends in partnership [48].

Also insistence on codesign and co-production of MHS practices, policies and procedures are clear implications of this dialogue [27]. Working in true partnership, of equal power, being part of the writing team and of the formal authorship is directly linked to recovery-oriented services and policies.

30.6 How Do We Implement HR's Enhancing Systems?

It is necessary to implement all these issues at both the levels of policy and practice. Using a human rights framework for both policy and practice needs a sort of 'gene transplant': psychiatry's genotype is about the history and development of institutions, not about individual aspirations and human rights.

> Seven years after the CRPD came into force the care available in many mental health facilities around Europe is still not only of poor quality but in many instances hinders recovery. The level of knowledge and understanding by staff of the rights of people with mental disabilities is very poor. It is still common for people to be locked away or to be chained to their beds, unable to move. Inhuman and degrading treatment is common, and people in facilities are often stripped of their dignity and treated with contempt. Violations are not restricted to inpatient and residential facilities; many people seeking care from outpatient and community care services are disempowered and also experience extensive restrictions to their basic human rights [16].

Deinstitutionalization was a starting point, and even now it is a necessary step that means substituting community for hospital care, and voluntary for involuntary care wherever possible. This could break the traditional nexus between custodial psychiatry and denial of human rights and social exclusion, or marginalization in institutional facilities and generally in mental healthcare.

There is another potential contradiction between the concepts of social inclusion as full citizens and of social integration as person with disabilities. Especially in Italy, some leaders of the service-user movement do not wish to be identified with the disability sector. They want the same rights as all other citizens and decline special consideration due to a disability. Hopefully, these viewpoints can be reconciled.

The issue now is how to form a convergence between historic evolution of getting out of and emerging from the institutions and their hierarchical organizations and together embracing CRPD as stakeholder partners of equal value.

30.6.1 Putting Rights-Based Service into Practice

The World Psychiatric Association issued a guidance for the implementation of community mental healthcare, in order to meet the requirements of CRPD and other associated treaties and conventions [49]. A set of principles is related to the value of community as well as the rights of individuals with mental health problems as persons and citizens. ‘Community mental health services emphasize the importance of treating and enabling people to live in the community in a way that maintains their connection with their families, friends, work and community. In this process it acknowledges and supports the person’s goals and strengths to further his/her recovery in his/her own community’. People must have equitable access to services in the ‘least restrictive environment’, while a community mental health service seeks to foster the service user’s self-determination and his/her participation in processes involving decisions related to his/her treatment and living conditions and recognizing the role of families in providing support and key relationships.

The passage and shift in focus from clinical and functional needs to citizenship rights, the social dimensions of recovery and empowerment are mediated by the role of community-based services as catalysts of resources and opportunities for individuals.

Trieste has been awarded internationally as innovative practice for the implementation of Article 19 of CRPD, that is, independent living and community participation (by the Zero Project in 2014) [50]. There was a complete shift from total institution to a fully community-based service, without barriers, and with a low threshold for access [40, 51, 52]. It has been working without an asylum from 45 years so far, with an open door system, 24 CMH centres, a system of supported accommodation and a small general hospital unit (today only 32 beds for the whole region of 1,200,000). Personal budgets are now the economic instrument to tailor individual recovery and social inclusion plans of care [41], while the integration of mental health services in a system of healthcare districts for community-based medicine (elderly, young and adolescent, disability, specialized medicine, etc.) ensures mainstream healthcare. Social co-operatives provide place-and-train employment in a system of real paid job and advancing career opportunities [40].

Therapeutic practice has been developed with the highest possible degree of freedom and respect, following the principle of respecting the service-user's power of negotiation.

This results in the lowest possible compulsory treatment rate per year (1/10,000) and the low incidence of forensic cases (under 10 in the whole region of population size *X* in the year 2016). At the same time, it has been possible, using a framework of citizenship rights, and inspiring mental health practice with them, to reduce suicide rate by 60% for the last 15 years [51] and violence, whose indicators are the number of patients in forensic care or in jail.

There are an increasing number of good practices related to human rights. These are systematically collected by the Zero Project as innovative practice or innovative policies in the framework of the CRPD [50]. Some are also recommended by the service-user organizations [20]. The WHO and other international organizations (IMHCN) are collecting them in a compendium for widespread dissemination. Often these are small, unique and isolated sound practices in a local context, thus invoking the challenge of how to spread the knowledge about them and to train other people or inspire similar experiences. Some examples of innovative practices in this field are listed in Table 30.2.

30.6.2 The Legal Battle: Advocacy and Legislation

Denial of human rights for people with mental illness is a festering sore, and escalation by the service user/consumer movement is a direct consequence of psychiatry refusing to discuss and negotiate human rights with people with living experience of mental illness who were directly involved in or concerned for their own and others' care. Consumer advocacy for human rights was largely understimated initially by psychiatry service-user organizations, which then engaged with the disability movement, and this led to involvement at the international and UN policy level.

For instance, in Germany, between 2011 and 2013, several landmark decisions by Germany's Constitutional Court and Federal Supreme Court led to a challenge and intense medical, legal and ethical discussions and developments. On the one

Table 30.2 Examples of innovative practices for HRs and recovery

Supported decision-making
– Personal Ombudspersons in Skåne, Sweden
– Traditional models of healing, Western Maharashtra, India
– Non-coercive alternatives to crisis by shared risk and responsibility and precrisis planning, UK
– Peer advocacy (relates also to Article 13 on Access to Justice)
– Advanced directives
Reasonable accommodations
– Reasonable accommodation in the criminal justice system
– Custody matters
– Reasonable accommodations for employment
Stakeholders involvement in care
– Peer support workers
– RACT in Norway and Sweden
Co-production
– Personal budgets for co-planning and delivery (Trieste, Italy, National Disability Insurance Scheme, Australia)
– Recovery services, incl. recovery of carers, recovery houses and crisis respite homes, sponsor or host families
Dialogical approaches
– Open Dialogue (Finland)
– Trialogue (Germany, Austria)
– The assembly model (Italy)—have a say, a voice
– The Mental Health Services (The MHS) Conference and Learning Network of Australia and New Zealand (an interactive crucible for mental health reform co-owned by all stakeholder groups)
– Whole life Action Learning Sets—starting from the personal experience and then working together to define aims (International Mental Health Collaborating Network)
Advocacy
– Associations of citizens and stakeholders: social action and advocacy against stigma and human rights violations (Italy, Spain)

hand, new legal formulations for coercive medication were instated; on the other hand, examples evolved of clinical practice abstaining from coercive medication without an increase of other forms of coercion [53].

Violence, coercion or abuse has been often seen as justified or sometimes even necessary to control a person with psychosocial disabilities. This is linked to insufficient training to defuse or de-escalate difficult situations, overcrowding, lack of supervision of staff, a culture of violence, abuse of power, lack of staff and especially lack of alternatives. It has to be considered as a treatment failure. Every person deserves to be treated with respect and dignity at all times.

The UN Special Rapporteur on torture, Juan Méndez, in his report to the UN Human Rights Council [22], has called for 'an absolute ban on all coercive and non-consensual measures, including restraint and solitary confinement of people with psychological or intellectual disabilities…in all places of deprivation of liberty, including in psychiatric and social care institutions'.

The differences between the two distinct substituted decision-making regimes, mental health and guardianship laws, are pointed out by international bodies. Mental health legislation is characterized as being meant for those with psychiatric diagnoses, with its focus on crisis intervention, involuntary assessment, treatment and detention. The substituted decision-maker is typically the treating clinician, e.g. psychiatrists, and mental incapacity is not a necessary criterion for civil commitment powers under most mental health legislation, at least until very recently, and even then, only in some countries.

Guardianship law applies to all people with impairments affecting mental capacity, in order to determine where 'deficits' are relevant to decisions that need to be made. 'Given the previous points, it follows a less restrictive approach than mental health legislation; the substituted decision-maker is (in ideal circumstances) a trusted person appointed by choice, often comprising a family member but could include public officials, such as a public advocate, financial administrator or a public trustee' [38].

In the mental health field, access to supports to exercise legal capacity could include the use of mental health advance statements or directives; access to informal support networks made up of peers, family members and partners; and the inclusion of mental health advocates and/or those nominated by the person with lived experience of mental illness to assist in healthcare decisions.

The paradigm shift to a rights-based approach to disability encapsulated by the CRPD poses potential challenges for the existing legal frameworks governing involuntary placement and involuntary treatment, taking into account overwhelmingly negative experiences of involuntary placement or involuntary treatment [38].

The European Commission Green Paper [54] already acknowledged that compulsory placement and treatment 'affect severely' 'patients'' rights and 'should only be applied as a last resort, where less restrictive alternatives have failed', and 'medication should be of limited duration'. Moreover, 'any restriction of personal freedoms should be avoided, with particular reference to physical containment' (European Parliament 2006) [38].

According to the European Committee for the Prevention of Torture, there can be no medical justification for forced restraints lasting over several days, and the Committee has deemed this type of mistreatment a violation of the European Convention on Human Rights [55].

For some authors, a 'generic' law, instead of a mental health law, like in the UK, is applicable to all individuals with a serious decision-making problem, whatever its cause; it should be based on decision-making capability, and then it would be consistent with the Article 12 requirement that individuals with disabilities shall 'enjoy legal capacity on an equal basis with others' [56]. In other words, it could only allow involuntary treatment when a person's decision-making capability for a specific treatment decision is impaired—whatever the health setting or cause of the impairment—and where supported decision-making has failed. In addition, involuntary treatment would require an assessment that such treatment gives the person's values and perspective paramount importance [57, 58].

Today in most countries, detention and involuntary psychiatric treatment are not based on impaired decision-making capacity, but on the status of being diagnosed with a mental disorder, often coupled with the risk of harm to self or to others. So informed consent is not just the right way for ascertaining decision-making capacity, as maintained by Freeman et al. [25]. In 12 European member states, these are still the two main conditions justifying involuntary placement, while just in Italy and Spain, no classification of danger in regard to risk levels or thresholds is mentioned [38].

Several cases raised legal controversies and were brought to the European Court of Human Rights, resulting in finding violations of human rights [59].

It is interesting to refer what is happening after a recent Parliamentary Assembly Recommendation of the Council of Europe [60], which concludes that 'any legal instrument that maintains a link between involuntary measures and disability will be discriminatory and thus violate the CRPD', such as the draft additional protocol to the Oviedo Convention (having a 'mental disorder' as the basis of the involuntary treatment and placement). Instead it recommends that the Committee of Ministers 'instruct the Committee on Bioethics to focus its work on promoting alternatives to involuntary measures in psychiatry, including by devising measures to increase the involvement of persons with psychosocial disabilities in decisions affecting their health'. Afterwards the Committee of Ministers has declared, on one hand, that 'involuntary measures in psychiatry must continue to be provided for in the laws of member States', even ensuring they are 'exceptional and used as a last resort in the absence of alternatives', either for a need of care of for preventing harm. On the other hand, it has agreed with the Assembly that 'the utmost should be done to promote alternatives to involuntary measures', through information exchange and sharing of best practices, with a view to the complementary development of guidelines with the direct involvement of disability rights organizations [61].

There is little research about the implementation of the convention into national legislation worldwide. The situation in India has been recently described by Kelly [62], while Battams and Henderson [63] have provided such a study for the context of Australia, and Kleintjes et al. [64] have analysed the specific aspect of mental healthcare user participation in policy development and implementation (cit. in [21]). New Zealand's mental health legislation requires reform to avoid discrimination [65]. The United Nations Committee has recommended that Australia should 'repeal all legislation that authorizes medical intervention without the free and informed consent of the persons with disabilities concerned, committal of individuals to detention in mental health facilities, or imposition of compulsory treatment, either in institutions or in the community, by means of Community Treatment Orders' [28]. In a systematic review, Steinert et al. [21] did not find examples of peer research, i.e. participatory research by mental health service users, and declared: 'Much more evidence is needed for answering the many questions that are posed by the UN-CRPD, such as how inclusion and equality can be realised for people disabled by mental disorders and what impact a change of policies, service provision, legislation, and attitudes would have on their mental health'.

30.6.3 Adopting and Adapting CRPD: The WHO QualityRights Programme

The World Health Organization strategy on HRs is embedded in four cornerstones [66].

1. Raise awareness and advocate for change, especially related to HRs violations—which often occur behind closed doors and go unreported.
2. Develop mental health policies and laws that promote human rights.

   Mental health policies and laws are absent or inadequate in most countries of the world, and yet they are critical to improving conditions for people with mental disabilities. WHO, in the framework of the Action Plan, is monitoring the implementation of legislation worldwide. While about a half of member states have a stand-alone mental health law (and 2/3 a policy or plan for mental health), only 42% of countries cover all the five main HRs (transition to community-based services, legal capacity, alternatives to coercive practice, procedures to protect rights and file complaints, inspections of HRs conditions by an independent body). In detail, 67% of countries' legislation promotes rights of people with mental disorders to exercise legal capacity, and 75% promotes 'least restrictive care' or alternatives to coercive practice [67].
3. Create mechanisms to assess and improve human rights conditions.

   Taking into consideration that many people with mental disabilities (assumed to have no capacity to make decisions for themselves) are detained in psychiatric institutions unjustifiably and against their will, the WHO works to unite and empower people to improve the quality of care and promote human rights. To this end, the WHO has launched the 'The QualityRights Programme' [68] which aims to improve both quality and human rights conditions in inpatient and outpatient mental health and social care facilities and empower organizations to advocate for the rights of people with mental and psychosocial disabilities.

   The WHO QRs Programme specifically helps to promote human rights, recovery and independent living in the community; to support improvements on the ground and at policy level; and to promote participation of people with mental health conditions. Its toolkit is an important means to assess and promote the implementation of the five core articles (n. 28, 25, 12, 14, 19) of the CRPD, and it has been already used in several countries, e.g. India, Afghanistan, Somalia, Egypt, Tunisia, Spain, Greece.
4. Train key stakeholders on the rights of people with mental disabilities.

   Training needs to be provided to:

- People with mental disabilities themselves as well as their families—so that they can claim their rights
- Health and mental health professionals—so that they understand the rights of their patients and apply these in practice

– The police force who are in daily contact with people with mental disabilities
– Lawyers, magistrates and judges who make important decisions concerning the lives of people with mental disabilities [66]

Recently, relevant training materials related to capacity building on human rights and recovery have been developed by WHO HQs in Geneva and are now available online. Capacity building on human rights issues among all stakeholders is seen as one of the most relevant means for training.

30.7 Ways Forward

Efforts towards a realistic way forward include calls for a broad discussion including mental health practitioners and a wide range of service user groups and family carers as well as specific interventions such as reform of guardianship laws or the promotion of advance directives in mental healthcare [24] and systematizing the implementation of a wide range of evidence-based approaches to decreasing involuntary care of all types, including the subcategories of forced medication and psychiatric incarceration, seclusion and restraint [2].

The international recognition of mental health as a global health imperative led to its inclusion within the 2030 Sustainable Development Agenda, as far as specific objectives are concerned [69]. It has been officially recommended to 'mainstream the right to mental health into health, poverty-reduction and development strategies and interventions, and explicitly include it in general and priority health policies and plans' [31].

The Special Rapporteur on Article 25 has particularly recommended a paradigm shift to community-based, recovery-driven psychosocial approaches (see Table 30.3).

Table 30.3 From recommendations of Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health [31]

To ensure that healthcare services guarantee the right to mental health for all, States should:
(a) Ensure that users are involved in the design, implementation, delivery and evaluation of mental health services, systems and policies
(b) Stop directing investment to institutional care and redirect it to community-based services
(c) Invest in psychosocial services that are integrated into primary care and community services to empower users and respect their autonomy
(d) Scale-up investment in alternative mental health services and support models
(e) Develop a basic package of appropriate, acceptable (including culturally) and high-quality psychosocial interventions as a core component of universal health coverage
(f) Take targeted, concrete measures to radically reduce medical coercion and facilitate the move towards an end to all forced psychiatric treatment and confinement
(g) Seek technical assistance from the WHO QualityRights initiative to assess and improve the quality of mental healthcare

30.7.1 A Practice of Liberation and Freedom

Any bold and uncompromising or non-negotiable assertion of the CRPD, by advocating its full list of claims for rights of individuals as 'the only way', will throw up many obstacles to overcoming social barriers to its fullest possible implementation. A more realistic possibility seems to be a focus on decreasing involuntary care and social exclusion in institutions and in society, with a social movement fostering political and social action combined with a change of institutional practice and thinking in mental health and social care.

Liberation is the unshackling and unlocking of the doors which allows us to breathe unfettered, so we can exercise and practise freedom.

Thus we need to explore particularly the issue of liberation and freedom in care processes, as opposed to a habitual culture of violent threat or physical isolation and restraint and denial of subjectivity.

'Liberty is therapeutic' was in the 1970s the motto in the Trieste experience, when the psychiatric hospital was definitely overcome and closed down. 'Freedom first' (Muusse, Van Rojen), the new slogan of the international movement for better care in a rights-based and person-centred approach, emphasizes that personal liberty is not the outcome but a precondition for care which overturns control mechanisms and supersedes them with people empowerment.

Which practices can promote freedom? Can they be described and operationalized? Which are related indicators? What connects keywords such as open door, open dialogue, free access and community engagement?

A service should question about the use of seclusion and compulsion as means to regulate behaviours, the gap in power driven by a paternalistic attitude and the access to opportunities and resources (a mere 'clinical' vs a 'comprehensive' and 'integrated' approach).

There are basic issues related to the system and the practice, e.g. to what extent empowerment is conditioned or limited by:

- The easy access to detention because of legislation
- The presence of locked units even in the more open system of care
- The lack of a clear open door policy
- The lack of low-threshold, easy and friendly access to services
- The lack of response to basic social needs and rights
- The lack of a discourse based on negotiation within trusting therapeutic relationships

We can think of gestures, small actions and incremental changes in practice, but it is needed a whole system change/a change of the thinking (recovery—whole life learning).

30.7.2 From Dialogue to Trialogue

A community approach is premised upon a co-responsibility among the users, their family and the service, in the search for the widest possible consensus and sharing, a constant willingness to seek solutions, a therapeutic exchange and the constant interaction/exchange between inside and outside.

The most effective method is that of recognizing the other's point of view and being truly interested in that person through an honest, frank, warm discussion, which does exclude a direct and 'hard' confrontation between operator and patient.

Clearly, human technologies are the most difficult to reproduce because they require the construction of reciprocal spaces and authenticity. On each occasion, they are activated in a unique way based on experimentation between oneself and the other and thus cannot be either predisposed or taken for granted.

Many dialogical practices and programmes, or approaches, are now developing more and more, stemming from a proper therapeutic field, by involving the person's whole social network, as in the Open Dialogue, a 'way of life' [70], or as a form of community awareness, through stakeholder representatives, e.g. in the whole life Action Learning Sets, recovery and discovery communities [35].

On issues such as the contentious request of replacing all substituted decision-making by supported decision-making altogether, we need a culture and practice of discussion and discourse between all stakeholders that allows us to think through and come up with realistic steps forward while not losing the vision of the CRPD. Trialogue groups with their long tradition of communication between (ex)service-users, family carers and friends and mental health workers beyond stereotypes can play a vital role in this phase of development of a rights-based approach to mental health problems and crises. In Trialogue, three main groups of individuals who have most experience with psychiatric problems and disorders and with the mental health system come together on neutral ground—outside familial, institutional and therapeutical/professional hierarchies and intra-stakeholder group clusters—in order to communicate on an equal footing. This training ground is gaining importance when the goal is advancing recovery orientation and a human rights-based approach in psychiatry [71].

The WPA commitment to a partnership approach based on human rights (WPA Madrid Declaration on Ethical Standards for Psychiatric Practice 2011) [72] is echoed by WAPR's 2015 policy document and statement supporting CRPD guidance and urging its incorporation, also in daily practices in the field of rehabilitation [73].

While recovery orientation [74] and a rights-based approach is requesting choice among a set of offers, even access to a range of evidence-based clinical and psychosocial interventions and service delivery systems is patchy. They are still far from being able to be taken for granted, and consistent access to them is in dire need for advocacy efforts from all stakeholders [75].

30.7.3 The Prospect of a New Legal Vision

In legal terms, are we going towards a 'disability-neutral' mental health?

> Mental health law fails to respect the 'autonomy' or right to 'self determination' of the patient in psychiatry in the same way as capacity-based law does for all other patients. Mental health law is thus discriminatory. There must be a generic law covering all persons who lack decision-making capability…The concept of 'will and preferences', used frequently in the CRPD, could be helpful. 'Involuntary' (if that remains the right term) interventions could be justified when a person is unable to express their will and preferences or when their currently expressed will and preferences are not their 'enduring' or 'authentic' will and preferences (as might occur during a confusional state) [76].

The new legal situation brought about by the CRPD with its freedom rights as well as with its far reaching entitlement rights has been widely accepted by the international community (172 ratifications by March 2017).

Anyway:

> There is a commonly held, yet false, assumption that people with mental health conditions lack the capacity to assume responsibility, manage their affairs and make decisions about their lives. These misconceptions contribute to the ongoing marginalization, disenfranchisement and invisibility of this group of people in their communities…One of the underlying reasons it is difficult to move through the obstacles to fully embrace the CRPD, is that discrimination continues to affect people with mental health conditions on many levels. Changing laws is only a partial solution. We have to change the ways that we relate to each other at every level, and to offer people information and tools to make the transition to a more equitable social reality [16].

The implementation of this new way of thinking and the actions consequently to follow will take time. They will only happen if service users, former service users, family carers and friends, mental health professional and human rights advocates fight for and gain consensus and solidarity on some points, such as choice of support in the community, alternative crisis intervention settings and participatory policy-making and research in order to lobby and gain support from relevant policymakers and civil society.

30.7.4 Practices Can Be Rights-Based

This goal should not stand alone but be offered in tandem with improving evidence-based, recovery-oriented mental health interventions and service delivery systems which are congenial to both service users and their families and which can reliably result in optimal outcomes. Availability, accessibility, acceptability and quality in community-based treatments are pointed out as the main features of a shift from services to personalized care and support [31].

It is really difficult to define what is innovation and which are good or even best practices, if not within certain parameters, e.g. according to ethics, evidence and/

or service-user and family satisfaction and experience. We don't only need evidence-based, but also values-based practices and services [77, 78], embedded in a firm ethical framework. Moreover, there are evidence-based practices and practice-based evidences, i.e. some evidences of good practices are rooted in the experience of care [79].

Issues related to the base of evidences, replicability, sustainability and feasibility are also to be considered for their acceptance and dissemination.

In defining best practices, we need to be clear and consistent about the evaluative criteria that make them so, together with minimum requirements for their operationalization according to local variability. A best practice in one place may not be so in another. Similarly, it is also needed to distinguish between practices that are innovative (but not yet determined as best practice) versus those that have been subjected to assessment and found to meet the selected criteria.

Substantive rights are imperative and non-negotiable, and they represent mainly an individual freedom to do or to be without others' consent, but they can remain abstract. Proclaiming equality can leave inequality based on power untouched. They are limited by others' rights or ethical validity, or simply power balance. They can be not ethical, for instance, if they don't touch the distribution of resources in a welfare state crisis [80].

Rights are connected to citizenship, then to a welfare state, to participation to a society and hence to democracy and social justice and equality. Improving individual competencies is another way to reach the optimal level of independent functioning in the society [81]. Certainly the most relevant level is the (whole) system (without large closed institutions) and not just a single isolate programme; but small programmes and projects, even when they are certainly not mainstreaming in a whole system, can be exemplary, true seeds of change.

30.8 Conclusion: Individuals vs Community, from Voluntary Care to Participation

In democratic societies that demand a balance between upholding the rights of people with psychosocial disabilities, e.g. SPMI, and the rights of the community, what are the keys to satisfying both? There are two main ways. One, and initially the easiest to implement, is to systemize an evidence-based range of ways of minimizing involuntary care [2]. 'De-stigmatising mental illness involves abandoning the use of invasive and inhumane practices as well as those practices based on the custodial approach' (European Parliament 2009) [38].

The second and more enduring way is to make key changes to allow full participation by consumer and family groups in the governance, structure and function of services and to provide them with formal regular input into mental health law reform and challenges of public and governmental discrimination, as they affect individuals with SPMI. Simultaneously the power imbalance in services between service users' families and service providers must be addressed [2].

Optimizing strategies to decrease involuntary treatment can be achieved by systematizing practices which foster therapeutic engagement and alliances and which

favour consultative and collaborative care with service users and their families. These should include early detection and intervention strategies, convenient access to services and facilities, and mobile, flexible, respectful, welcoming and age-appropriate engagement practices, joint decision-making strategies, jointly constructed individual treatment and recovery plans, early warning sign/relapse signature plans and advance directives, as well as involving routine and regular consultation with individual consumers and their families. These strategies have well-established or promising evidence bases, but few mental health services systematically apply them. Applying evidence-based strategies of minimizing coercive practices like seclusion and restraint is an important subset to achieve this goal [2].

Social inclusion, welcoming and valuing of the continuing input of service users and families and human rights advocates are the keys to upholding human rights in the reform of mental illness services and laws.

Whether in both high-income and medium- to low-income countries, the goal of continuous significant lowering of the frequency and length of involuntary and/or coercive care, with stepwise practically achievable targets, is less absolutist and more attainable than the stance taken in CRPD, but it is no less rigorous or ambitious.

However, the new frontier is not about divergent and alternative paths: it is not just about fighting against old and new asylums (i.e. against involuntary treatments and institutional placements), and developing community-based services and reforming legislation, versus advocating for citizen's rights and empowering people with mental health conditions. We need to forge an amalgam or convergence of both strategies.

While many in psychiatry currently believe that CRPD is too idealistic and absolutist to be practically applied in totality to present-day psychiatry, there is an emerging evidence base for the proposition that optimizing human rights is inherently therapeutic and contributes to healing and that the restoration of both liberty and full citizenship is a precondition for mental health and wellbeing. A more positive and constructive view that more of us could share is that CRPD is setting the direction not necessarily just for today's deliberations, but it has set the horizon we aspire to reach and explore for the future.

Achieving equity of human rights also entails challenging social exclusion and inequality, by acting on social determinants of health to achieve greater equity of quality and stability of home, work, income, supports, relationships and social participation.

Political, legal and social action has to be combined with our own emancipation as clinical professionals from institutional thinking and practices in mental health and social care, to vastly improve the prospects of a whole life and full citizenship and rights for persons with psychosocial disabilities.

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Public Mental Health

31

Jonathan Campion

Abstract

Globally, mental disorder and self-harm accounts for 22.0% disease burden (as measured by years of healthy life lost to disability). Even this figure underestimates the large burden which is due to a combination of high prevalence, most lifetime mental disorder arising before adulthood, and mental disorder having a wide range of impacts. These impacts include higher rates of health risk behaviour, physical illness (non-communicable and communicable) as well as reduced life expectancy, educational and employment outcomes. Annual global economic cost of mental illness was estimated to be $2493 billion in 2010 and projected to grow to $6046 billion by 2030. A range of cost-effective evidence-based interventions exist to treat mental disorder, prevent associated impacts, prevent mental disorder from arising and promote mental wellbeing including for those recovering from mental disorder. Many such interventions also result in early net economic savings which can be calculated at national, regional and local levels. However, coverage of public mental health interventions is poor: Only a minority of people with mental disorder receive treatment even in high-income countries with far less coverage in low- and middle-income countries. Even lower coverage occurs for interventions to prevent associated impacts such as premature mortality, prevent mental disorder from arising or promote mental wellbeing. The public mental health intervention gap has a broad range of impacts and associated economic costs. Public mental health practice takes a population approach to mental health and facilitates improved provision, outcomes and coordination of public mental health interventions to sustainably reduce burden of mental disorder and promote population mental health. Assessment of the size, impact and cost of the

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national, regional or local public mental health intervention gap supports improved coordination with other sectors, strategic planning, advocacy for resourcing and improved coverage of interventions. Public mental health capacity can also be enhanced through education and training, settings based approaches, use of technology, implementation of mental health policy, legislation and adopting a human rights approach to access. Public mental health practice facilitates better integration between different sectors and appropriate resourcing which can be supported by estimating the local impacts of improved coverage of public mental health provision including associated economic savings.

31.1 Introduction

Public mental health takes a population approach to mental health which includes treatment of mental disorder, prevention of associated impacts, prevention of mental disorder and promotion of mental wellbeing. It considers both outcomes and coverage of these interventions including for higher-risk groups. Such an approach facilitates improved coordination and provision of public mental health interventions as well as reduced associated inequalities.

This chapter on public mental health considers the impact of mental disorder and wellbeing, public mental health interventions and their economic impacts, the implementation gap, assessment of public mental health unmet need and action to address this unmet need in order to realise the broad range of associated opportunities.

31.2 Impact of Mental Disorder

Mental disorders account for a large and growing proportion of disease burden which systems need to address. Burden of disease for any country can be assessed using the disability-adjusted life year (DALY) which is a time-based measure combining years of life lost (YLL) due to premature mortality and years of healthy life lost to disability (YLD) [1]. Since the majority of lifetime mental disorders arise before adulthood and are chronic or intermittent, burden of disease for mental disorder as measured by YLD is higher than by either DALY or YLL and higher than for cardiovascular disease, cancer or communicable disease and maternal, perinatal and nutritional causes (Table 31.1). The most recent global burden of disease assessment estimated that the global proportion of burden of disease due to mental disorder and self-harm was 22.0% as measured by YLD compared to 8.6% as measured by DALY [1] although this varies between countries and regions. For instance, across the European region, proportion of burden of disease due to mental disorder and self-harm was higher at 24.4% as measured by YLD and 12.8% as measured by DALY [1]. Furthermore, between 1990 and 2010, absolute disability-adjusted life-years (DALYs) due to MNS disorders increased by 41% [2].

However, even these WHO figures are underestimates since they do not take account of the interconnectedness between mental disorder and other health conditions [3] or associated excess mortality. Furthermore, they do not include several

Table 31.1 Global and European burden of disease due to mental disorder compared to cardiovascular disease, musculoskeletal disease and cancer as measured by years of healthy life lost to disabilities (YLDs) and disability-adjusted life years (DALYs) (2015) [1]

	Global (YLDs) (2015) [1]	Global (DALYs) (2015) [1]	European region (YLDs) (2015) [1]	European region (DALYs) (2015) [1]
Population (millions)	7344.4	7344.4	904.5	909.9
Total burden	719,536,456	2,668,295,388	97,078,335	297,475,942
Mental disorder and self-injury				
• Childhood behavioural disorders	6,386,066	6,386,066	611,998	611,998
• Depressive disorders	54,214,632	54,214,632	7,669,698	7,669,698
• Anxiety disorders	24,621,020	24,621,020	3,422,458	3,422,458
• Bipolar disorder	8,997,662	8,997,662	1,313,406	1,313,406
• Schizophrenia	15,010,219	15,632,692	1,736,693	1,814,131
• Eating disorder	1,385,112	1,506,392	285,426	303,719
• Autism and Asperger's syndrome	10,044,578	10,044,578	1,176,465	1,176,465
• Alcohol use disorder	7,890,008	13,048,894	1,716,065	3,826,375
• Drug use disorders	9,843,656	17,628,729	1,758,294	3,832,886
• Other mental and behavioural disorder	9,606,273	9,606,273	1,365,031	1,365,031
• Alzheimer's and other dementias	9,894,627	28,972,839	2,609,166	7,178,132
• Self-harm	332,498	37,672,153	60,362	5,543,179
Mental disorder and self-harm (total)	158,226,351	228,331,930	23,725,062	38,057,478
% of total burden	22.0	8.6	24.4	12.8
Cardiovascular disease (total)	25,598,512	407,636,500	4,760,373	78,819,290
% of total burden	3.6	15.3	4.9	26.5
Musculoskeletal disease (total)	103,817,908	107,885,833	16,727,281	17,171,726
% of total burden	14.4	4.0	17.2	5.8
Cancer (total)	8,560,368	243,650,521	2,391,405	51,140,969
% of total burden	1.2	9.1	2.5	17.2
Communicable, maternal, perinatal and nutritional	113,631,997	829,418,902	10,316,240	25,767,215
% of total burden	15.8	31.1	10.6	8.7

mental disorders occurring in childhood (e.g. emotional disorder) and adulthood (e.g. somatoform disorder and personality disorders). An even larger proportion of population experiences subthreshold mental disorder which increases risk of transition to mental disorder and also has a broad set of impacts.

A number of important reasons explain the large size of impact of mental disorder:

31.2.1 Prevalence

Mental disorders are common and affect a considerable proportion of a population at any one time. For instance, 12-month global prevalence was 9.8–19.1% for anxiety, mood, externalising disorders (ADHD, oppositional defiant disorder and conduct disorder) and substance use disorders and 0.8–6.8% for serious mental illness [4] with rates varying by region and country. Another study summarising data from 27 EU member states, Iceland and Norway estimated that 31.2% of the European population (136.2 million people) had experienced a mental disorder in the previous year [5]. In India, at least 20% of the population has a mental disorder which requires treatment [6]. Mental disorder also affects 10–20% of children and adolescents worldwide [7]. Burden disproportionately falls on low- and middle-income countries (LMICs) where 80% of people with mental disorder live [3].

31.2.2 Mental Disorders Start Early in the Life Course and Are Often Long-Standing

Majority of lifetime mental disorders arise during childhood and adolescence with half of lifetime mental disorder arising by age 14 and three-quarters by the mid-20s [8, 9] which is several decades before most other types of illness. Furthermore, once mental disorders have arisen, they are often chronic and recur throughout the life course. Table 31.2 highlights the age at which different mental disorders begin [8].

Table 31.2 Age of onset of mental disorder: average age at which 25–75% of different mental disorders begin [8]

Mental disorder	Age at which 25–75% of lifetime mental disorder arises
Impulse control disorders	
• Oppositional defiant disorder • Conduct disorder • Attention deficit hyperactivity disorder (ADHD)	7–15 years 9–14 years 7–9 years
Anxiety disorders	
• Phobias • Panic disorder, generalised anxiety disorder, PTSD	7–14 years 25–53 years
Mood disorders	25–45 years
Psychosis	Late teens to early 20s
Substance disorders	18–29 years

31.2.3 Mental Disorders Have a Broad Range of Impacts

During childhood and adolescence, impacts of mental disorder include a several-fold increased risk of different health risk behaviours (such as tobacco smoking, alcohol use, drug misuse, self-harm, physical inactivity and poor diet), physical illness (both communicable and non-communicable), school exclusion (Table 31.3), worse educational outcomes and offending [11, 12].

Mental disorder during childhood and adolescence subsequently results in a broad range of adverse impacts during adulthood [11, 12]: Health-related impacts include higher rates of adult mental disorder [13], health risk behaviours, physical illness (both communicable and non-communicable) [3, 14–16] and 10–20-year reduced life expectancy although this is worse where universal health coverage is unavailable. Globally each year, more than 8 million people die from mental disorder [17].

The largest cause of premature mortality in people with mental disorder is associated with physical disease and in particular cardiovascular disease. In LMICs, excess mortality is similar with the large majority dying from physical illness especially infectious illness [18]. Furthermore, a large proportion of the 804,000 suicides occurring across the world each year [19] are by people with mental disorder [20, 21]. For instance, mental and substance use disorders were estimated to be responsible for 62% of DALYs allocated to suicide [22].

A large proportion of overall health risk behaviour is by people with mental disorder. In the case of smoking which is the single largest cause of preventable death and responsible for 11.5% of global deaths (6.4 million) in 2015 [23], 43% of smokers aged 11–16 in Great Britain have either emotional or conduct disorder [10], while 42% of adult tobacco consumption in England is by people with mental disorder [24]. Since a large proportion of health risk behaviour also arises before adulthood and is associated with onset of mental disorder and subsequent physical illness, this represents a key public health opportunity [11].

Table 31.3 Levels of different health risk behaviours (smoking, alcohol use, drug use and self-harm) and exclusion in 11–16-year-olds in Great Britain with emotional and conduct disorders compared to national levels [10]

Health risk behaviour in 11–16-year-olds in Great Britain	Emotional disorder (5% of 11–16-year-olds in Great Britain) (%)	Conduct disorder (7% of 11–16-year-olds in Great Britain) (%)	National (Great Britain) (%)
Smoke regularly	19	30	6
Drink alcohol twice a week	4	10	3
Ever drug use	20	28	9
Ever self-harmed (self-report)	28	21	7
Have no friends	6	8	2
Excluded from school once	4	15	2

Mental disorder also impacts on areas outside health including educational and employment outcomes, socioeconomic deprivation and debt, social skills development, crime, violence both victimisation [25] and perpetration [26] as well as stigma and discrimination [11, 12]. For instance, 80% of all crimes (including violent crime) in Britain are committed by people who had conduct disorder and subthreshold conduct disorder in childhood and adolescence [27]. Furthermore, impacts are intergenerational with maternal mental disorder a risk factor for child undernutrition [28].

The large disease burden results in high economic costs: In 2010, the estimated annual global economic cost of mental illness was US$2493 billion with US$823 billion as direct costs and US$1671 billion as indirect costs reflecting the broad range of impacts [29]. However, these costs are projected to grow to US$6046 billion by 2030. Even when using DALYs to assess impact which underestimates the burden due to mental disorder (Table 31.1), estimated costs of mental illness during 2011–2030 were US$16,300 billion with US$7300 billion costs incurred by LMICs. Another study estimated €523.2 billion annual costs of mental disorder in the European Union [30].

31.2.4 Lack of Coverage of Effective Public Mental Health Interventions

Only a minority of people with a mental disorder receive any treatment even in higher-income countries, while coverage of interventions to prevent associated impacts, prevent mental disorder from arising and promote mental wellbeing is far less (see Sect. 31.8). This implementation gap results in preventable suffering, a broad range of impacts, associated costs and unnecessary perpetuation of disease burden.

31.3 Public Mental Health Interventions

A range of effective public mental health interventions exists across the life course [11, 12] which would have large impacts across different sectors with appropriate coverage. Public mental health interventions can be divided into mental disorder treatment, mental disorder prevention and mental wellbeing promotion. Another way of considering public mental health interventions is by mental disorder prevention and mental wellbeing promotion at primary, secondary and tertiary levels as outlined in the next sections.

As for other diseases such as cardiovascular disease, treatment alone is not enough to sustainably reduce burden of mental disorder with an Australian study showing that even if everyone with mental disorder received best available treatment, disease burden would be reduced by only 28% [31].

31.4 Prevention of Mental Disorder

Mental disorder can be prevented at primary, secondary and tertiary levels as is the case for other disorders [12, 32]:

1. Primary prevention: Prevention of mental disorder occurring by addressing risk factors
2. Secondary prevention: Early identification of mental disorder to treat and prevent its progression
3. Tertiary prevention: Working with people with established mental disorder to prevent associated impacts and relapse as well as promote recovery

Each level of prevention requires implementation of different types of evidence-based interventions by different organisations. Effective coordination of the work of different organisations is facilitated by an assessment of levels of risk factors, mental disorder and appropriate level of coverage of interventions according to need [33, 34].

For each level of prevention, groups at higher risk of mental disorder require proportionately greater levels of intervention to prevent widening of inequalities [11, 12, 35, 36]. Examples of child and adolescent groups with several-fold increased risk include children with special education needs, physical illness, with a parent with mental disorder, children looked-after (by the state) and young offenders. Examples of adult higher-risk groups include those from particular ethnic backgrounds, people with learning disability, women during the perinatal period [37], carers [38], homeless people, offenders [39] and lesbian, gay, bisexual and transsexual people. While higher-risk groups benefit more from prevention, larger groups at less elevated risk also benefit. Therefore, a proportionate universalistic approach towards different levels of prevention and promotion can both target higher-risk groups and accommodate larger population groups. Selective prevention refers to interventions which target such higher-risk groups, while indicated prevention targets individuals identified as having increased risk for a disorder but who are asymptomatic.

31.4.1 Primary Mental Disorder Prevention

Prevention at a primary level involves addressing relevant risk factors. The number of people with a particular disorder is directly related to the average level of the underlying symptoms or risk factors in the general population [40, 41] so that greater levels of risk factors for mental disorder in a population or specific group are associated with higher rates of mental disorder.

A public health approach recognises wider determinants and lifelong impact of mental health. As for action on cardiovascular disease, addressing such

determinants is important to prevent mental disorder and promote mental wellbeing [11]. A population approach takes account of the size of impact of different factors, the proportion affected by such factors and levels and outcomes of effective interventions to address such factors which can be assessed in a structured way [12, 32–34]. A small population decrease in the level of risk factors can thereby result in significant reduction in levels of mental disorder and suicide.

Risk occurs by an interaction between genetic, psychological, social and environmental factors. Their interaction is mediated by hormonal/stress response and inflammatory pathways. Epigenetics describes modifications to genetic material which influences how genes function without changing DNA sequence and is likely to be a key mechanism mediating impact of risk factors, e.g. sexual abuse history linked to antisocial behaviour is associated with hyper-methylation of serotonin transporter gene [42].

During childhood and adolescence, factors associated with increased risk of mental disorder include [11, 12, 33]:

- Genetic factors.
- Factors during pregnancy and at birth:
  - Low birth weight [43].
  - Smoking during pregnancy is associated with increased risk of conduct disorder [44] and ADHD [45].
  - Alcohol consumption during pregnancy which is associated with increased risk of conduct disorder, hyperkinetic disorder and intellectual disability [46].
  - Premature birth is associated with increased risk of mental disorder in offspring [47].
  - Maternal disorder during pregnancy is associated with premature birth and low birth weight [48]. Maternal stress during pregnancy is associated with child behavioural problems and impaired cognitive and language development.
- Socioeconomic factors such as poverty [49] and household income [50] underpin many other risk factors for mental disorder [35]. For instance, socioeconomically disadvantaged children 2-3 times more likely to develop mental disorder [50].
- Food insecurity [51].
- Socio-demographic factors such as gender, age, ethnicity and family type. For instance, children from one-parent families have twofold risk of mental disorder compared to children from two-parent families [10].
- Parental factors:
  - Poor quality of early attachment relationships [52] which may have greater impact in LMICs [53].
  - Parental mental disorder affects 20% of parents [54] and is a significant predictor of lifetime onset of mental disorder in their children [55]. Level of increased risk is similar for maternal and paternal mental disorder [56]. Parental mental disorder also leads to poor infant growth [53].
  - Parenting which is one of the most consistently powerful influences on emotional and behavioural development of children [27]. Furthermore, the asso-

ciation between childhood conduct problems and variables such as large family size and single parenthood may be largely mediated by parenting practices [57]. Poor parenting is associated with increased risk of conduct disorder in childhood [58] and negative child emotional outcomes [59], while non-physical punishment is associated with increased risk of child mental disorder [60].

  - Parental employment [10, 61].

- Adversity and abuse: Childhood adversity accounts for 30% of all mental disorders and is one of the strongest predictors of mental disorder particularly when associated with maladaptive family functioning (such as parental mental disorder, child abuse, neglect) [62]. Child adversity is moderately associated with adult smoking, heavy alcohol use, poor self-related health, cancer, heart disease and respiratory disease (OR 2–3), strongly associated with adult mental ill-health, problematic alcohol use and sexual risk taking (OR 3–6) and most strongly associated with adult problematic drug use and interpersonal and self-directed violence (OR > 7) [63]. Impact of bullying [64] on risk of developing mental disorder is long term [65]. In England, child abuse is associated with increased risk of depression (OR 2.9), PTSD (OR 4.0), psychosis (OR 2.7), alcohol dependence (OR 1.8) and drug problems (OR 2.1) [66]; repeated sexual abuse during childhood and adolescence is associated with even higher rates of adult mental disorder including depressive disorder (OR 6.2), PTSD (OR 6.8), probable psychosis (OR 15.3), alcohol dependence (OR 5.2), eating disorder (OR 11.7) [66] and attempted suicide (OR 9.4) [67]. Maltreatment also worsens the course of mental disorder [68]. The scale of child abuse in combination with the size of risk impact highlights the need for urgent action since over half of all children aged 2–17 years (1 billion children globally) experienced emotional, physical or sexual violence in the previous year [69], while a quarter of adults report being abused as children and a fifth of women report being sexually abused as a child [70].
- Screen time which is the main waking activity of children in high-income countries [71, 72] is associated with poor wellbeing [73], depressive symptoms, psychological distress [74], self-harm and suicidal ideation [75]. Screen time also displaces many other activities such as physical activity, play and socialisation which are important in promoting mental health. Evidence suggests a dose-response relationship where each additional hour of viewing increases the likelihood of experiencing socio-emotional problems [76]. Studies also suggest screen time has a direct impact on mental health; exposure to television before the age of 3 is associated with increased risk of attention problems by the age of 7 [77], while screen time in teenage years is associated with increased risk of attention problems, learning difficulties, long-term academic failure [78] and psychological difficulties [79].
- Alcohol consumption and associated alcohol use disorder are associated with price, availability, marketing and licensing [80]. Alcohol, tobacco and drug use are several times more common in children and adolescents with mental disorder (Table 31.3) which highlights the need for early targeted approaches for both treatment and prevention.

- Other child factors including special education needs and physical illness [10].

During adulthood, factors associated with mental disorder include [11, 12]:

- Socio-demographic factors such as gender, age, ethnicity and marital status.
- Socioeconomic-related factors including deprivation [35], lower household income [81, 82] and other related factors including food insecurity [51], inadequate housing, fuel poverty [83], unemployment [82] and recession [84]. In particular, debt appears to be a key mediator between lower household income and increased risk of mental disorder [85, 86].
- Childhood mental disorder [13, 87, 88].
- Employment-related issues such as job strain, effort-reward imbalance, low decision latitude, high demands, job insecurity [89], excessive hours [90], workplace bullying [91] and jobs of poor psychosocial quality [92].
- Physical illness: For instance, risk of depression is doubled in people with diabetes, hypertension, coronary artery disease, heart failure and cancer, tripled in those with stroke, end-stage renal failure and COPD and more than seven times more common among people with two or more chronic physical conditions [93]. Furthermore, comorbidity complicates help seeking and treatment [3].
- Smoking [94, 95].
- Violence [2, 70, 96] including domestic violence [97], conflict and complex emergencies [98–100], alcohol-related violence (associated with 53% of violent crime in England and Wales) [101] and violence towards particular groups such as older people [102].
- Social isolation and poor social capital including in low-income countries [103, 104]. Social isolation also results in early mortality [105].
- Dementia: Potentially modifiable risk factors include lack of childhood education (responsible for 8% of risk), midlife hearing loss (9%), smoking (5%), depression (4%), lack of exercise (3%), social isolation (2%), hypertension (2%), diabetes (1%), obesity (1%) [106] and affective disorders [107].

Interventions which address risk factors can prevent subsequent mental disorder and associated impacts. Childhood is a key prevention opportunity since most mental disorder arises before adulthood, and childhood mental disorder is also a risk factor for adult mental disorder. Both prevention and early treatment prevent a range of associated impacts across the life course. Prevention at primary level can dramatically reduce the development of mental disorder. For instance, new episodes of major depressive disorder can be reduced by 25–50% when preventive interventions are offered in stepped-care format [108].

While risk factors such as family type may themselves not be amendable to intervention, they indicate those at higher risk of mental disorder who disproportionately benefit from prevention interventions. Examples of interventions which address important risk factors include [11, 12]:

- Actions to reduce socioeconomic inequalities: Lower household income is associated with increased risk of mental disorder in childhood, adolescence and

adulthood [10, 50, 81]. Since inequality and deprivation are underlying drivers for a range of other risk factors for mental disorder [35] and other conditions, they are particularly important to address although this requires political will. If all children had the same risk as the most socially advantaged, this would result in reduction of 59% for conduct disorder, 34% for emotional disorder and 54% for hyperkinetic disorder (birth cohort studies) [109]. A range of evidence-based interventions can reduce health inequalities [110, 111] although national government policy including taxation is also important. More specific interventions include prevention and action to address debt [86] and fuel poverty [112].

- Parental support: Interventions targeted at mothers include smoking cessation [113, 114], brief interventions for alcohol misuse during pregnancy, interventions to prevent prematurity [47] and low birth weight, breastfeeding support and home visiting programmes. Interventions for parents include parent training programmes which can prevent antisocial behaviour and delinquency [115] but also have a broader range of impacts on both parent and child including reductions in unintentional injury and abuse of children by parents [116] as well as antisocial behaviour by their children [13]. Home visiting programmes reduce child behavioural problems [117].
- Other parental interventions include prevention, early detection and treatment of parental mental disorder [48] with parental treatment reducing risk of childhood mental disorder by 40% [118]. Maternal postpartum depression can be prevented through psychosocial and psychological interventions [119] with some evidence for interpersonal therapy, CBT [120] and peer support [121, 122].
- Addressing food insecurity [123]
- Action to address child adversity which is responsible for a large proportion of adult mental disorder [62, 63]: This highlights the importance of both prevention and early intervention to address child abuse through parenting programmes [116, 124], home visiting programmes [117], school-based programmes to prevent violence [125] including bullying [126] and sexual abuse [127], safeguarding to address child abuse, prevention of alcohol misuse [80] and addressing domestic violence [128]. Seven strategies for reducing violence against children include implementation and enforcement of laws, norms and values, safe environments, parental and caregiver support, income and economic strengthening, response and support services and education and skills [129].
- Early detection and treatment of childhood mental disorder which prevents a proportion of adult mental disorder [130, 131].
- Employment-related stress and mental disorder through workplace-based interventions [132, 133].
- Social isolation through volunteering, befriending services, time banks, learning, arts and other community activities [12].
- Prevention of depression through primary care-based psychological and educational interventions [134] and in older people [135] including with psychological interventions [136].
- Screen time limits which have been recommended by the US Department of Health as one of its national ‘health improvement priorities’ and a key ‘disease prevention objective’ [137, 138].

- Physical activity which can prevent or delay onset of mental disorder [139]
- Prevention of dementia through childhood education, physical activity, social engagement and smoking cessation as well as management of hypertension, hearing loss, depression, diabetes and obesity [106].
- Suicide prevention through restricting access to lethal means including pesticide [140], school-based awareness programmes and treatment of depression [141].
- Prevention of smoking uptake through school-based interventions [142], mass media campaigns [143] and plain packaging [144].
- Reduction of alcohol consumption and associated problems through action on price, availability, marketing and licensing with reducing alcohol affordability as the most effective way of reducing alcohol-related harm [80].
- Prevention of drug misuse [145].
- Prevention of violence by prevention of alcohol misuse [80], addressing domestic violence [128] and prevention of violence to women [146].
- Anti-stigma and discrimination interventions although evidence is lacking from LMICs [147].

Promoting protective factors for mental wellbeing can also prevent mental disorder particularly in higher-risk groups [12] (see Sect. 31.6). For instance:

- Breastfeeding is associated with reduced behavioural problems.
- Home visiting programmes improve child emotional and social development as well as reduce child behavioural problems [117].
- Parenting programmes improve parental mental health [148], emotional adjustment and behaviour in under 4-year-olds [149], child conduct problems in 3–12-year-olds [150] and safety at home [116].
- Early childhood education programmes [151]
- School-based mental health promotion programmes can reduce classroom misbehaviour, anxiety, depression [152], conduct problems, emotional distress and drug use [153].
- Work-based mental health promotion programmes can prevent stress and mental disorder [154].
- Dementia can be prevented by childhood education, physical activity and social engagement [106].

Examples of effective interventions to prevent mental disorder at primary level with information on cost-effectiveness are highlighted in Table 31.4. However, most relate to high income countries with absence of evaluation of cost effectiveness in LMICs.

31.4.2 Secondary Mental Disorder Prevention

Secondary prevention involves early identification and intervention of mental disorder to treat and prevent its progression. Evidence-based treatment exists for every

Table 31.4 Examples of cost-effective interventions to prevent mental disorders at primary, secondary and tertiary levels

Primary prevention	• School-based interventions to [155]: – Reduce bullying resulting in net savings of £14 for each £ spent – Prevent conduct disorder through social and emotional learning programmes resulting in net savings of £84 for each £ spent • Education: Increasing educational qualifications of UK women from none to basic qualifications would reduce total cost of depression among women by £230 million a year or £4.9 billion over the working lives of these women [156] • Debt advice services result in total returns of £3.6 for each £ spent with net savings by year 2 with resulting from increased employment and productivity [155] • Prevention of depression in older people is highly cost-effective at €4367 per depression/anxiety-free year gained [157] • Prevention of loneliness in older people through psychosocial group therapy can reduce health-care costs by €943 for each person involved [158] • Reducing alcohol affordability: Over 10 years, a minimum price of 40p and 50p per unit across the UK would result in savings of £3.1 billion and £7.1 billion, respectively [159]
Secondary prevention	• Health visitor support to detect and treat women with postnatal depression results in net savings of £0.80 for each £ spent [155] • Parent training interventions for conduct disorder result in net savings of £8 for each £ spent, £7334 for each family receiving a group parenting intervention and £6250 for each family receiving an individual family intervention [155] • Early detection and treatment of depression at work results in net savings of £5 for each £ spent, most of which accrues to the employer [155] • Early intervention of psychosis results in net returns of £18 for each £ spent with net savings to the health sector by the end of the first year [155] • Early intervention during the phase preceding psychosis (clinical high-risk state) results in net returns of £10 for each £ spent with net savings to the health sector by year 2 [155] • Screening and brief interventions in primary care for alcohol misuse result in net returns of £12 for each £ spent with net savings starting by year 1 [155] • Suicide risk assessment in primary care: Improving the skills of GPs to assess suicide risk results in net savings of £44 for each £ spent [155]
Tertiary prevention	• CBT for people with medically unexplained symptoms results in net savings of £1.75 for each £ spent with NHS savings by year 2 [155] • CBT for people with schizophrenia results in overall net savings to the health and social care system of £989 per person [160] • Family therapy for people who have significant emotional connection to someone with schizophrenia results in estimated savings of £4202 per individual with schizophrenia over 3 years [161] • Crisis resolution home treatment teams can reduce costs of services for people with mental disorder by up to 30% [161] • Stigma prevention campaigns result in £421 saved per person with depression [162] and £0.70–£1.90 return on investment over 1 year [163] • Smoking cessation for people with mental disorder is cost-effective [161, 164, 165]. A cessation intervention for smokers identified in psychiatric hospitalisation did not result in higher short-term mental health-care costs and was highly cost-effective over the long-term with ICER of $428 per QALY [166] • Needle exchange has 1 year return on investment of 6.38–7.58 to one [167]

mental disorder including for LMICs [168, 169] and is summarised in relevant UK NICE guidance [12]. Since the majority of lifetime mental disorder arises before adulthood, this should be reflected in appropriate level of provision of treatment services before adulthood.

In particular, parenting interventions are recommended as first-line treatment for children with conduct disorder [13] which in the UK affects 6% of 5–16-year-olds [10] and attention deficit hyperactivity disorder [170] which affects 3.5% of 5–16-year-olds [10]. Early intervention for conduct disorder is more effective than later intervention [13]. Since 40–70% of those with conduct disorder develop antisocial personality disorder [171], prevention and early intervention for conduct disorder in childhood also prevent antisocial personality disorder and associated violence in adult life. Early intervention for different mental disorder is also effective during adulthood [12] and results in a range of improved outcomes and reduced inequalities. Early recognition of mental disorder can be facilitated by training of health professionals, screening of higher-risk groups and improving mental health literacy of the population including through internet-based resources [172].

Examples of effective interventions to prevent mental disorder at secondary level with information on cost-effectiveness are highlighted in Table 31.4.

31.4.3 Tertiary Mental Disorder Prevention

Tertiary prevention involves targeted intervention for people with established mental disorder by optimising evidence-based treatments to improve outcomes and prevent relapse and other impacts including suicide. This includes addressing health risk behaviours preventing physical illness and detecting physical illness early to reduce premature death and morbidity in people with mental disorders. Successful partnership working with service user and carers is particularly important [173] as is effective collaboration between primary care, secondary mental health care and other providers.

Mental disorders are associated with a range of inequalities which can be prevented by early [11, 12]:

- Access to appropriate evidence-based interventions to treat mental disorder, improve outcomes and prevent relapse.
- Monitoring of physical health and health risk behaviour.
- Early intervention for physical health conditions such as hypertension [174, 175] and treatment of those at high risk of developing diabetes [176].
- Early intervention for higher rates of health risk behaviour including smoking, alcohol and drug misuse, physical inactivity, poor nutrition, obesity, poor dental health and higher-risk sexual behaviour [12]. Smoking cessation is particularly important since smoking is the single largest cause of preventable death, and 42% of adult tobacco consumption in England [24] and 44% in the USA [177] are by people with mental disorder. Smoking cessation and reduction interventions are

effective for people with mental disorder [165, 178, 179] and can be provided by primary care [180], secondary care [178] and pharmacists [181]. Since smoking is responsible for the largest proportion of health inequality in those with mental disorder, targeted smoking cessation for people with mental disorder can significantly reduce health inequalities. Furthermore, impact of smoking cessation on anxiety and depressive symptoms is at least as large as antidepressants [182].
- Action to address associated impacts such as debt [86], poor housing, lack of education and unemployment.
- Action to address stigma and discrimination [147].
- Action to reduce higher rates of experience of violence [25] and perpetration of violence [26] through improved treatment coverage for particularly alcohol use disorder, drug use disorder and conduct disorder [13] which also prevents antisocial personality disorder [171], as well as targeted interventions for domestic violence [128] and prevention of alcohol misuse [80].

Suicide prevention is done through restricting access to lethal means, school-based awareness programmes and treatment of depression [141].

Examples of effective interventions to prevent mental disorder at tertiary level with information on cost-effectiveness are highlighted in Table 31.4.

31.5 Mental Wellbeing and Associated Impacts

Mental health and wellbeing is a complex construct that has been defined in numerous ways including as 'a state in which the individual realises his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community' [183].

Mental wellbeing has been linked to several constituents which include pleasure, engagement, relationships, meaning and achievement [184]. Pleasure (hedonic wellbeing) is important but limited in several ways, while engagement and meaning (eudaimonic wellbeing) include aspects of mental wellbeing that are more than just pleasure. Engagement refers to absorption in tasks such as work, exercise or cultural activities, while meaning links to wisdom and for some spiritual or religious traditions. Meaning and engagement have particularly large impacts [185, 186] which have relevance to both measurement and intervention focus.

Analysis of a survey of 32,000 individuals in 21 European countries found that those with high levels of hedonic wellbeing were also likely to have high eudaimonic wellbeing [187]. However, many happy individuals had low eudaimonic wellbeing, while those with meaningful lives were not necessarily satisfied. Sociodemographic variables associated with hedonic and eudaimonic wellbeing were similar although men had lower levels of hedonic wellbeing and higher levels of eudaimonic wellbeing compared to women; retirees had lower levels of eudaimonic wellbeing although similar levels of hedonic wellbeing to the general population, while those in full-time education and looked-after house/children had higher

hedonic wellbeing although similar eudaimonic wellbeing. Levels of income only had a minor effect on hedonic and eudaimonic wellbeing.

Levels of child wellbeing vary considerably between countries [188, 189]. Levels of adult wellbeing also vary between different countries which indicate different levels of risk and protective factors and opportunities for intervention. For instance, in Europe the proportion who [190]:

- Rated life satisfaction level as 7 or more out of 10 varied from 38.3% in Bulgaria to 91.0% in Denmark (EU average 69.3%)
- Felt that what they do in life is worthwhile varied from 47.8% in Greece to 91.4% in Denmark and the Netherlands (EU average 78.5%)
- Rated their happiness as 7 or more out of 10 varied from 48.0% in Bulgaria to 90.6% in Finland (EU average 74.1%)

A survey including more than 160 countries showed a U-shaped relation between life satisfaction and age in high-income, English-speaking countries, with lowest levels of wellbeing in 45–54-year-olds [191]. However, the pattern was different in other countries with respondents from the former Soviet Union, Eastern Europe and Latin America showing progressive reduction in wellbeing with age, while wellbeing in sub-Saharan Africa showed little change with age.

Mental wellbeing is associated with a range of impacts relevant to different sectors [11, 12]. Health impacts include reduction and prevention of mental disorder in children and adolescents including persistence [192], mental disorder and suicide in adults, physical illness, health-care utilisation and mortality [191, 193]. Wellbeing is also associated with improved recovery from physical illness [194]. Broader impacts of mental wellbeing include:

- Improved educational outcomes
- Increased productivity at work, fewer missed days off work, higher income
- Social relationships/contentedness
- Reduced antisocial behaviour, crime and violence
- Reduced health risk behaviour such as smoking/alcohol/drug misuse
- Improved resilience/ability to manage adversity

Promotion of mental wellbeing can also be effective in preventing mental disorders and promoting recovery of those with mental disorders.

31.6 Promotion of Mental Wellbeing

Health promotion interventions target the determinants of health and wellbeing rather than illness and can take place at an individual, community or structural level. This aims to improve individual wellbeing, enable healthier and more sustainable communities, facilitate environments which support improved health and achieve structural changes in policy and law which benefit health and reduce health

inequalities. There is some overlap with interventions to treat disorder since treatment of disease also addresses a major determinant of poor wellbeing in its own right.

A range of effective interventions exist to promote mental wellbeing [11, 12, 195]. As for prevention of mental disorder, mental wellbeing promotion can occur at three levels:

1. Primary promotion involves interventions which promote protective factors for mental wellbeing.
2. Secondary promotion involves early intervention to promote the mental wellbeing of people who have recently experienced reduced wellbeing.
3. Tertiary promotion involves interventions to promote the mental wellbeing of people with long-standing poor wellbeing.

Each level requires both a universal approach and the targeting of groups at higher risk of poor mental wellbeing [12]. In England, adults with lowest 15% levels of mental wellbeing have 8–30 times higher levels of mental disorder compared to people with highest mental wellbeing levels [82]. Since prevalence of mental disorder is high (Table 31.1), people with mental disorder represent a large proportion of people with poor mental wellbeing and therefore require targeted mental wellbeing promotion to support recovery from mental disorder.

31.6.1 Primary Mental Wellbeing Promotion

The following factors influence mental wellbeing [11, 12, 82, 196]:

- Individual: Genetic background; personality traits; socio-demographic factors including age, gender and marital status; self-esteem and autonomy; and resilience including emotional and social literacy
- Health: Mental disorder, subthreshold mental disorder and physical health
- Social: Relationship with parents and/or carers; maternal (antenatal and postnatal) care; early upbringing and experiences including attachment patterns with parents and/or carers; social support, relationships and networks; and community factors such as trust and participation
- Environmental: Schools, work, housing and living environments
- Socioeconomic factors
- Violence and abuse
- Activities including education, employment and other purposeful activities such as physical exercise
- Values such as honesty and altruism
- Meaning, purpose, spirituality and wisdom
- Culture including the arts
- Sleep

However, certain protective factors for wellbeing appear particularly important in some cultures and at certain stages of life. For example, in the UK, for young children, these include primary school context and friendships, home life and family relationships and living in a less deprived neighbourhood; for school-aged children, they include a school environment free from bullying and classroom disruption, feeling supported and sharing meals; for adults, they include good employment and conditions at home [196]. Similarly, certain factors appear to be particularly associated with poor wellbeing: In the UK during school and teenage years, these include substance misuse, excessive computer gaming and disruptive behaviour at school, while during adulthood, they include deprivation, fuel poverty, poor housing, stressful work and mental disorder [196].

As with mental disorder, increased population levels of protective factors for mental wellbeing are associated with increased population levels of mental wellbeing. The population impact of risk and protective factors depends on both the size of impact and the proportion of the population affected by such factors which can be assessed in a structured way [32–34]. A small increase in the level of protective factors experienced by a population can have a major impact on overall population wellbeing levels which can also prevent mental disorder and suicide.

Interventions to enhance protective factors for mental wellbeing above are carried out by different organisations, and public health has a key role in local coordination. A range of effective interventions across the life course exist to promote mental wellbeing at a primary level [11, 12]. Population coverage is facilitated by targeting particular places such as parenting centres, preschools, early childhood education [151], schools [152, 153, 197, 198], the workplace [199], nursing homes [200] and communities. Availability of high-quality childcare and early education services is particularly important for vulnerable children at risk of developing (or who are already showing signs of) social and emotional and behavioural problems [201, 202]. Interventions to promote the mental health of young people can be implemented effectively in LMIC school and community settings [203].

Examples of effective interventions to promote mental wellbeing at primary level with information on cost-effectiveness are highlighted in Table 31.5.

31.6.2 Secondary Mental Wellbeing Promotion

Secondary mental wellbeing promotion involves early interventions to promote the mental wellbeing of people who have recently experienced reduced wellbeing. They include those outlined in primary promotion above although require a more targeted approach as well as coordination with services already being provided. Examples of effective interventions to promote mental wellbeing at a secondary level with information on cost-effectiveness are highlighted in Table 31.5.

Table 31.5 Examples of cost-effective interventions to promote mental wellbeing at primary, secondary and tertiary levels

Primary promotion	• Preschool programmes – Early childhood education programmes for higher-risk children result in returns of $4.19 for each $ spent [204] – Home visiting long-term benefits: Total value of benefits per family is more than $27,000 over a 15-year follow-up period compared with costs of around $6300 [205] – Child-parent centres for low-income families for children between age 3 and 9 provided $11 return for each $ spent mainly due to increased earnings, tax revenues and averted crime costs [205] – Preschool impact on earnings: Gross lifetime earnings are £12,500 higher per person and £19,000 higher per household for a child who had attended a high-quality preschool than for a child who had attended a low-quality preschool [206] • School-based programmes – Prevention of conduct disorder through school-based social and emotional learning programmes results in total returns of £84 for every £ spent with most of the net savings accruing to the criminal justice sector [155]. Cost savings over 2 years are more than twice the initial investment, with cumulative gross savings per child of £6369 after 5 years and £10,032 after 10 years – Good behaviour game to reduce aggressive/disruptive classroom behaviour and prevent criminality results in savings of $31 for each $ spent [207] – Life skills training that is a classroom-based intervention to reduce risk of alcohol, tobacco and drug use and violence results in net savings of $38 for each $ spent [207] – Reading recovery is a structured literacy tutoring intervention for struggling readers typically in first grade and results in savings of $10 for each $ spent [207] – Peer tutoring programmes use students from the same classroom or higher grades to provide one-to-one assistance to other students struggling to read and result in savings of $12 for each $ spent [207] • Work-based mental health promotion can result in total returns of £10 for each £ with most net savings accruing to the employer after 1 year [155] • Physical activity: Brief physical activity interventions cost £57–14,002 per QALY [208]. Walking and physical activity programmes in older people to promote mental wellbeing cost £5000–£12,000 per QALY, while group exercise programmes cost £4915 per QALY [209] • Befriending services: Net savings are £225 per person each year if resulting improved quality-of-life measures are included [161] and £271 per older woman after 10 months [210] • Time banks use hours of time as community currency, with participants contributing practical help or resources in return for services provided by fellow time bank members. Economic modelling suggests that net savings per time bank member are £850 each year [211]
Secondary promotion	• Community navigators result in £420 net savings in the first year [211]
Tertiary promotion	• Employment support: Individual placement support for people with severe mental illness across six European sites was more cost-effective as a way back into competitive employment than standard vocational rehabilitation services [212] • Supported housing [161] • Peer support results in potential savings of €5 for each £ spent through reduced inpatient care [213] • Physical activity and healthy eating interventions for people with mental disorder are cost-effective in both men (€3357/QALY) and women (€3766/QALY) [214]

31.6.3 Tertiary Mental Wellbeing Promotion

Promotion of the mental wellbeing of people with long-standing poor wellbeing including from established health problems also requires a more targeted approach and coordination with services already being provided. Such interventions help promote recovery from existing health problems and prevent recurrence. Examples of effective interventions to promote mental wellbeing at a tertiary level with information on cost-effectiveness are highlighted in Table 31.5.

31.7 Public Mental Health-Related Policy

Many mental health policies are adopting a public mental health approach. For instance, objectives of the UK's mental health strategy include prevention of mental disorder and promotion of mental wellbeing [215]. Similarly, WHO's Mental Health Action Plan highlights the need to promote mental wellbeing and prevent mental disorder as well as treatment and prevention of associated outcomes [36]. It also highlighted public mental health relevant need to provide comprehensive, integrated and responsive mental health and social care services in community-based settings and implement effectively and strengthen information systems. More recently, the United Nations Sustainable Development Goals made mental health a core part and committed to treatment and prevention of non-communicable disease including mental disorder as well as promotion of mental wellbeing [216] in contrast with the absence of mental health in the Millennium Development Goals published in 2000. Public health has been slower to integrate mental health although the UK's public health white paper highlighted its importance [217].

31.8 Public Mental Health Intervention Gap

The population impact of effective public mental health interventions depends on their implementation, coverage and outcomes. However, despite the impacts of mental disorder and poor wellbeing and the existence of a range of cost-effective public mental health interventions which can demonstrably result in a range of economic savings even in the short term [12], their coverage is inadequate, and no country has yet implemented to scale.

For instance, across the European Union, only 10% of people with a mental disorder receive notionally adequate treatment [5] although coverage in lower-income countries is far less and virtually non-existent in some [218, 219]. This contrasts to treatment rates for most non-communicable disease which commonly exceed 50% even in low-income countries [220]. Even fewer people receive interventions to prevent associated impacts of mental disorder (such as premature mortality), prevent mental disorder from arising or promote mental wellbeing. This is important since sustainable reduction in disease burden from mental disorder can only occur with such interventions [31].

Such an implementation gap results in preventable human suffering, a broad range of impacts and associated economic costs [32, 33]. Furthermore, it represents a breach of the right to health [221].

Several reasons contribute to this implementation gap including systematic discriminatory attitudes towards mental health which also affects help seeking as well as lack of [35]:

- Recognition of symptoms of mental disorder and awareness of effective interventions by the general population as well as health professionals.
- Public mental health understanding among public health, primary care, secondary mental health care, social care and those commissioning services about numbers affected, associated impacts and costs, associated risk and protective factors, evidence-based interventions and their coverage. For instance, only 33% of countries regularly compile any mental health service activity data [218].
- Mental health expenditure: Compared to associated 22.0% of global burden of disease [1]: Reported mental health expenditure across all country income groups was less than 5% of general government health expenditure although this was much less for lower-income countries [218]. In India and China, the two largest countries, less than 1% of health expenditure was allocated to mental health [219]. Furthermore, mental health receives only 1% of development assistance [222].
- Staffing resource: The level of mental health staff was only 9/100,000 population globally although varied from 1 to 50/100,000 population between different countries) [218].
- Mental health policy: This was absent in 32% of countries [218] although is usually not implemented to scale even where it exists.
- Estimates of the coverage of mental health programmes which are usually unavailable [223].
- Assessment of public mental health unmet need and proportion of the population requiring different public mental health interventions either at local [34] or national level [224].

31.9 Addressing the Public Mental Health Intervention Gap

In order to have population impact, effective public mental health interventions require appropriate implementation and coverage which can be enhanced by:

- Improving understanding about mental health
- Settings based approaches including primary care and other providers
- Use of technology
- Mental health policy development
- Regulation, legislation and a human rights approach
- Examples of initiatives to address the treatment gap in LMICs
- Public mental health practice

31.9.1 Improving Understanding About Mental Health

Public health campaigns, media or social/digital marketing of resources are important to improve mental health literacy of the population [172], demand for appropriate intervention and facilitate early recognition and treatment of mental disorders. Similar interventions to address stigma increase the numbers seeking treatment, facilitate earlier presentation, prevent relapse and support improved resourcing for public mental health interventions. Such interventions include the use of less stigmatising terms for mental disorder [225] and training for mental health workers [226]. Targeted approaches are important for particular groups including children and young people, parents, teachers and health professionals.

Appropriate training to a range of health, public health, policy and other groups should also include improving mental health literacy regarding symptoms of mental disorder as well as a public mental health practice (see Sect. 31.9.6).

31.9.2 Settings Based Approaches

Coverage of different public mental health interventions is facilitated by implementing integrated mental health care across particular settings where large proportions of the population spend time such as antenatal classes, preschool, school, workplace and care homes for older people. Such approaches enable several public mental health interventions to be implemented in a particular setting more efficiently and to scale.

Since the majority of lifetime mental disorder arises before adulthood, childhood and adolescence are key opportunities to implement interventions to both prevent mental disorder and offer early treatment. Schools have a particularly important role to play: For instance, most parents of children with mental disorder in Great Britain seek advice from teachers in contrast to a minority of parents approaching primary care or mental health professionals [10]. Some estimates suggest that early intervention for mental disorder during childhood and adolescence could prevent 25–50% of adult mental disorder [130] and thereby also prevent a wide range of associated impacts including suicide and self-harm. Since different mental disorders have different ages of onset (Table 31.2), such age groups need targeting.

A range of other support exists including family and carers, peers, elders and faith-based organisations. Traditional healers can also provide a potentially important source of mental health care and signpost to relevant treatment settings particularly in areas where mental health-care provision is poor although also to minority populations in higher-income countries [227]. Some evidence suggests such healers can provide effective psychosocial intervention, and several countries are attempting to incorporate traditional healers into their formal health-care systems.

Primary care is a particularly important health care setting for improving coverage of public mental health interventions as well as further referral to secondary mental health care if required. Integration of mental health into primary care is supported by appropriate resources and training of primary care staff. In the absence of

primary care or appropriately trained professionals, shifting of tasks from more to less well-trained individuals can improve coverage [228, 229]. Non-specialist health workers show potential to improve coverage and outcomes for a range of mental disorder [230].

31.9.3 Use of Technology

Technology also has a role in improving implementation in several ways including [231]:

- Mental health care delivery in clinical settings in LMICs
- Mental health training and education of health workers in LMICs
- Detection and diagnosis of mental disorders in LMICs
- Videoconferencing in LMICs which is also cost effective [232]
- Mobile phones offer a way of screening, detection, improving appointment attendance and medication adherence, providing ongoing encouragement and psychosocial support in LMICs [231, 233], delivering psychotherapy [234], supporting assessment and treatment for people with psychosis [235] and improving smoking cessation rates [236]. Mobiles can also boost effectiveness of psychotherapy and behavioural interventions [237]
- Internet can be used to deliver CBT for adult common mental disorder [238], PTSD including in conflict zones [231] and smoking cessation [239] while combining direct contact and internet based interventions can improve treatment outcomes and coverage for common mental disorder [240]
- Telephone support in LMICs can promote treatment adherence and clinical outcomes in people with mental disorder as well as reducing alcohol consumption
- Online self-help programmes can provide access to resources and support as well as offering a discrete way of seeking support

31.9.4 Mental Health Policy Development

Development of an evidence-based mental health policy is also an important step and should include information about the size, impact and costs of public mental health intervention gap, impacts and economic savings from improved coverage (see Sect. 31.9.6) and actions to reduce the implementation gap. This can be supported by a coordinated approach from relevant stakeholders and relevant briefings to key decision makers.

31.9.5 Regulation, Legislation and a Human Rights Approach

Regulation and legislation can support improved access to public mental health interventions through protection of children from abuse as well as reducing

availability of alcohol and access to means of suicide. Legislation can also support a rights approach to mental health which is important in improving access to public mental health interventions [221]. The 1948 Universal Declaration of Human Rights mentioned health as part of the right to adequate standard of living, while the right to health was recognised as a human right in the 1966 International Covenant on Economic, Social and Cultural Rights. The Commission on Human Rights created the mandate of Special Rapporteur on the right of everyone to the highest attainable standard of physical and mental health in 2002. More recently, the United Nations Human Rights Council adopted a resolution entitled 'Mental health and human rights' which reiterated key universal human rights and specific rights protections required for people with mental disorder [241]. As well as treatment, it should include the right to effective interventions to prevent mental disorder and promote mental wellbeing.

31.9.6 Examples of Initiatives to Address the Treatment Gap in LMICs

Initiatives to reduce the public mental health intervention gap have focused on treatment.

Examples of initiatives to reduce the treatment gap in LMICs include integration of mental health care into primary care, use of front-line health workers rather than mental health professionals as advocated by WHO's Mental Health Global Action Programme (mhGAP) [169] and community case finding [168, 242, 243].

A recent example of implementation initiatives in low-income country settings to improve coverage of mental disorder treatment included PRIME (PRogramme for Improving Mental health carE) and included on:

- Challenges to implementation covering lack of priority for mental health over other health needs of countries, poverty, different cultural settings, broader health system challenges such as weak coordination between national and local authorities, inadequate medication supply, weak health management information systems, burden on front-line health-care workers, lack of human resources, inflexible bureaucracy and lack of accountability among providers, limited community awareness, stigma and discrimination towards people with mental illness and different explanatory models which may influence uptake of services [244].
- Methodology of evaluation of mental health-care plans required at different population levels including community-based cross-sectional surveys to measure change in population-level contact coverage, facility-based surveys to assess change in detection of disorders, disorder-specific cohorts to assess effect on patient outcomes and case studies to evaluate implementation [245].
- Methodology to estimate resource needs and costs in order to successfully scale up implementation of district-level mental health services over 5–15 years [246]. This can inform policy makers about financial and human resource implications of implementing integrated mental health-care packages in other countries.

- Development of district mental health-care plans in Ethiopia [247], India [248], Nepal [249], South Africa [250] and Uganda [251].
- Comparison of common elements and country-specific adaptations of plans in different settings [252]. Many differences between countries were driven by resource context, with greatest similarities between low-income countries (Ethiopia, Nepal and Uganda) and between middle-income countries (India and South Africa). Despite these differences, common elements included shared objectives and a common overall planning framework; high levels of participation and engagement with local stakeholders; focus on community, health facility and health organisation levels; challenges of overburdened primary health-care systems; and limited impact of training without new mental health resources, referral pathways, improved medication supply and reorientation of health facility managers.

31.10 Public Mental Health Practice to Address the Gap

Sustainable reduction in disease burden from mental disorder and promotion of mental wellbeing across populations require appropriate coordination, coverage and outcomes of evidence-based public mental health interventions. Such interventions are provided by different organisations across various sectors including health (primary and secondary care), public health, social care, welfare, housing, education, criminal justice and voluntary sector.

Public mental health practice can support coordination, planning and allocation of responsibilities and resources across such different organisations and sectors as well as improved coverage, outcomes and monitoring of progress in four key steps [32, 224]:

1. Needs assessment of:
   (a) Level of provision of public mental health interventions
   (b) Size, impact and cost of unmet need for effective public mental health interventions at least nationally
   (c) Impact and associated economic savings resulting from improved provision
2. Use of such information to inform strategic and mental health policy development, commissioning, inter-agency coordination and wider advocacy in order to improve coverage and outcomes of public mental health interventions
3. Implementation at population level with different public mental health interventions being provided by various organisations
4. Evaluation of intervention coverage and outcomes to inform further implementation plans

Since different localities and countries have different levels of unmet need, a needs assessment should include local, regional and national levels of [34]:

- Levels of mental disorder and wellbeing
- Levels of risk and protective factors

- Proportion from different higher-risk groups
- Coverage and outcomes of public mental health interventions
- Estimated economic costs of mental disorder to both health and other sectors
- Size and cost of the gap in provision of public mental health interventions
- Expenditure on different types of public mental health intervention
- Estimated economic savings to different sectors from improved coverage of a range of public mental health interventions

Mental health needs assessments carried out by the author have supported inclusion of mental health relevant information for several million people across England which in turn has supported inter-agency coordination, policy and strategic development, commissioning decisions and improved population coverage of public mental health interventions. This work found that engagement by relevant organisations and sectors was facilitated by division into assessment of level of intervention provision and unmet need focusing on:

- Treatment of mental disorder including early intervention (secondary prevention)
- Treatment services provided by particular sectors such as primary care, secondary mental health care, social care and voluntary organisations
- Mental disorder (primary) prevention
- Mental wellbeing promotion (primary, secondary and tertiary)

Initial assessment of the coverage of public mental health interventions facilitates coordination of the work of different organisations, and such a population approach requires the involvement of public health [33, 34] although psychiatrists also play an important role [253]. However, mental health is poorly represented in needs assessments in the UK for a number of reasons including lack of mental health in public health training which perpetuates the public mental health implementation gap [34]. Since the majority of professionals from public health, primary care, secondary mental health care, social care and funding bodies are unaware of the size, impact and cost of their public mental health unmet need, relevant education and training is a critical step to address this gap. This includes appropriate integration of mental health into public health training, public health into mental health training and training about how to carry out mental health needs assessments. Broader public mental health training and education is also important for the wider population with schools, workplaces and different media outlets having particularly important roles.

The costs of providing a significantly scaled-up package of specified cost-effective interventions for prioritized mental and neurological disorders is estimated at US$3–US$4 per person per year in LMICs and at least double that in upper-middle-income countries [254].

Effective advocacy is required for appropriate level of resource at national level which can be supported by regular assessment of the national size, impact and cost of the public mental health gap as well as impact and associated economic savings

of improved coverage [224]. For instance, comprehensive coverage across England of several public mental health interventions outlined in England's mental health strategy [155, 216] would result in conservative net savings of [224]:

- £4147 m after 5 years and £6532 after 10 years from school-based social and emotional learning programmes to prevent conduct disorder for a 1-year cohort of 10-year-olds
- £9726 m from school-based interventions to reduce bullying for all 5–18-year-olds
- £386 m from parenting interventions for parents of a 1-year cohort of 5-year-olds with conduct disorder
- £4518 m after 2 years from workplace screening and early treatment of depression and anxiety disorder for all employees
- £568 m after 1 year and £1040 m after 5 years from suicide awareness training for all GPs in England
- £62 m after 1 year and £477 m after 10 years from early intervention for all adults developing psychosis in a year
- £457 m after 1 year and £1693 m after 7 years from primary care-based screening and brief intervention for all hazardous and harmful/mild dependent drinkers
- £310 m after 3 years to the health sector from CBT for all adults with schizophrenia in previous year
- £18,864 m after 1 year to employers from provision of a simple set of interventions to promote wellbeing of all employees

Such practical approaches support implementation of evidence-based public mental health interventions which in turn supports the objectives of various national and international mental health policy [33, 199, 200]. It also supports integration of mental health across disease categories and into all aspects of relevant policy, planning and implementation.

31.11 Conclusion

A range of cost-effective public mental health interventions can prevent mental disorder and promote mental wellbeing at primary, secondary and tertiary levels. Such interventions result in a broad range of impacts and associated economic savings even in the short term. Since only a minority of those who would benefit from such interventions actually receive them, this failure to implement according to population need results in a broad range of human suffering, associated impacts and economic costs. Opportunities exist to improve coordination, coverage and outcomes of public mental health interventions in order to sustainably reduce burden of mental disorder and promote population mental wellbeing. Assessment of the size, impact and costs of such an intervention gap at both local and national level as well as the impact of improved coverage is an important first step in improving public

mental health intervention coverage. This is followed by integration of relevant information into mental health policy, commissioning decisions, implementation and evaluation. Relevant public mental health education and training to a broad range of sectors is also important. Access to effective public mental health interventions is an important rights issue. However, given the economic cost of the intervention gap and economic savings of a range of public mental health interventions, improved coverage, outcomes and integration of such interventions is also a key part of sustainable economic development.

Declaration of Interest Jonathan Campion has carried out mental health needs assessments for local authorities and mental health trusts for which his employer received payment.

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Psychiatric Rehabilitation in the Twenty-First Century

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Abstract

During the past century, various kinds of psychiatric rehabilitation were developed continuously. In the past, psychiatric rehabilitation was aimed in housing after deinstitutionalization. Supported housing services have contributed to more freedom and more social skills for patients when compared to earlier hospital-based services. To integrate these people into their communities, vocational rehabilitation is significant in recovery process. Supported employment which provides individual placement in competitive employment has several benefits. As impairments in psychosocial functioning are common in people with severe mental illness (SMI), the social skills training should be integrated into a multimodal treatment program and adjusted to the individual needs.

Moreover, having cognitive deficit in patients with SMI is related with functional outcome concerning employment, independent living, and community and social functioning. Thus, many interventions of cognitive rehabilitation designed

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by using the concept of neuroplasticity such as cognitive remediation therapy, cognitive adaptation training (CAT), and computer-assisted cognitive retraining (CACR) were developed and have become more popular in the twenty-first century. Finally, metacognitive training (MCT) as a combination of cognitive behavioral therapy, psychoeducation, and cognitive remediation aims to provide insight for various cognitive biases has been developed. However, the studies to prove the effectiveness of these interventions need to be further investigated.

32.1 Introduction

Psychiatric rehabilitation or psychosocial rehabilitation is a process that facilitates the opportunity for individuals who are impaired, disabled, or handicapped by a mental disorder to reach their optimal level of independent functioning [1, 2]. Changes in the field of psychiatric rehabilitation are growing. Thirty years ago sheltered workshops were considered best practice, but later these workshops have fallen into disfavor in some settings. Twenty years ago, group homes which also offered life skills training were heralded as the best choice for people disabled by mental illness. Ten years ago and continuing to the present time, supported housing, together with vocational rehabilitation which includes supported employment, is still considered the promising approach in working with psychiatrically disabled person [2]. Recently cognitive rehabilitation which aims to improve cognitive impairment has received much interest as cognitive deficits in severe mental illness (SMI) especially in schizophrenia are significantly correlated with poor functioning outcome [3].

Psychiatric rehabilitation in the past century was aimed in housing and vocational rehabilitation because most of severely mentally ill persons especially schizophrenic patients were affected from functional deterioration in many areas of life such as self-care and independent living, social functioning, working, or studying that often made them become homeless persons. Thus, interventions which might alleviate positive and negative symptoms and protect them from human right violation were promoted to implement among patients with SMI since the past century. According to the concept of human rights which was set out in 1948 [4] and was broaden to use for persons with disabilities from mental health problems. However, after discovering that severe mental illness and neurodegenerative diseases affected many aspects of cognitive function and cognitive impairments were related with functional outcome concerning employment, independent living, community functioning, and social functioning. Therefore, intervention designed to improve neurocognitive function via concept of neuroplasticity may be needed in the treatment of severely mentally ill person with cognitive deficits in the twenty-first century.

Comparing with antipsychotic drugs which are now classified into first- and second-generation antipsychotics, psychiatric rehabilitation may also be divided into first- and second-generation approaches. However, the difference between antipsychotics and psychiatric rehabilitation is that for psychiatric rehabilitation we can combine first- and second-generation approaches for the same patient which are

suitable for the area of impairment and phase of diseases of each patient. However, prescribing both first- and second-generation antipsychotics for treatment of individual patient is not recommended.

In this chapter we will describe psychiatric rehabilitation for both first- and second-generation approaches which is still used or will receive more attention in this twenty-first century.

32.2 Sheltered and Supported Housing

As mentioned earlier, persons with SMI frequently suffer from reduced daily living skill, and many of them are in need of specialized housing and care arrangements.

Beginning in the 1960s and 1970s, deinstitutionalization from large mental state hospitals occurred in many European countries and North America, while this started later in other parts of the world. This process resulted in significant challenges for community psychiatric and housing services. Originally, the main aim was to change institutional care into community-based housing [5]. Unfortunately, a marked proportion of patients were referred from hospitals to large homes for persons with mental disorders, sometimes pejoratively named as "trans-institutionalization."

In some European countries, concerns have been expressed that the range of available housing is insufficient or of a poor quality [6]. It has been hypothesized that insufficient provision of needed support in community housing resulted in "revolving door" for patients experiencing repeated hospital admissions within a short period of time. In many countries the number of psychiatric hospital beds was dramatically reduced, e.g., in Austria from 1.34 hospital beds per 1000 inhabitants to 0.42 beds. This resulted in dramatic rising numbers of supported housing places, e.g., in Berlin the number of places for mentally ill patients in supported housing increased by threefold over one decade [6]. Nevertheless, a subgroup of severely mentally ill patients were not able to get access to appropriate housing and became homeless.

32.2.1 Forms of Supported Housing

The different forms of supported accommodation are difficult to define, owing to the existence of various systems to classify them, the multiple dimensions of staff status and staffing ratios involved, and the heterogeneity of the patients who end up in such accommodation [7].

32.2.2 Usefulness of Supported Housing

In the last decade several overviews [8] were published analyzing research about the effects of supported housing, frequently having compared with hospital-based rehabilitation programs. A study performed in a community hostel reported that patients

had a better quality of life and greater freedom compared to patients in hospital-based rehabilitation units with similar levels of psychopathology and impairment. Several studies reported that a large proportion of persons with longer-term mental illness prefer living in community rather than in hospitals [6]. A study analyzing environmental factors on outcome found that community settings were associated with better client outcomes than hospital environment [9]. High levels of resident involvement, autonomy, and program clarity were reported as essential aspects of environmental quality in sheltered homes. Taylor et al. [8] cited an Italian study that facilities with higher levels of restrictiveness and fewer links with community-based activities experienced higher rates of hospital readmission.

Taylor and coworkers [8] also concluded from several studies that there is no clear consensus on the optimal number of residents in community-based residential mental health facilities. Nevertheless, it was reported that higher density in supported housing facilities increases residents' stress and decreases their privacy.

32.2.3 Findings from Intervention Studies

Chilvers and colleagues [10] performed a systematic review on randomized or quasi-randomized trials in order to determine the effects of supported housing schemes compared with outreach support schemes or standard care for people with SMI living in the community. Unfortunately, they could not identify any studies from randomized trials for their review. Chilvers et al. [10] concluded that due to the absence of evidence, decisions on the provision of alternative forms of accommodation that continued can only be based on a combination of professional judgment, patient preference, and availability. They suggest that policymakers should consider supported housing schemes with caution. Further, they recommend supported housing schemes should not be implemented without plans for evaluation using rigorous methods or should be delayed until further evidence of their effectiveness exists.

Until today, in several European countries, a small proportion of patients cannot easily be discharged from psychiatric hospital wards directly into the community. Macpherson and colleagues [11] searched for studies comparing the effects of 24 h residential rehabilitation with standard hospital treatment. They found only one study with 22 participants with important methodological shortcomings and limitations. Again, studies using appropriate research methods were urgently recommended.

When not limiting the inclusion criteria of supported housing studies merely to randomized controlled trials (RCTs), overall 28 studies were found [6]. Several nonrandomized studies showed that supported housing can have positive effect with moderate to high satisfaction according to clients' assessments. One of the largest studies worldwide in this area was the British "Team for the Assessment of Psychiatric Services (TAPS)" study: More than 700 former long-term psychiatric inpatients showed at the 5-year follow-up stability in psychiatric symptoms with negative symptoms clearly reduced. As compared with controls, significant improvements in social behavior and domestic and life skills were found. After 5 years,

nearly all patients were happy to be discharged from mental hospitals. These findings were later supported by other studies [6].

However, several authors (e.g., Chilvers et al. [10]; Fakhoury et al. [6]) criticized the research methods used in the majority of studies concerning supported housing. Many studies have been uncontrolled follow-up studies, cross-sectional surveys, or nonrandomized controlled trials (RCTs). Despite all these limitations, it seems surprising that some findings (e.g., improvements in social behavior) are rather homogenous all over the world and in different contexts.

32.2.4 Housing First Approach

For a long time, there was only small evidence in which interventions are effective for homeless people suffering from mental disorders. Most services were developed mainly on clinical considerations, but were supported only by small descriptive studies or nonexperimental designs. At the end of the 1990s, the "housing-first" approach, a new and unconventional model, was suggested [12]. While the traditional housing approaches require from patients first to start with psychiatric treatment and to stop drug and alcohol abuse, the housing-first approach offers people who are homeless their own apartments, without any preconditions. In the last 15 years, there have been numerous RCTs showing the effectiveness of this approach among homeless mentally ill persons [5, 13]. Reviews on housing first have shown that this is a very successful approach concerning homeless and mentally ill persons' ability to find and maintain stable housing for a longer period of time. Further, these reviews confirmed that randomized controlled designs are useful and feasible for evaluating the efficacy even of such complex interventions.

In the last few years, the housing-first approach for persons with SMI who are not homeless has also been discussed in Europe [14]. In contrast to North America, in Europe and Asia the proportion of homeless people among severely mentally ill persons is markedly lower. Thus, until now it is not clear if the results of studies in the USA or Canada could be transferred to Europe and the rest of the world. Despite differences in the healthcare systems, some European service planners think about considering the housing-first approach due to political discussions about the UN convention on the rights of persons with disabilities [15].

Article 19 of the UN convention on the rights of persons with disabilities states with regard to living independently and being included in the community:

(a) Persons with disabilities have the opportunity to choose their place of residence and where and with whom they live on an equal basis with others and are not obliged to live in a particular living arrangement;
(b) Persons with disabilities have access to a range of in-home, residential and other community support services, including personal assistance necessary to support living and inclusion in the community, and to prevent isolation or segregation from the community;
(c) Community services and facilities for the general population are available on an equal basis to persons with disabilities and are responsive to their needs.

32.3 Vocational Rehabilitation Program

About 80% of people with SMI are unemployed. Working offers to these people many advantages: (1) developing basic processes such as a sense of responsibility and judgment, and improving self-esteem; (2) decreasing the number of hospitalizations; (3) developing social skills, thus regaining a certain amount of personal power and control; (4) acquiring a social and vocational identity or gaining the ability to like others; (5) and developing the possibility of being granted full citizenship in the community [16]. The meaning of work can change according to the country. The work can be perceived as an obligation for ensuring an individual's social security, or it can be a personal choice during the recovery process.

32.3.1 Two Models for Vocational Training

Grossly, we can have two main categories in vocational program: train-place and place-then-train [17]. Train-place programs aim to help participants develop specific skills to allow them to reintegrate the workplace. The vocational agencies advocate step-by-step process whereby clients complete a rehabilitation program before getting a competitive employment. There are seven stages of vocational services according to this model: (1) assessment of clients' competencies and skills, (2) assessment of clients' coping strategies, (3) skills training, (4) sheltered workshop, (5) transitional employment, (6) searching for competitive employment, and (7) maintaining competitive employment. The vocational agencies offering prevocational programs, such as sheltered workshop, enclaves, transitional programs, hospital-based programs, industrial therapy, volunteer placement, clubhouse, mobile work crews, and work-ordered days, are considered to be offering in the train-place programs [17].

Place-then-train model aims at placing the person in real work setting prior to offering them specific training to help them quickly achieve their vocational and community integration goals. This approach focuses on rapidly placing the person in a competitive employment position. Supported employment services including individual placement and support model or Australia's open employment model are in this category. It should be noted that these two train-place and place-then-train approaches are not mutually exclusive when implemented in the community that some vocational agencies offer supported employment programs to individuals who have already received prevocational services. Another approach in certain countries is social enterprise model to offer remunerative work just as any other firm in a setting with a high ratio of individuals with severe mental illness or other disabilities.

32.3.2 Several Vocational Rehabilitation Programs [18]

32.3.2.1 Sheltered Workshop

Sheltered workshops, hospital-based programs, industrial workshops, or enclaves were provided for people with SMI who presented a low level of functioning and who were not ready to integrate to workplace. Sheltered workshop creates an

environmental security and an opportunity to develop basic work skills and habits. The work task is repetitive and monotonous, and the time-limited aspect of sheltered workshops can become an obstacle to regular workplace integration if clients never move on to other jobs, so these workshops have decreased the popularity in some settings.

32.3.2.2 Transitional Programs

Transitional employment was offered to the members of clubhouses. This is negotiated by vocational staff with employers and usually takes the form of part-time community jobs where another person replaces the client if they experience a relapse. Most of the work can be taught without the need for specific skills, which are by the rotating group of clients over an extended period of time. One study from Thailand found that 76.7% of stable psychotic patients improved their functional status within 4–6 months during the follow-up time [19]. In certain settings, prevocational activities within sheltered workshops are mandatory before accessing transitional employment. The disadvantages are that the jobs are often unskilled and time limited; regardless of their job performance and satisfaction, the workers will need to vacate the position.

32.3.2.3 Social Enterprise/Social Firm

This is described as a program midway between sheltered work and competitive work and is similar to work crews, where groups of clients are trained and supervised among both handicapped and ordinary workers in a business. The aim of social enterprises is to offer a holistic setting where the participant's vocational and mental health goals can be met. The social firm should be financially viable and profitable without subsidies. The major advantages of this model are real-world remuneration and a sense of belonging to the enterprise, not to mention the accommodations offered to compensate for deficits or symptoms.

32.3.2.4 Supported Employment

This program typically provides individual placement in competitive employment in accord with client preferences and capabilities, without requiring extended prevocational training. The most widely known approach under this model is individual placement and support (IPS), which integrates vocational and mental health treatment teams and has zero exclusion criteria. The choose-get-keep psychiatric rehabilitation approach from Boston offers support in competitive work settings but only after extensive prevocational career exploration. The advantage of this program over other vocational services is that the clients actually obtain real-world competitive jobs and facilitating their integration while working against the stigma of mental illness.

32.3.2.5 Integration with Other Psychosocial Programs

Up to two thirds of individuals with severe mental illness cannot achieve or maintain basic social roles such as employee, spouse, parent, and integrated member of the community. Social and vocational interventions effectively enhance social and vocational functioning for individuals with schizophrenia. Cognitive remediation in

conjunction with vocational rehabilitation has proven to enhance performance on measures such as attention and working memory, along with employment outcomes compared with those who receive vocational intervention alone [20]. Integrated supported employment program that incorporates social skills training showed higher employment rate and longer job tenure.

Even though each service follows a specific model with precise goals, there can be overlaps and adaptations. As Harding et al. [21] pointed out, there are four components to help people with severe mental illness integrate into the workplace: (1) flexibility, (2) collaboration, (3) a unified theoretical framework integrated from different disciplines, and (4) database system across the rehabilitation process. Various combinations, adaptations, and integrations of specific vocational services components are used in order to help people with severe mental illness attain their vocational goals. New interventions for improving neurocognition and social cognition in schizophrenia are also leading new integration of interventions for improving social and vocational outcomes. But occupation rather than employment is a central concept of recovery that recovery-oriented service delivery must take this into account.

32.4 Social Skills Training

Poor psychosocial functioning is a core feature of schizophrenia and other severe mental illnesses. Deficits in social functioning affect virtually every aspect of life, including self-care and independent living, quality of social relationships, and the capacity to work, study, or parent. Although psychopharmacological treatment is essential to achieve symptom reduction in schizophrenia, it is by no means a sufficient therapy on its own. In order to promote recovery and improve the quality of life of affected people, a full range of psychological, pharmacological, social, and occupational interventions should be offered.

Social skills training is a psychosocial treatment which aims to improve their functioning in their communities [22, 23]. Originating in the social skills model, the social skills training has been designed to address deficiencies in the three main components of social competence: receiving skills (i.e., social perception), processing skills (i.e., social cognition), and sending skills (i.e., behavioral responses). Social skills training programs differ in content, duration, and implementation setting; however, they all share a similar approach based on social learning theory. The strategies for teaching new skills involve goal setting, role modeling, behavioral rehearsal, positive reinforcement, corrective feedback, and home assignments to practice skills and promote generalization.

The training is most often used to address the social deficits characteristic of schizophrenia and in some cases of severe affective disorders; however, it can also be applied in order to facilitate socialization in children with autism spectrum disorders or attention deficit hyperactivity disorder. Depending on the child's age, more emphasis can be put on teaching social norms and social "rules" and making the expectations of others understood than on helping to gain competences for independent living.

As mentioned above, social skills training can be applied in different settings for various reasons; however, group setting is the principal modality for implementing the training. Delivering the training to a group of patients helps reduce stigma and provides a context for participants to learn from each other's real-life experiences and an opportunity for self-help and peer support. It is also the most cost-effective way to implement the training. Nevertheless, it is also possible to conduct social skills training with individuals or families, and there are some evident advantages of each of these modalities as well. The training process and the acquisition of skills might be more swift in an individual setting, whereas including family members could directly influence communication and problem-solving strategies which, in turn, results in reductions in the stress-inducing "emotional temperature" of the family.

Although social skills training is generally considered a well-established intervention to improve social competences, there are somewhat conflicting findings in the literature regarding its effectiveness. The first two comprehensive meta-analyses conducted in this field were fairly optimistic with the authors concluding that effects of the training were large for behavioral outcomes directly related to the focus of the intervention, but much smaller effects for improved instrumental role functioning or independent living skills. Pilling and colleagues [24] published a meta-analysis including only randomized, controlled trials (RCTs) and reported that there was no clear evidence of benefit of social skills training in any of the investigated outcome measures. However, this conclusion has been rated as questionable due to the authors' methods for combining results from studies using very different types of outcome measures. A meta-analysis of 19 RCTs by Pfammatter and colleagues [25] yielded large effects of social skills training on skills acquisition, with smaller, but significant effects on assertiveness, social functioning, and general psychopathology. In the most comprehensive meta-analytic investigation to date which included 23 RCTs, Kurtz and Mueser [26] categorized domains of beneficial outcomes on a proximal–distal continuum (according to the presumed site of action of the skills training interventions). The authors found large positive effects for more proximal measures such as content mastery and smaller but still significant effects on more distal measures of community functioning, negative symptoms, and relapse prevention.

The results regarding the effectiveness of social skills training indicate that the transfer of verifiable gains in social skills to daily life is of central importance. The generalization of social skills can be promoted, for example, by community-based in vivo skills training or by enlisting "indigenous supporters" (i.e., relatives or friends of the patient) to prompt the use of skills in real-life situations. A recent approach with promising results is incorporating virtual reality technologies for improving the motivation of patients engaging in social skills training. The effects of social skills training on social functioning might be further enhanced by the combination of the training with interventions aimed at improving cognitive functioning such as cognitive remediation.

Another meta-analysis [23] mentioned that the relevance of current results might be limited due to cultural differences, as it is unknown if such interventions might be transferred from cultural background to another one. Further, the type of setting

offering social skills programs might influence the results. They recommend large multicenter randomized controlled trials using the same research methods in different settings and different cultures.

32.5 Cognitive Rehabilitation

Cognition is referred to a complex collection of mental skills that includes attention, perception, comprehension, learning, remembering, problem solving, reasoning, etc. [27, 28]. After a brain injury or being suffered from any disease which affects the brain, these neurological and mental processes will be interrupted.

Mental illness affects not only emotional or psychotic symptoms but also cognitive impairments. Patients with psychiatric disorders often experience that it is harder for them to pay attention, remember and recall information, process and respond to information quickly, and think critically including organized planning and problem solving [29]. According to Devere [30], there are numerous studies that found how SMI and neurodegenerative diseases impact various aspects of cognitive function. Cognitive deficits are significantly correlated with functional outcome concerning employment, independent living, community functioning, and social functioning [3]. Moreover, there is a hypothesis which is supported by evidences that intervention designed to improve the brain structural and functional integrity via neuroplasticity could mitigate cognitive impairments especially in schizophrenia [3]. Even in the elderly, although the brain reserve is hard to avoid, retaining cognitive reserve as close to the previous level may be possible [31]. To improve these cognitive functions, cognitive rehabilitation is crucial to lead the patient with a variety of clinical conditions to a more productive life [29].

32.5.1 Principle of Cognitive Rehabilitation Therapy

Cognitive rehabilitation therapy is a systematic, functionally oriented service of therapeutic cognitive activities and an understanding of the person's behavioral deficits [27, 32]. These services are directed to achieve functional change by reinforcing, strengthening, or establishing previously learned patterns of behaviors or establishing new patterns of cognitive activity or mechanisms to compensate for impaired neurological systems [27, 32]. Even though cognitive rehabilitation therapy was used firstly for the treatment of traumatic brain injury (TBI), later, there are many therapists and researchers who attempt to apply this intervention to treat patients with other brain-related diseases including psychiatric disorders such as schizophrenia, Alzheimer's disease, etc. [33].

Cognitive rehabilitation therapy was aimed to improve real-life functioning, living, and work status [27], by using mixed theories and models from a number of different areas including neuropsychology, occupational therapy, speech and language therapy, and special education [34]. These holistic and integrated programs must form part of the multidisciplinary approach [27]. However, some cognitive rehabilitation programs may rely on a single strategy. Before implementing each

program, a comprehensive assessment concerning impaired component skill or cluster of skills should be done [27]. The following five cognitive skill areas should be assessed and treated [27]:

1. *Attention skills*: sustained, selective, alternating, and divided
2. *Visual processing skills*: acuity, oculomotor control, fields, visual attention, scanning, pattern recognition, visual memory, and visual cognition or perception
3. *Information processing skills*: auditory and other sensory processing skills, organizational skills, speeds, and capacity of processing
4. *Memory skills*: orientation, episodic, prospective, encoding, storage, consolidation, and recall
5. *Executive skills*: self-awareness, goal setting, self-initiation, self-inhibition, planning and organization, self-monitoring, self-evaluation, flexible problem solving, and metacognition

After analyzing preferable results according to a practical cognitive model, a cognitive rehabilitation task or series of tasks is then designed to restore a specific cognitive function or compensate by adapting to the presence of a cognitive deficit [1]. In addition, when applying knowledge about neuroplasticity using physical exercise as an analogy, the intervention which will promote neuroplasticity, reshape neural network, and change cognitive functioning durably should spend sufficient duration to engage the second phase of learning [3]. Moreover, simple cognitive exercise should precede complex tasks because cognitive rehabilitation is likely to be more effective if simple cognitive processes are embedded before higher-level processes are mastered. Finally, interventions are most effective if they are tailored individually to each person's capabilities and limitations. To gain maximal benefit, it is important for the patients to have the tasks slightly above the threshold of challenge [3, 35].

Factors that might be responsible for the success in rehabilitation are the development of patients' awareness to their deficit via the cognitive exercises which are quantifiable and scoreable, showing the result as graphs to monitor improvement, and lead to promote self-motivation and self-esteem [27]. Moreover, the structured program approach to the materials, the daily concrete feedback and goals, the relatively short divided time frames to finish blocks of activity, the promotion of patient self-confidence including sense of mastery, and the massed practice available through homework exercises. Finally, factors from activation of neurological pathways through properly targeted repetitive cognitive tasks and the development and utilization of compensatory strategies to improve performance and process training which is comfortable for patients to accept constructive feedback.

32.5.2 Type of Cognitive Rehabilitation [36]

According to the approach for schizophrenic patients with cognitive deficit, cognitive rehabilitation therapy or cognitive training programs can be classified into three groups: training programs to enhance cognition, compensatory rehabilitation programs, and computerized cognitive training. Details of these programs are described as follows.

32.5.2.1 Training Programs to Enhance Cognition [36]

This intervention focuses on restoring cognitive functioning and correcting the underlying deficit, with the goal of learning how to do what was done before. These programs which were designed to improve some specific abilities are described as follows:

1. *Cognitive Remediation Therapy (CRT)*
   It was developed by Wykes and colleagues [37] based on an original program from Morice and Delahunty since the early 1990s. According to the leading developers and evaluators of cognitive remediation, the definition of cognitive remediation therapy for schizophrenia is "a behavioral– training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition, or metacognition) with the goal of durability and generalization" where social cognition is defined as "the mental operations that underlie social interactions, including perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviors of others." [38] CRT objectives include increasing the capacity and efficiency of cognitive functions, teaching global and transferable cognitive schemata to guide response, improving metacognition, increasing motivation, generalization of skills, and use of social support [39, 40]. The program consists of three modules, namely, cognitive shift module, memory module, and planning module [36]. In general, the training protocols use three or four techniques supplemented by extended practice in carrying out tasks to improve the automatization of the information processing necessary for each task [38] in order to build confidence and skill.
2. *The Newcastle Programs*
   It was contributed by Morice and Delahunty from Australia in 1996 [36, 41]. They tried to develop and examine three different programs. The first program, the modified Brenner program, was a modified version of integrated psychological therapy (IPT) for schizophrenia that was aimed to train the patients and their family members to solve the problem together. The second program, the computer-assisted program, is a computer exercise focused on practicing specific neurocognitive functions such as attention, perception, and reasoning. The result from these two aforementioned programs demonstrated progression in most WAIS-R tests but not in the same way when executive functioning was tested. Thus, the third program, the frontal/executive program, was created to enhance executive functions especially planning skills and cognitive flexibility [36].
3. *Cognitive Enhancement Therapy (CET)*
   It was developed by Hogarty and Flesher [42] to train neurocognitive skills and social skills for people with stable schizophrenia through the integration of computer-based cognitive exercises in attention and problem solving, with an active social-cognitive group experience designed to facilitate perspective taking, gistful processing of information, and social context appraisal. The intervention involves weekly sessions for up to 2 years [3]. Moreover, some researchers had attempted to apply it in treating patients with first-episode psychosis. However, it was designed only for persons with IQ above 80 and being psychopathologically stable [36].

4. *Attention Shaping* [36]
   It is used for modifying behavior, including cognition by focusing on selective repetitive reinforcement of successive approximations to required behaviors but not reinforcing to inappropriate behaviors.
5. *Integrated Psychological Therapy (IPT) for Schizophrenia* [36, 43]
   This is a group intervention which comprises of five subprograms, namely, cognitive differentiation, social perception, verbal communication, social skills, and interpersonal problem solving. Start practicing basic skills such as concentration, concept forming, abstracting ability, perceptive ability, and memory first before more complex forms of social behavior will be trained later.

32.5.2.2 Compensatory Rehabilitation Programs

These interventions focus on improving wider aspects of functions by using unimpaired cognitive process or applying to develop desired behavior for compensating cognitive deficits. However, these programs might be more suitable for people with significant cognitive impairment whose performance capacity might not be restored to achieve their premorbid level. The programs in these groups are, for example [36], as follows:

1. *Errorless Learning (EL)*
   In this program, each training task will be broken down into minute tasks. The most simple task will be practiced firstly, and then the more complex tasks will be trained later gradually. During repetitive training in every step, the patients will be educated to follow instructions for executing tasks perfectly and errorless [36]. EL takes benefits of implicit learning processes, learning without conscious awareness, to improve implicit learning systems that may restore impaired working memory and explicit memory processes [35].
2. *Cognitive Adaptation Training (CAT)* [36]
   It focuses on training patients with cognitive deficit to use environmental assistance and signs to promote executive function by organizing their routine activities such as using task checklists and alarmed drug packaging and sequencing their routine tasks properly. These strategies need to be employed after the patients' cognitive functions, pattern of behaviors, and environment were assessed holistically.

32.5.2.3 Computerized Cognitive Training [36]

These computer programs help the patient to improve only part of cognition which were practiced. Moreover, attention skills are the main focus of these computerized programs rather than problem-solving skills. Even though each patient rarely has social interaction during practicing and there are few studies supporting their effectiveness, these computer programs still have several benefits. For instance, the program can adjust the degree of difficulty systematically depending on each patient basis. Moreover, patients and therapists can check the outcome of learning process from receiving feedback immediately and getting various types of designed reinforcement. Here are examples of these programs:

1. *Gradior* [36]
   This cognitive training system designed by the INTRAS Foundation is aimed to rehabilitate cognitive functions such as attention, perception, memory, orientation, calculation, and language for patients with brain injuries, dementia, neuropsychiatric disorders with neurological deficit, and mental disorders or intellectual disabilities.
2. *RehaCom* [36]
   This computer program comprises of distinct modules such as attention and concentration, divided attention, working memory, spatial operations, logical thinking, visuoconstructive abilities, etc. Patients can select to practice with skills related to them.
3. *The Neuropsychological Educational Approach to Rehabilitation (NEAR)* [36]
   This training technique is developed within educational psychology to attract participants and make the patients practice different cognitive skills with computer according to contextualized format.
4. *A Game-Based Neurofeedback Training System* [44]
   Neurofeedback training (NFT) was developed and tested for enhancing cognitive performance in the elderly by promoting sustained attention based on the knowledge that ability to sustain attention potentially leads to improve cognitive ability. Therefore, the game-based NFT system was composed of 12 sessions for attention training and implemented twice a week. Jirayucharoensak and colleagues found that most Thai participants can modify their amplitude of certain brain wave ranges and produce specific patterns of cortical activity which are related to improved cognitive performance level after following this NFT protocol.
   Nowadays, there are various softwares or applications regarding computer-assisted cognitive retraining (CACR) for using with computers and tablets including smartphones for restoring cognitive function and training compensatory techniques in patients with various neuropsychiatric conditions. However, the studies to prove the effectiveness of these methods need to be further investigated [45].

32.6 Metacognitive Training

Metacognitive training (MCT) is a therapeutic intervention that draws on concepts used in cognitive behavioral therapy (CBT), cognitive remediation, and psychoeducation. MCT aims to raise awareness for cognitive biases and provide corrective experiences to clients [46]. Cognitive biases represent distortions in the selection, appraisal, and procession of information. These distortions can be helpful to some extent (e.g., a specific amount of mental rigidity is necessary to maintain long-term goals); however, they become dysfunctional when misrepresented. A growing body of research indicates that cognitive biases might contribute to triggering or maintaining psychotic symptoms in schizophrenic disorders and play a crucial role in delusions [47]. MCT for psychosis attempts to weaken delusional beliefs by helping

patients gain insight into the cognitive biases behind delusions [48]. It is focused on thinking patterns irrespectively of the content, thereby indirectly altering the metacognitive structure that is thought to underlie psychosis.

MCT was developed at the University Medical Center Hamburg-Eppendorf, and its version for psychosis is available in 33 languages. Other versions of MCT have been developed for other mental disorders. MCT for psychosis was originally designed to be delivered for a group of 3–10 patients; however, there is an individual form of the training as well. The training consists of eight modules. Each module describes the respective topic, explains how it can contribute to the formation of illness, and contains exercises aimed at challenging the functionality of cognitive biases and showing alternative thinking strategies. Consistent with the indirect approach of the intervention, most exercises are delusion-neutral; however, some of them offer an opportunity to address paranoid themes directly.

MCT addresses various cognitive biases such as that of "jumping to conclusions," "bias against disconfirmatory evidence," and attributional biases. Furthermore, there are modules concerning metamemory problems, theory of mind, and self-esteem. The jumping to conclusion bias refers to a tendency to gather less information or less reliable information than healthy controls before arriving to strong conclusions. Bias against disconfirmatory evidence refers to belief inflexibility or incorrigibility which might also play a central role in delusional conviction. Both the jumping to conclusions and the bias against disconfirmatory evidence appear to be present not only in patients with acute delusions but also in remitted patients and individuals at risk for psychosis [49–52]. Regarding attributional biases, patients with schizophrenia seem to show an inclination to externalize both positive and negative events rather than consider multiple causes, i.e., myself, others, and circumstances. Metamemory problems are indicated by an overconfidence in the accuracy of false recollections together with a reduced memory vividness and reduced confidence for autobiographical events. Deficits in theory of mind—i.e., the inability to recognize and represent the beliefs, thoughts, and intentions of others—have also been found to be present in psychosis by many studies; however, their specific contribution is unclear. Finally, regarding self-esteem, cognitive biases such as overgeneralization or catastrophizing alongside dysfunctional coping strategies are also addressed by MCT.

Jiang and colleagues [53] found in their meta-analysis a small but significant effect of MCT on positive symptoms; however, according to this study the wide diversity in the measures used to assess the outcomes made it impossible to come to a general conclusion. The meta-analysis by van Oosterhout et al. [54] concluded that studies do not support the positive effect of MCT on positive symptoms, data gathering, and delusions. However, Eichner and Berna [55] claim that this aforementioned meta-analysis excludes three positive studies. After the investigation of 15 studies, they found a small to moderate effect on delusions and positive symptoms. This effect on delusions were reduced but remained significant, when potential biases were considered. Acceptance of the intervention was generally reported to be high among patients with schizophrenia.

Most of these studies were conducted with patients with a relatively short duration of illness. However, MCT could as well be an important instrument of rehabilitation in low-functioning chronic schizophrenic patients [56]. Positive results were found among these patients in the self-rated frequency of delusional thinking and delusional belief conviction. Furthermore, based on patients' ratings, cognitive biases such as jumping to conclusions and catastrophizing were significantly reduced. Even more importantly, however, the completion of the training seemed to increase clinical insight at a larger scale than cognitive behavioral therapy. This is relevant as insight is a crucial factor in seeking optimal treatment and in therapeutic compliance.

Conclusion

At the beginning of treatment of patient with SMI who suffered from declined functioning in many aspects of their lives, various kinds of psychiatric rehabilitation were developed continuously to improve their functions in all involved areas. Moreover, after de-hospitalization of these patients from large mental hospitals occurred successfully across many parts of the world, supported housing services have contributed to more freedom and more social skills for many patients. Unfortunately, in a relevant proportion, patients moved from one institution (psychiatric hospital) to another institution (sheltered home), which is in contrast to the original idea of deinstitutionalization. In some regions, the most severely ill were not able to stay in the housing services provided by communities resulting in homelessness. Nevertheless, for the majority the development of supported housing was positive as compared to earlier hospital-based services. But, psychiatrists and service planners are challenged by the limitations of the available services.

To integrate these people into their communities, working can make them develop factors which are important to recovery such as responsibility, judgment, self-esteem, social skills, and personal power and control including vocational identity. Even though there are two main models for vocational training program which were train-place and place-then-train, supported employment which provides individual placement in competitive employment without prevocational training found that there are benefits over other vocational services in obtaining real-world competitive jobs and facilitating their integration while working against the stigma of mental illness especially when this intervention is integrated with other psychosocial programs which promote neurocognition, social cognition, and social skills.

As impairments in psychosocial functioning are common in people with SMI, the improvement of social skills is also an important treatment target. The social skills training clearly shows positive effects on psychosocial functioning, and participation in a training program might positively affect a number of dimensions important for recovery. However, this type of rehabilitation should be adjusted to the individual needs of the patient and integrated into a multimodal treatment program.

Moreover, it is also found that patients with SMI especially schizophrenia are suffering from cognitive deficit which is an obstacle to restore their previous function. Based on knowledge regarding neuroplasticity, some of these interventions are applied to restore specific cognitive impairments such as cognitive remediation therapy and cognitive adaptation training (CAT) which are used to train patients to adapt themselves with cognitive deficit for regaining their productive life. Even though computer-assisted cognitive retraining (CACR) has received popularity, it cannot replace the benefits of individual or group intervention which is useful to promote social functioning.

Finally, metacognitive training (MCT) as a hybrid of the approaches of cognitive behavioral therapy, psychoeducation, and cognitive remediation aims to provide insight for various cognitive biases that is thought to underlie psychosis such as that of "jumping to conclusions," "bias against disconfirmatory evidence," and attributional biases as well as a corrective experience. The training is a feasible, well-structured intervention which is likely to represent a safe, highly acceptable and promising intervention in psychosis. MCT could complement standard treatment approaches or be administered for patients to whom cognitive behavioral therapy is not an available option. However, more studies to prove the effectiveness of these interventions have been recommended.

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Prevention in Psychiatry: A Narrative Review of Conceptual Basis and Current Status

33

Adarsh Tripathi, Kabir Garg, and Afzal Javed

Abstract

Psychiatric disorders are among the most common causes of disability and burden worldwide. It has been estimated by the World Health Organization that close to 450 million people worldwide suffer from some sort of psychiatric illness. Even though the psychiatric disorders are usually diagnosed in the early adulthood, it has been found that the usual age of onset is in teens, and then they persist into adulthood, causing major impairments. Thus prevention in mental health is of utmost importance. The current narrative focuses on defining the concept of "preventive psychiatry," current scientific evidence base and possible future directions of these initiatives.

33.1 Introduction

Psychiatric disorders are among the most common causes of disability and burden worldwide. It has been estimated that close to 450 million people worldwide suffer from some sort of psychiatric illness [1]. Neuropsychiatric conditions have been calculated to cause up to 13% of the global disability-adjusted life years (DALYs), with psychiatric disorders making up to five out of the top ten causes [2]. Even though the psychiatric disorders are usually diagnosed in the early adulthood, it has

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been found that the usual age of onset is in teens [3], and then they persist into adulthood, causing major impairments. The incidence of mental illnesses is associated with further array of deleterious effects in the adulthood. These complications include unemployment, fall in average income, impairments in family life, and social functioning [4]. Surely enough, these disorders deserve to be targeted with aggressive and widespread preventive efforts. While preventive psychiatry has historically been largely overlooked area, encouraging developments in recent past have emerged.

The current narrative review focuses on defining the concept of "preventive psychiatry," current scientific evidence base and possible future directions of these initiatives.

33.1.1 Health and Positive Mental Health

"Health" has been defined by the World Health Organization (WHO) as "a state of complete physical, mental and social well-being and not merely an absence of disease or infirmity" [5]. The term can also be applied to " a state of fitness and ability, or to a reservoir of personal resources that can be called on when needed" [6]. In both the above definitions, it is clear that there can be no concept of heath without mental health. It is also imperative that mental health is just not the absence of mental illnesses but much more, and it is intimately connected with physical health and behavior [7]. Mental health has been defined by WHO as "a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" [7]. This concept of mental health has been further described in the terms of "positive mental health" which the WHO describes as "an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to the goals, expectations, standards and concerns" [5]. Thus this concept of positive mental health includes facets like optimism, well-being, resilience, and quality of life [8] and is very important, as the concepts of mental health promotion and prevention rely heavily on it for their aims and outcome measures.

33.1.2 The Need for Promoting Mental Health

Mental health affects all facets of human existence. It can be considered to have " both material and immaterial, or intrinsic values: for the individual, society and culture" [7]. The relationship between the human life and mental illnesses is bidirectional. A major example of this can be the culture, which is a sum total of views, beliefs, and practices, and differs from region to region thus even if the diagnoses remain the same across different region, the predisposing, perpetuating, and protecting factors, along with the expression of disease itself that varies greatly [9]. Mental health is also important for "social capital." Social capital is defined as "features of

social organization such as networks, norms, and social trust that facilitate coordination and cooperation for mutual benefit" [10]. While there is still debate on the extent and measurements of this determinant, there is no confusion when it comes to its utility. It is recognized that social capital enables promotion of social and economic growth [11]. A very recurrent question that arises every time this discussion is held is the validity of need for dedicated prevention and health promotion efforts while there exist health promotion interventions in general. Mental health and the physical well-being are intertwined. Both affect each other and influence each others' outcome [8]. Thus it can be understood that mental health promotion is essential for being able to achieve global health. And it is true that the basic tenets of mental health promotion and preventive psychiatry remain same as prevention practices in general, yet the outcomes of general health promotion and mental health promotion can vary greatly [8]. Also, a major difference is the fact that while general health promotion is broad spectrum and runs the risk of ignoring mental health, the mental health promotion focuses on psychiatric illnesses [12]. Preventive psychiatry has unfortunately been an ignored concept until recently, yet the importance and principles of prevention and risk factor in mental health have been historically identified. Freud tried to promote the understanding of the influence of events of childhood on the psychopathology in adult patients [13]. Prevention has also featured in the health policies of developed countries during the past decades. In the USA, President's Commission on Mental Health from era of Jimmy Carter impressed upon the importance of prevention in the planning of mental health policy [14]. Thus it can be easily seen that preventive psychiatry and mental health promotion are in no way "novel" concepts. The initial part of the twentieth century witnessed the initiation of preventive psychiatry as a discipline [15]. This was observed in the mental hygiene movement that aimed for prevention of psychiatric diseases and promotion of mental health at the community levels [16, 17]. Earlier, a majority of the skepticism associated with psychiatric prevention was based on the fact that little knowledge existed about the etiopathogenesis and perpetuating factors of mental disorders. The biological and psychological models were two separate entities and armed with this little know-how, effective preventive strategies were not possible [15]. However, knowledge about these facets of psychiatric disorders has increased by leaps and bounds over the last few decades. Biological and psychological factors have been amalgamated into the biopsychosocial model [18], which provides a good understanding for a majority of diseases, even if it still has some gray areas. Neuroimaging and molecular mapping have contributed immensely to our understanding of psychiatric disorders. Genetic predispositions have been identified, and the role of epigenetics is increasingly being studied [19]. This has resulted in the field of preventive psychiatry to expand into a multidisciplinary area and fueled interest and growth in mental health promotion and prevention.

Professional bodies at the highest levels have identified the burgeoning importance of prevention in psychiatry. The World Psychiatric Association has a consensus statement on preventive psychiatry [20] that identifies and elaborates the importance of prevention in psychiatry and also lays down the possible activities and pathways for mitigating the development of preventive psychiatry globally. The

statement accepts the necessity of the biopsychosocial approach in psychiatry and states that prevention and health promotion are important, albeit complex tasks that require cooperation between mental health professionals, professional bodies, governments, policy makers, legislatures, NGOs, etc. and a leadership role, even if "covert" to be assumed by psychiatrist and psychiatric bodies in guiding these efforts. In addition to statement on primary, secondary, and tertiary prevention, it also comments upon the essential nature of "quaternary prevention," i.e., reducing the impairment in the lives of the family and community of the patient, including destigmatization. For pursuance of such goals, the WPA also established the section on preventive psychiatry in 1996. The section actively promotes cooperation among members and agencies from member nations and regularly holds academic activities including publications, workshops, and symposia in international meetings, providing guidance to member bodies on the issues relating to preventive psychiatry.

33.2 Concept of Preventive Psychiatry

33.2.1 Prevention Versus Promotion

Although the terms "promotion" and "prevention" have been used interchangeably, there do exist differences between the two. Mental health promotion often refers to the positive mental health [2]. It focuses on the determinants of the mental health and aims to increase positive mental health, to reduce inequalities, to build social capital, to create health gain, and to narrow the gap in health expectancy between countries and groups [21]. Such activities include the creation of individuals and conditions that promote optimal psychological development and functioning. It is an "enabling process" which is "done by, with and for the people." Prevention of mental health may be considered an aim and outcome measure of mental health promotion, which is inherently a broader concept [22]. Mental illness prevention pertains to mental health problems, including the symptoms, disorders, and strains related to temporary or persistent distress [2]. It focuses on reducing risk factors and enhancing protective factors. This activity is aimed at decreasing the "incidence, prevalence, and recurrence" of psychiatric illnesses, reducing the duration of symptoms, eliminating risk factors and conditions associated with mental illnesses, and also reducing the impact of the illness on not only the patient but also the family and the society [23].

33.2.2 Levels and Types of Prevention

It is the preventive paradigm which carries the division into primary, secondary, and tertiary prevention, something that is recognizable by almost all the medical professionals. Leavell and Clark proposed this three-tier concept of prevention, as back as the 1960s [24]. The primary prevention refers to preventing the disease at the

pre-pathogenesis stage. Secondary prevention that is also known as health maintenance aims to promote early detection, screening, and prompt treatment along with limiting disability. The tertiary prevention is done at the later stages of the disease and is directed at the recovery, rehabilitation, and restoration of the functionality of an individual [25]. The secondary and tertiary prevention received popularization, much at the expense of the primary prevention, causing a shift of attention away from it [15]. Secondary and tertiary efforts in majority of cases are effectively treatment measures. This has caused the distinguishing line between the preventive efforts and regular clinical practice to blur. There is thus a major need to draw the clinician's attention back toward the aspects of health promotion and disease prevention [15]. The preventive efforts can also be classified on the basis of the population covered. Universal prevention includes the interventions that target the general public or a whole population group which is not identified on the basis of increased risk. The selective prevention targets the individual or subgroups of population that have the higher risk of developing a mental disorder, based on biological, psychological, or social risk factors. Indicated or targeted prevention is done for the high-risk individuals with minimal but identifiable signs and symptoms, indicating toward a mental disorder, but those who do not meet the diagnostic criteria of a disorder at that time [23]. This review is primarily focused on primary prevention of psychiatric disorders.

33.2.3 Concept of Risk and Protective Factors

Exact etiopathogenesis of most psychiatric disorders is still far from known. Mental health prevention effort, therefore, targets the determinants having a causal relationship or otherwise predisposing an individual to mental illnesses. Recent understanding places and immenses importance on the ability to identify and predict risk factors as the foundation of the future of preventive psychiatry [26].

Risk factors are those that are associated with an increased probability of onset, increasing the severity and duration of illness. Protective factors refer to conditions that can improve people's resistance to the risk factors [27]. These factors have been strongly linked to development and prognosis of psychiatric illnesses [28]. Both these factors, risk and protective, can be further classified based on their domains, such as individual, social, family related, economic, or environmental [2]. Furthermore, they can be generic, i.e., common to multiple psychiatric disorders. Interventions targeting such risk factors usually generate a broad spectrum of preventive effects. For example, poverty and child abuse have been found to be linked with depression, anxiety, and substance abuse; thus programs targeting these risk factors are expected to yield benefits to all the three diseases. On the other hand, disease specific risk factors are related to particular disorders.

The major socioeconomic and environmental risk factors have been found to be related to wider issues such as poverty, displacement, isolation, lack of education and proper nutrition, racial discrimination, violence, war, unemployment, and others [2]. The lack of basic necessities and deprivation hinders large masses from

leading an acceptable quality of life [29]. At the same time, protective factors in this domain include empowerment, minority integration, social participation, tolerance, social services, social support, and community network. These protective factors guide the development and delivery of preventive interventions and health promotion.

The other major domain of individual and family-related factors includes the biological, cognitive, emotional, behavioral, and interpersonal factors. They have been found to have major effects in the sensitive periods in the life, and their effects carry impact across generations [2]. An in-depth discussion of these risk and protective factors appears in the publications by the World Health Organization, Prevention of Mental Disorders: Effective Interventions and Policy Options [2] and Promoting Mental Health: Concepts, Emerging Evidence, and Practice [7].

33.2.4 Populations at Risk

While the importance of prevention in psychiatry cannot ever be overemphasized, it should also be understood that these efforts cannot be dished out with random abandon. It is very important that the involved parties (clinicians, policy makers, professional bodies) identify the populations and communities in need of the interventions and then target them for maximum effectiveness. Even though it has been identified that almost the whole population is at need for the mental health promotion rather than just the already ill or about to be ill [12], there still is the need to identify what intervention is to be applied where and to prioritize considering the finite and often inadequate amount of mental health resources at disposal [8]. A proposed solution for this is to construct different programs: some directed to discrete population groups, others focusing on general public and a separate set targeting those at imperative risk or already suffering from mental disorders [12, 30, 31]. These groups should however be comprehensive enough to include all the age groups, while identifying the unique, but not necessarily mutually exclusive challenges to mental health. For example, school children and teens have to deal with academics and peers while also being in the usual age of onset for disorders such as psychosis and substance use [8]. This is also the period when major behaviors and traits are developed either healthy or otherwise [32]. It has been seen that interventions done in this time period are likely to yield significant changes with long-lasting results [33]. Mental health has been found to have important bearings on the academic performance of this age group [34]; furthermore, ignoring this issue prevents them from achieving their complete potential [35]. Similarly, the old and aging population are affected by factors such as insecurity, financial dependence, physical ailments, and lack of adequate social support [36]. Loss of social status and reduction in social network play an important role in the genesis and perpetuation of psychiatric illnesses in this age group [8]. The population in between these extremes of ages also is very important. The adult population forms the major workforce, and the other two groups (children and elderly) usually depend on

them. This is also the usual age of starting of a majority of psychiatric disorders. This age group has been identified as a significant site for the prevention efforts [12, 30, 31]. Special groups are identified not just on the basis of the age. Women, of all ages, have been seen to have higher rates of certain psychiatric disorders. It is also more likely for a woman to be shouldering the responsibility of the primary caregiver, and thus there is a need for increasing awareness about mental health and well-being [37]. It has been seen that the two genders understand and respond to stressors differently. Females are also more prone to certain mental illnesses due to hormonal influences, proneness to violence, discrimination, exploitation, and unique life cycles [38, 39]. Females also are prone to financial and emotional dependence with restriction in life decisions and lack of empowerment, all of which has been identified as factors promoting development of psychiatric disorders [39]. And a unique risk factor the females are exposed to is pregnancy. Perinatal depression is a serious mental disorder, more so in the developing nations. While the effects on the mothers are easily fathomable, it has been found to be linked with infant malnutrition and growth retardation in early childhood and scores of other behavioral problems in adolescence [40–43]. Successful intervention in treating and preventing perinatal depression thus offers a significant mental health promotion strategy. The success stories are present in countries such as Pakistan [44] and India [45]. Another identified high-risk group is the migrant population [46], more so if the migration is involuntary such as wars, natural calamities, or other hostile conditions. Migrants have to face a cultural transition and also sometimes are at receiving end of backlash and persecution by the native population. It has also been seen that in addition to increased incidence of psychiatric disorders in the migrants, they also do not seek help and are reluctant to come forward [46].

War and terrorism not always lead to migration. A large portion of the native population are left to fend for themselves in these areas of upheaval and are often stripped off of the basic tenets of human life such as adequate food, shelter, education, and health, deprivations that keep them from leading the kind of life that everyone values. These deprivations are strong risk factors for development of psychiatric disorders, and as can be expected, psychiatric help is beyond the reach of these individuals [47].

Then there are communities that are perceived as “different” or even “immoral” by the prevalent cultural standards, for example, the LGBT (lesbian, gay, bisexual, and transgender) community. This community has been found to have specific mental health needs and risk factors [48]. First and foremost is the massive stigma attached to them, along with the discrimination and persecution at the social and even legal front. They also have significant stress in managing their personal identity in view of their sexual orientation. These stressors exist from the early ages right until the old age [49]. This list is in no way complete or exhaustive when it come to the issue of identifying groups at risk and their risk factors, a complete discussion of which is beyond the scope of the current article, but it serves to explain this particular construct of preventive psychiatry.

33.3 Evidence-Based Efforts and Interventions

33.3.1 The Evidence for Prevention

Using the original definition of evidence-based medicine by Sackett [50], evidence-based prevention and health promotion use the best available current evidence in making decisions regarding the activities and interventions to be applied to populations for achieving the best possible outcomes in terms of reducing the incidence of the diseases and helping individuals to exert a greater degree of control and improvement in their health status [51]. The need to demonstrate evidences for effectiveness cannot be overemphasized as these interventions are labor- and capital-intensive process and pressures always exist for accountability in spending public money by the governments themselves or by nongovernment organizations. A large number of programs have been found to yield good results across multiple studies. For a growing number of programs, replication studies have been carried out across different cultures and socioeconomic-political settings.

33.3.2 Examples of Effective Interventions

The fight against the burden of mental disorders requires not just theories and philosophies but also feasible interventions suited to the needs and resources of the local community with adequate motivation and backing from the political and clinical personnel. Over the last few decades, many studies in mental health promotion and disorder prevention, which may be considered to be overlapping [52], have been done and have demonstrated that such interventions improve not just the mental health status but also the physical health and the overall social and economic development [52]. The interventions can be divided into macro-, meso-, and micro-levels.

The marco-interventions include general, wide-based strategies such as improving nutrition. It has been found that nutritional interventions tend to give best results when clubbed with counselling and psychosocial care [52]. A major example of nutrition supplementation could be the iodine fortification of common salt which has been found to protect against mental retardation and lead to healthy development and better education outcomes while simultaneously protecting against multiple physical ailments [2, 53]. Another important example is the provision of supplementary nutrition in form of "midday meals" in Indian schools which has, in addition to nutrition fortification, also led to improved school attendance and retention, which in itself is a protective factor against mental illnesses [54]. These nutrition supplementation interventions have been found to be cost effective [2]. Another macro-intervention has been the improving of housing conditions. Poor housing is an indicator of poverty and has widely been a target to improve public health. Systematic reviews have suggested that this has a positive impact on perception of safety, community participation, and self-reported mental and physical health [55]. Improving access and quality of education remains another

important macro-strategy. Observational data from Indian states found that improving education yielded benefits that went beyond simple improvement of literary skills, these led to improved sense of pride, self-worth, and purpose, leading to greater confidence in oneself [56]. Using subsidies to close the gender gap in the education has also been suggested to be a viable strategy for achieving this [57]. Using this strategy, significant improvement in female utilization of educational services has been observed in Bangladesh [58] and Pakistan [57]. Community interventions using recognition of local risk and protective factors have been developed focusing on the empowerment of people. An example can be the Communities That Care (CTC) program from the USA, which was subsequently adopted in countries of Netherlands, the UK, and Australia [59–61]. It is a community violence and aggression prevention program that includes activities working simultaneously at multiple levels of community (through media and policy changes), the schools (improving curriculum and teacher training), the family (parental training), and individual level. A major target area of macro-strategies has been the misuse of addictive substances. The strategies employed include the taxation and controlled availability of such items, supportive environments for substance reduction (banning workplace and public smoking), and targeted interventions to reduce substance use during pregnancy. All of these have shown varying degree of success [52] especially in the cases of smoking and alcohol use [62, 63].

The "meso-" and "micro"-interventions involve a more personalized approach in the delivery of the interventions. These have focused on areas such as early development where home visiting as a method has been tried in at risk areas. Most home-based interventions focus on the educational strategies to improve the resilience and the competence of families and parents. It is understandable that having emotionally and socially competent adults as parents would be the key to success in raising healthy and well-adjusted children [15]. Thus programs targeting young parents and addressing their problems such as depression [64] and substance abuse [65] and also the programs providing training and education regarding aspects of parenting, such as promoting breastfeeding [66], have been found to yield significantly positive outcomes in terms of mental health and overall development of the child. Various evidences involving home visits for pregnant women in prenatal and perinatal periods have yielded positive results in mothers and eventually the newborns [67, 68]. Such results, including higher IQs, reduced behavioral problems; lesser incidences of substance use and delinquency have also been found to extend to the age of up to 15 years [69]. For preschool children and families at risk, community programs promote elementary reading skills and socio-emotional well-being. An example of this approach can be the "Perry Preschool Project" from the USA where half-day preschool interventions combined with weekly home visits for children from improvised backgrounds led to better cognitive development, academic achievement, and school completion along with fewer conduct problems and arrest up to age of 27 years [70, 71]. The speech and language skills of children from improvised families that have been found to develop slowly than their better-off counterparts have also been found to improve if they are subjected to early educational and stimulation interventions.

School is another important delivery platform of preventive interventions. And there are adequate evidences that providing universal programs to students can bring about positive changes in mental health [7]. They can be either targeting the entire school in an integrated approach or may just focus on only a part (e.g., children in a specific class) of a specific group of students exposed to certain risk factors. Usually, universal school-based programs focus on general risk factors such as subpar academic performance, aggression, bullying, isolation, etc. and have shown to increase the students' competence and resilience and have also found to yield reductions in depressive symptoms [72–74]. The older students in the middle and high school grades however face new challenges including exposure to delinquent behavior, substance use, and peer pressure. Programs focusing on skill building in this age group have been found to serve the dual purpose of promoting mental health and preventing substance use [7, 75]. It has also been proposed making changes to the overall school psychosocial environment ("child friendly schools"). The components of such an institution comprise of fostering a friendly, rewarding, and supportive environment, promotion of active learning and participation, and doing away with physical forms of punishment [76]. As with other intervention strategies, it has been observed that multicomponent programs that focus simultaneously on the children as well as the school ecosystem yield better results than either of the strategies alone.

The adult populations, who are the workforce of any community, understandable are exposed to an additional barrage of risk factors arising out of the workplace and work-related determinants. Job loss and dissatisfaction have been found to lead to serious repercussions on mental health. Providing unemployment benefit does not seem to be the answer as in survey; not working and receiving welfare has been found to be associated with negative cognitive beliefs, lower maternal health, less social support, and avoidant coping strategies [77]. Support and job search training for youths from low-income groups has been proposed as an effective strategy to improve coping with unemployment and reducing the negative mental health outcomes. An example is the JOBS program that has been locally adapted and applied in the USA, China, and Finland and has been found to have positive effects in terms of reemployment, the quality of jobs, and reducing depression and distress [78, 79]. However, just finding jobs is not the answer. Work-related determinants contribute to mental health problems including but not limited to burnout, anxiety, depression, etc. Thus, the interventions need to be targeted at either the coping strategies of the workers or the working environment. These include teaching stress management techniques, relaxation methods, social skills, and fitness training. These have been found effective in reducing the adverse psychiatric outcomes in workplaces.

Such interventions have been designed and tried for different populations based on the local risk factors and resource availability. Many of these have been tried in developing and low-income group countries as well. Although this list is neither exclusive nor exhaustive, one can appreciate the concept of tailoring and delivering interventions based on the area, the individual, and the population affected at large.

33.4 Preventive Psychiatry and Administrative Psychiatry

33.4.1 Multidisciplinary Collaboration

The preventive efforts in psychiatry do not mean only isolated programs. The need to incorporate prevention with the mental health administrative services has been identified since long [25]. There are however, certain challenges in this endeavor. A major roadblock is the tussle between the discipline of medicine, which is focused on health care for individuals and the public health, focused on well-being of the population. As a matter of fact, even many psychiatrists and mental health professionals that are in administrative capacities have been found to be unaware of preventive paradigm of psychiatry [25]. It stands to reason thus that psychiatric administrators may collaborate with public health physicians, researchers, and public health administrators more broadly. Another major problem that arises in preventive psychiatry is the allocation of resources, as the health services have to deliver both the treatment and the prevention services. Even now, psychiatric clinical practices are guided, even if unintentionally, by principles of prevention, especially the selective and indicated prevention [14]. Administrative psychiatrists can for one encourage practice of prevention-based psychiatry on a daily basis [25]. Some suggestible areas for service improvement by incorporation of prevention paradigms include (1) early detection of mental illnesses and substance abuse, (2) preventing relapse, (3) promoting healthy lifestyle modifications, and (4) suicide prevention and smoking cessation programs. Apart from making improvements to the service delivery, another equally important method is through policy [25]. This requires advocating for preventive psychiatry interventions to bureaucratic and legislative bodies. Administrative psychiatrists' work goes way beyond the clinics, and their collaboration is not limited just to government bodies but should also include communities, professional organizations, and NGOs. All of these collaborations open up areas for advocating, increasing experiences, and exchanging ideas on the issues of preventive psychiatry.

33.4.2 Education and Training

The education and training system is entrusted with churning out competent workforce and leadership. It is thus very important to include prevention and health promotion in curriculum of the undergraduate and postgraduate medical trainees and other allied mental health professionals [14]. Training in prevention and health promotion is an area broadly lacking in the current education system [25]. These principles need to be at par with the education in diagnosis and treatment of disorders. In the recent years postdoctoral fellowships and even super-specialization courses have been made available in the field of psychiatry, but such training opportunities are virtually nonexistent when it comes to public health or community psychiatry.

33.4.3 Research

Psychiatric professional bodies and administrators are often the guiding, funding, and regulatory figures in supporting and sustaining research efforts. These bodies can play an important role in the inclusion of prevention paradigms in the research activities [25]. While some may argue that a large number of current psychiatric research projects do have future goals that contribute to understanding and practice of mental health promotion and disease prevention, the need to promote research with well-defined, focused prevention and promotion-relevant aims and hypotheses still persists [31]. As has been discussed in this article, there is currently a growing body of literature on preventive interventions targeted mainly on children and adolescents [80]. A number of interventions have been tested and proven effective in controlled studies; the focus has now understandably expanded to include the issue of cost effectiveness [25]. Some identified areas of research for prevention efforts, in addition to the current endeavors, include interventions to promote adherence to treatment, reducing disability in patients of mental illnesses and studies on substance cessations and improving diet and lifestyle practices, the so-called primordial and tertiary prevention [81]. The collaboration between the psychiatric researchers and public health preventive medicine researchers can also be expected to yield good results with the cumulative expertise of the people involves and is an area that should be promoted by the regulatory and administrative bodies.

33.5 Recent Developments

33.5.1 Legislative Changes

As discussed above, not just clinicians but also the legislative and executive stakeholders in developed parts of the world have started to identify the importance of the constructs of preventive psychiatry, and this has started to reflect in their health policies and plans. For example, the Affordable Care Act (ACA) in the United States of America (USA) emphasizes upon the importance of health promotion and provides significant opportunities for mental health promotion [82]. Significant provisions include the promotion of integrated treatment at the primary health-care delivery level, allowing an amalgamation of primary health care with psychiatry and insurance reforms requiring coverage of prevention interventions such as smoking cessation counselling. It also sets up $15 billion worth of Prevention and Public Health Fund [83] while also creating the National Prevention, Health Promotion, and Public Health Council, which developed the National Prevention Strategy (NPS). The NPS has multiple priorities aligning with the goals of mental health promotion such as promoting positive early childhood development, proving support to individuals and families at need, promoting violence free environments, and promoting early identification and early access for psychiatric disorders [84]. Similarly, the Public Health White Paper for England [85] focuses on health promotion and well-being, making the individual and community partake in the responsibility of

promoting health rather than just the government. It focuses on issues of health improvement (making lifestyle changes, removing inequalities, and improving social conditions), health protection, and service delivery systems, even if the emphasis on service delivery promotes secondary and tertiary prevention and possibly neglects primary prevention [13]. While the effectiveness of preventive interventions has been identified in high- and low-income countries, the majority of results have been drawn from the developed world. As encouraging as they may be, these results cannot be generalized as there exist a vast socioeconomic-cultural diversity that mandates controlled replication studies before large-scale community programs can be rolled out. The World Psychiatric Association thus also identifies steps that need to be carried out to health promotion endeavors. These include previously identified steps such as strengthening the information gathering system, tailoring of culturally appropriate measurement instruments to gauge the need and monitor the progress of preventive interventions, bridging the policy gaps among the member nations on the issue of mental health promotion and ensuring sustainable, well-targeted financial sources.

Another salient example is the recently released National Mental Health Policy of India which incorporates mental health promotion and disease prevention as one of its key goals [86]. The steps included are redesigning the anganwadi centers and anganwadi workers to cater to early childcare and introduction of mother-child sessions on parenting skills, training of teachers and introduction of life skills training programs in the schools and colleges, and increasing awareness among the policy makers, planners, and governments of need to alleviate poverty and inequalities and a special emphasis on women's mental health. This indicates a significant stride toward providing impetus to mental health promotion and preventive efforts and can serve as a template for other low- and middle-income countries that very often lack adequate policy and legislative efforts in this direction [54].

33.5.2 Future Directions

As is appreciable from the review above, multiple strategies have been identified for prevention of psychiatric disorders. The need of the hour is to support a wider dissemination of knowledge and strategies, increasing cooperation globally to facilitate planning of more and more appropriate services and incorporation of these services in the routine health-care, educational, and social infrastructure. This needs implementation research and identifying roadblocks. Improving skills of mental health professionals by providing adequate training opportunities, ensuring adequate funding by provision of policy and legislative changes and improving collaborations of various stallholders are likely to help in effective realization of preventive strategies at the ground level.

A major component of future activities in this area needs to be the identification and assessment of needs and setting priorities [87]. A way to do this could be encouraging participation by the citizens, nonprofit organizations, and advocacy groups [8, 46] may not be needed. Another major activity that would need to be

carried out is the increasing awareness dispelling myths about mental illnesses as a majority of public in multiple countries have poor knowledge and attitude toward mental illnesses, which in turn decreases the help seeking and acceptance of mental health care [88]. Use of mass media, especially television and print media, may serve to this end [8]. There is also a need to support the research the etiology and progression of neuropsychiatric illness in relation to the biological risk and protective factors and thus promote collaboration among the realms of preventive and translational psychiatry [15]. At the same time developing a person-centered approach—i.e., formulating the interventions that are culturally sensitive and suited to the needs of the individual— with appropriate identification of her unique sets of strengths and weaknesses is a something to strive for [89].

Conclusion

Psychiatric illnesses, as with other physical ailments, have identifiable and modifiable risk factors. What separates it from the other disciplines is perhaps the ever-evolving complex interplay between the environment, culture, society, and individual that results in a large amount of variety. Psychiatric prevention, even though historically a neglected aspect of medicine, is increasingly receiving attention and action over the past 2–3 decades. There have been coordinated efforts to design and deliver preventive interventions at different levels and have been found to yield beneficial effects. The settings include homes, communities, schools, and workplaces with collaboration between the mental health professionals, allied personnel, and policy makers. The roles of psychiatrists in these include planning, delivery, advocacy to leadership and, guiding the stakeholders through the process. It must however be remembered that despite the recognition from various quarters of world, including international and professional bodies working in the field of public health, a large amount of work still needs to be done, more so in the low- and middle-income group and developing countries. It is thus imperative to continue to develop adequate resources and infrastructure at the local, regional, and international level to adequately counter the scourge of the increasing mental health burden. This requires efforts from all aspects of community and requires the psychiatrists, more than ever, to become aware and vocal in bringing preventive aspects of psychiatry to the forefront.

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Preventive Psychiatry as the Basis of an Undergraduate Medical Curriculum

34

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Abstract

The development of effective medical curricula is becoming increasingly challenging, due to the evolution of undergraduate medical education and ever dwindling resources. A paradigm shift is required for the evolution from traditional forms onto more innovative forms of curriculum development. On the other hand, despite compelling evidence on its clinical and cost-effectiveness, preventive psychiatry (mental illness prevention and mental health promotion) has been largely underrated, including in local and international policy, public health, clinical practice and also in education. As a substrate for the development of a medical curriculum, preventive psychiatry offers certain educational advantages owing to the importance of preventive thinking across psychiatry and the rest of medicine, its proximity to important educational outcomes (including crucial attitudes), its inclusion of generic clinical skills like communication skills, reflective capacity and empathy, its integrative and anti-stigma potential. Here preventive psychiatry is considered as a conceptual base on which a better undergraduate medical curriculum could be developed.

34.1 Preventive Psychiatry in Medical Curricula

It is widely accepted that prevention is better than cure. In addition to a broad and specific evidence basis supporting it, this assertion also receives logical and ethical support. The ethical case is justified by fulfilment of the basic ethical principles of medicine: preventing illness and promoting health maximise beneficence and

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non-maleficence, as well as autonomy and justice for the individual and the society as a whole, even before the emergence of illness.

Illness prevention and health promotion have been applied successfully in clinical medicine. Conversely, in psychiatry, prevention and promotion have not developed adequately, perhaps due to the multifactorial causal nature of psychiatric disorders and the difficulty in identifying specific preventive targets. This is enhanced by the challenge of proving an effective preventive intervention when its effect is expected in the distant future and in diffuse ways, not to mention the frequent political resistance to apply something without proof of obvious and easy-to-measure short-term benefits. Since the emergence of early evidence supportive of preventive psychiatry [1–3], ample additional evidence has come to light on the effectiveness of mental illness prevention and mental health promotion [4–8]. Despite this undisputed supportive evidence, preventive psychiatry is rarely prioritised over pressing clinical matters, even if the latter are clearly less clinically effective and cost-effective in the medium-long term.

Likewise, in medical education preventive psychiatry is underestimated and under-represented. This was once explained by the relative scarcity of a convincing evidence base [9], but this is no longer the case.

Preventive psychiatry is under-represented in current formal curricula of medical schools for a number of reasons: for instance, the benefits of teaching preventive psychiatry are hard to appreciate. Also, the nature of the current structure of curricula and their exams are made in such a way as for open curriculum subjects to get preferential treatment. It may also be due to the dual educational nature of preventive psychiatry. Despite many decades of deliberation, and despite a number of curricular structure changes, preventive psychiatry (or even more broadly, preventive medicine) is still not convincingly part of the undergraduate medical curriculum.

The WPA Section of Preventive Psychiatry, in collaboration with the WPA Section on Education, identified the need to explore to which extent preventive psychiatry is actually taught in medical schools around the world. Unpublished preliminary results of the Education and Prevention Intersectional Collaboration (EPIC) survey, served by the WPA Section of Preventive Psychiatry to over 500 medical schools around the world revealed a low response rate (13%), of which, however, the majority taught preventive psychiatry, regardless of whether it was explicitly mentioned in their curricula. This may be an indication that awareness of preventive psychiatry is not widespread among medical schools, but its value is appreciated among those who are aware of it.

The World Psychiatric Association undergraduate curriculum for psychiatry [10] promotes mental illness prevention and mental health promotion extensively. Similarly, in 2002, the WPA institutional programme on the core training curriculum for psychiatry [11] recommended preventive psychiatry as one of the basic components of the didactic curriculum for core training in psychiatry. The WPA has been one of the major promoters of preventive psychiatry, attested by the work of its scientific sections [12], as well as by campaigns of its leadership.

34.2 The Dual Nature of Preventive Thinking and Medical Education

Preventive medicine (illness prevention and health promotion) has been on the agenda for medical education for a long time. A 1923 issue of the British Medical Journal [13] strongly advocates for preventive teaching to permeate the medical curriculum, going as far as to suggest that "The preventive attitude of the student cannot merely be left to opportunity. It must be provided for". Psychiatry subsequently appeared strongly in the educational agenda of the World Health Organisation in 1961 [14], where its role is seen as formative towards the development of generic medical attitudes, in addition to the development of specific psychiatric competencies ("…(the student)… must also absorb ideas and develop attitudes which are basic to his future role as a doctor."). Following the pivotal World Conference on Medical Education held in Edinburgh in 1988 [15], the Edinburgh Declaration was drafted, in which the need for specific curricula on illness prevention and health promotion was emphasised. The World Federation for Medical Education went further to establish psychiatry as one of the six key specialties where the importance of health promotion was "indisputable".

From a philosophical perspective, these concepts are familiar. Aristotle, in his *Nicomachean Ethics*, made a brilliant distinction between what he called "intellectual virtue" (*διανοητική αρετή*) and "moral virtue" (*ηθική αρετή*) [16]. Loosely, to parallel Bloom's taxonomy [17], intellectual virtue relates to knowledge and skills, while moral virtue relates to attitudes. The difference of the two is most obvious in the way that they can be taught; on one hand, intellectual virtue may be taught didactically, openly, with the teacher being responsible for delivering knowledge to the student. On the other hand, moral virtue may be taught by example, between the lines, silently, with the student being responsible for being receptive to the experiences he/she is exposed to and for developing his/her attitudes accordingly.

Therefore:

The *teaching* of intellectual virtue (i.e. knowledge/skills) is *described in* the open curriculum

The *learning* of moral virtue (i.e. attitudes) is *implied by* the hidden curriculum.

This brief historical account reveals why it has proven very difficult to incorporate preventive thinking in medical education (either in psychiatry or the rest of medicine). This is probably because, educationally, preventive thinking has a dual nature: it is emphatically both an intellectual and a moral virtue. It composes of knowledge and skills, but also attitudes. It belongs both to the open and the hidden curriculum. Practically, in order for a doctor to practice preventive medicine, he/she must be firstly competent in knowledge and clinical skill, but also necessarily have developed a preventive attitude (e.g. to think ahead instinctively). This dualism makes preventive thinking difficult to incorporate as an explicit subject in a medical undergraduate curriculum, but equally easy to miss if it remains unexpressed.

The dual educational nature of preventive thinking may explain why its teaching has remained elusive, but also highlights the need to formalise preventive teaching as part of the undergraduate medical curriculum. Importantly, the dual educational nature of preventive psychiatry also highlights its potential usefulness in curriculum development.

34.3 Undergraduate Medical Education Needs a Paradigm Shift

Undergraduate medical curricula present with significant challenges, some of which may be tackled by using preventive psychiat ry as a basis for curricular development:

Content Inflation
Just like any curriculum, undergraduate medical curricula need to be relevant by adapting to changing times. One of the main modern challenges medical curricula face in this respect is content inflation. The latter is a consequence of the ever-growing amount of important new knowledge that medical students are expected to accumulate and assimilate. In the process of responding to this pressure, curricula are expected to evolve and achieve no less than to constantly redefine medical doctors [18].

Resource Depletion
Reducing curricular material burden is a common conundrum faced by anyone who has been involved in curriculum development; on one hand, vital new knowledge must be somehow included, while on the other hand, time and resources are depleted. One solution would be to empower students to pursue their own learning rather than to depend on didactic delivery. This assigns an active role to the students in their own learning, while at the same time it limits teaching time and content. While this approach is conceptually a "process-based" approach, and superficially contrary to the more currently prevalent "outcome-based" approach, in reality turning the process into an outcome confers significant advantages. Another (mutually inclusive) solution would be to use a curriculum basis which would be friendly towards the development of attitudes, as well as towards that of necessary knowledge (even if acquired in a self-directed way).

Bias towards Knowledge and Skills versus Attitudes
Another inherent problem of currently used curricula is their bias towards knowledge and skills as opposed to attitudes, which is why topics like professionalism, ethics, and stigm a often fe ature last or less prominently. This is not surprising, given the nature of curricula themselves; they are *expected* to describe what is meant to be taught, not imply what needs to be learnt. Basing curricular development on a subject that sits comfortably between the open and the hidden curriculum, and covers knowledge, skills and attitudes equally may help rebalance these important priorities. This is where the dual educational nature of preventive psychiatry may become useful.

Lack of Integration

Most medical school curricula nowadays make efforts to be "integrated" and thus include various types of educational activities, as well as a cross-discipline element. However, by experience, when this is applied artificially, it requires vigilance and intensive monitoring to ensure its functionality; therefore often it fails. Alternatively, if the curriculum was based on a topic that was by nature cross-sectional and required by default an "integrated" approach, then perhaps it would be easier to achieve that educational goal.

34.4 Can Preventive Psychiatry be the Basis for the Development of a Better Undergraduate Medical Curriculum?

> "The superior physician helps before the early budding of disease"
> Huang Ti (2697-2597 BC)
> The Yellow Emperor's Textbook of Medicine (Huang Ti Nei Ching Su Wen)

Preventive psychiatry can play a pivotal role in the reform of undergraduate education in medicine, as it combines two educationally advantageous concepts: preventive thinking and psychiatry. Taken together, these two offer an ideal ground for future doctors to develop their knowledge, skills and, most importantly, attitudes.

Preventive psychiatry's natural residence dually in the open and the hidden curriculum renders it a very convenient medium for medical students to learn the basics but also develop the most important lessons psychiatry has to offer at undergraduate level: attitudes. They may develop a holistic, person-centred approach, which is capable of helping new doctors develop themselves for new roles. The development of preventive thinking has the benefit of habitualising students to a holistic, humanistic, person-centred stance [19].

Concepts like resilience and mental capital may form part and parcel of daily practice. Equally, doctors with a robust preventive attitude will be more attuned to health promotion and public health issues, thus having a broader humanistic vista [20].

Furthermore, psychiatric skills such as communication skills, reflective practice and empathy are vital generic skills for any doctor. They do not differ to the skills students are expected to acquire elsewhere, while in the context of preventive psychiatry, they may be developed in a more effective, insightful and informed manner. More importantly, they may be applied with a mindset beyond the limits of an "on the spot" diagnosis and management, but with the intention of constructing a diagnostic formulation capable of supporting a prospective plan for the patient, thus achieving both acute management and illness prevention/health promotion.

Pressures on content volume and allocated time for teaching psychiatry make it important for educators to concentrate on the most time-effective but also

content-effective ways, without sacrificing what undergraduate medical students really need to know. By its mere nature, preventive psychiatry may be the right subject to cover knowledge, skills and attitudes that are crucial across medicine. Preventive psychiatry is an ideal aspect of psychiatry, which combines public health, preventive medicine, professionalism and psychiatry, all into one subject.

Preventive psychiatry may be a good educational paradigm given the practical reason that psychiatric problems are common in all parts of medicine. Just to exhibit some examples, up to 17% of medical inpatients have a secondary psychiatric diagnosis, and up to 39% of GP attendants have a somatoform disorder and up to 20% major depressive disorder [21]. Therefore, learning psychiatry at an undergraduate level is very important for all future doctors, so that they may recognise and diagnose primary psychiatric syndromes, psychiatric manifestations of physical illnesses and physical manifestations of psychiatric problems. The usefulness is clear for those not inclined towards psychiatry and possibly more for those who aim to become primary care doctors.

Because preventive psychiatry applies to other specialties and psychiatric subspecialties in this cross-sectional manner, one could characterise it as a "horizontal" educational target, cutting across many "vertical" traditional educational topics. This contextual relevance makes it an educationally time- and content-effective medium of teaching psychiatry and medicine.

Last, but certainly not least, basing a curriculum on preventive psychiatry (i.e. mental illness prevention and mental health promotion) would serve to destigmatise mental illness among new doctors [22, 23] and would position illness prevention on par with the promotion of health, reminding future doctors of the continua that exist between mental illness and mental health. The World Health Organisation, in its 2013–2020 Action Plan [24], recognises the strong link between illness prevention/health promotion and the reduction of stigma.

34.5 Conclusion and Future Directions

Preventive psychiatry is a promising but largely overlooked subject. Its clinical value in terms both of effectiveness and cost-effectiveness has low visibility, but is hard to dispute. Its educational value is exceptional, due to the fact that preventive psychiatry has a dual educational role, strongly promoting attitudes as well as knowledge and skills. Hence, its educational potential use as a curriculum base, especially in undergraduate medical education, is notable. It is suggested that further research is pursued in this area, with an ultimate scope to consider the development of a new undergraduate medical curriculum with preventive psychiatry at its core.

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Trends in Schizophrenia Diagnosis and Treatment

35

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Abstract

This review provides an overview of the concepts, methods and current status of the classification and diagnosis of schizophrenia and of the guidelines in schizophrenia treatment since the respective previous issue of *Advances in Psychiatry* had been published in 2009. While research evidence has greatly advanced the understanding of the aetiopathogenesis of schizophrenia, the diagnostic criteria of schizophrenia remain clinical ones. Classification criteria have been revised for the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) of the American Psychiatric Association. These and the revision of the

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classification of schizophrenia in the *upcoming 11th version of the International Classification of Diseases* issued by the World Health Organization (ICD-11) will be reviewed. Furthermore, a substantial number of studies have advanced schizophrenia treatment in pharmacotherapy and psychosocial therapies, and this increasing evidence makes it ever more important to establish clear guidelines to assure the transfer of evidence-based diagnostic and therapeutic procedures into clinical practice.

35.1 Introduction

Looking back at the report on schizophrenia in the third volume of the *Advances in Psychiatry* issued in 2009, it is evident that considerable advances have been made. International working groups have formed to study the genetics of schizophrenia in genome-wide association studies yielding tremendous progress. Also, in the course of the development of the fifth revision of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) of the American Psychiatric Association in 2013 and the still ongoing development of the eleventh revision of the *International Classification of Diseases* (ICD-11) by the World Health Organization (WHO), the available research evidence for innovative classification models for schizophrenia was thoroughly reviewed and assessed. In addition, a large number of studies have helped to establish advanced and highly detailed guidelines for the treatment of schizophrenia [1], and especially remarkable is the progress in the fields of psychosocial therapies including psychotherapy and vocational rehabilitation. However, similar to 2009, progress in the field of the development of novel pharmacotherapeutic drugs has been limited, and none of the novel findings about the aetiopathogenesis of schizophrenia have yet reached a state of evidence warranting the inclusion of aetiopathogenetic information in the diagnosis or classification of schizophrenia. This review will focus on the areas of the aetiopathogenesis, diagnosis, classification and treatment of schizophrenia, their advancement since 2009 and their future developments. For the sake of brevity, any selection of topics for our review is subjectively biased.

35.2 Aetiopathogenesis

In the aetiopathogenesis of schizophrenia, it is clear that this is a multifactorial, multistep *process* with a large degree of interindividual variability of its nature and course but with a final common and highly typical clinical picture. While group analyses show consistently that genetic factors and environmental and psychosocial factors all may play a role, there appears to be a high degree of interindividual heterogeneity as to the specific factors involved in individual patients, their time course, nature and degree of their influences, and the accompanying "pathoplastic" factors modulating the clinical manifestation.

35.2.1 Genetic Factors

A large number of genetic polymorphisms have been identified in a range of genes associated with the development of schizophrenia, and these were mainly linked to synaptic functions and immune functions, as was shown in multiple genome-wide association studies, which were the most important technological advances for the field of schizophrenia genetics since 2009 [2]. Similar studies now also link microRNAs involved in dopamine neurotransmission to schizophrenia risk [3]. Protein-interaction analyses linked with genetic analyses hint at a central role of synaptic dysfunctions in the aetiopathogenesis of schizophrenia [4]. The absolute contribution of each of these genes appears small, and polymorphisms do not seem to be disease specific, as they may occur in healthy persons or persons with other mental disorders. However, the evidence linking genetic factors involved in synaptic signal transmission with other neurobiological factors associated with schizophrenia is providing an increasingly clearer picture of the genetic foundation of schizophrenia. It remains to be seen if the multitude of genetic associations known to be associated with the development of schizophrenia can be combined in the future with protein analyses, neuroimaging technologies or neuropsychological tests, a field of research facing considerable challenges [5]. There is still the looming attraction of an increase of the predictive value of neurobiological tests for the future development of schizophrenia in individuals with an increased risk of disease development, who may then profit from prevention or early intervention. Such techniques today employ sophisticated machine-learning algorithms to analyze complex interactions of a range of putative risk factors including neuroanatomical and neurofunctional measures [6, 7]. Future studies need to show which algorithms work best.

35.2.2 Neurobiological Factors Associated with Schizophrenia

Taking together genetic and other neurobiological studies published since 2009, a picture emerges of the neurobiology of schizophrenia with two major aspects: a link to alterations of brain neurotransmission leading to impaired neurocircuit functions and a link with neuroimmunological processes. These will be the focus of this part of this review. An exhaustive review of the many neurobiological factors associated with schizophrenia is beyond the scope of this review, but the interested reader will find useful and more comprehensive systematic reviews issued by the World Federation of Societies of Biological Psychiatry in recent years (see, e.g. [8]). As is the case for genetic association studies, the neurobiology of these “other” factors is complex, and many factors may play a role with considerable interindividual variability. A common ground of many theories appears to be that schizophrenia is based on neurogenetic vulnerability genes, which are, however, not sufficient by themselves to cause the disorder. Further neurobiological factors need to come into play, and psychosocial and environmental stressors may need to be added to complete the aetiopathogenetic picture of schizophrenia. The search for reliable and specific clinical markers and biomarkers/endophenotypes for the early detection of schizophrenia

is ongoing, and current results suggest that there will be a range of biomarkers (probably disease stage specific) with considerable interindividual variability [9].

In brain neurotransmission, novel analysis methods of functional or anatomic neuroimaging, magnetencephalography and electroencephalography data have shown that the normal hierarchical organization of brain neurocircuits (with hubs and nodes functioning as relay spots of interaction between subnetworks of the brain in the sense of a functional modular architecture of the brain) is disturbed in schizophrenia patients [10]. Studies have also shown that neuroanatomical alterations play a role, most prominent of which is a dysmyelination leading to white matter dysfunction and a "disconnection" between brain areas in schizophrenia [11, 12]. Disturbed brain modularity appears to be a common pathophysiological pathway onto which genetic, anatomic and functional alterations lead in the aetiopathogenesis of schizophrenia. This seems to result in reduced cognitive flexibility, which appears to be at least partly mediated through glutamate-mediated neurotransmission [13]. The development of the hierarchical organization of the brain structure and its function is completed during adolescence, and this may explain why schizophrenia typically manifests during late adolescence. An important road for future developments may be the development of a combination of assessment approaches of brain connectivity, network structure and anatomical alterations, as has been shown for combining magnetoencephalography and functional magnetic neuroimaging data to analyze brain network connectivity data in schizophrenia [14].

Another factor which has received increasing research interest is the role of the immune system in the aetiopathogenesis of schizophrenia. There are genetic studies showing that the immune system may be involved [2]. Moreover, clinical evidence indicates that many patients with primary autoimmune encephalitis may present with symptoms of mental disorders including psychotic symptoms [15] suggesting the more general hypothesis that inflammatory states of the brain may be associated with schizophrenia [16, 17]. More specifically, patients with N-Methyl-D-aspartate (NMDA) receptor autoantibody-associated encephalitis may present as a schizophrenia-like mental disorder, and such antibodies have been found in several percent of all schizophrenia cases [18]. Early detection and the rapid initiation of appropriate treatment are paramount in these cases. Besides these clinical findings, recent evidence also implies brain microglial cells as playing a role in the pathophysiology of schizophrenia by mediating synaptic pruning and disturbing brain neurocircuits [19, 20]. However, while the NMDA receptor autoantibody-mediated cases can be clearly defined using modern autoantibody detection technologies, it is more challenging to dissect the role of brain immunocompetent cells in the aetiopathogenesis of schizophrenia. Still, this approach promises to open new diagnostic and/or therapeutic potential for the future.

35.2.3 Psychosocial Factors

This area of research is now focusing on the interaction of psychosocial stressors with brain development or other neurobiological factors. For example, recent studies provided links between dopamine neurotransmission and psychosocial stress

[21] or the cortical axis and the development of mental disorders [22]. Urbanicity may affect neural stress processing and may even have a role in brain development [23, 24]. Childhood neglect is associated with structural brain alterations and psychopathological symptoms of disorganization in schizophrenia [25], and different modes of childhood maltreatment may lead to different effects on adult psychopathology and brain disconnectivity [26]. These studies lend support to the hypothesis that psychosocial stressors and trauma may act not only psychologically but may actually lead to long-lasting alterations of brain structure and functions, which manifest only later in life. Surveys consistently show high rates of trauma experiences in people with mental disorders and also indicate preferential trauma disorder patterns [27]. Future research will need to show how to best detect such psychosocial exposure early in life, how to prevent them, and how to mitigate their late consequences on mental health with a view to develop new prevention and early intervention strategies for schizophrenia.

An important area of research into the psychosocial factors in schizophrenia since 2009 has been the elucidation of the role of psychological mechanisms in the development of schizophrenia. This research mainly focuses on the association of schizophrenia with the aberrant salience of thoughts (linked also to functional network alterations and disturbances of striatal dopamine-mediated neurotransmission; [28, 29]), a proneness for jumping to conclusions [30] and others [31]. These are today also considered in the development of cognitive behavioural therapies for people with schizophrenia.

35.2.4 Environmental Factors

As had already been known in 2009, a large variety of extrinsic factors like in utero infections, malnutrition and substance abuse (especially cannabinoids) seem to influence the manifestation of schizophrenia in individuals predisposed due to genetic factors. Traditionally, gene-by-environment interactions and epigenetic pathomechanisms have been implicated to explain the role of environmental factors in the pathophysiology and aetiopathogenesis of schizophrenia. The hypothesized impact of environmental factors may be on such epigenetic processes (biological) or it may be on psychological or social processes [32]. Recent research also indicates that other biological factors than epigenetic processes may mediate environmental stressor actions in the aetiopathogenesis of mental disorders, like effects on dopamine neurotransmission [33]. Based on register data, researchers are turning their interest now to the interactions of a number of factors in individual cases, for example, by studying the association between prenatal infection, peripubertal psychosocial trauma and the development of schizophrenia [34]. Providing such links may help to understand why "multiple hits" of genetic, environmental and psychosocial factors are necessary to explain disease development in individual cases. Recently, environmental pollution has also received renewed interest, but a review showed that the evidence base of this area of research was small [35].

There has been little progress to explain the often considerable time lag between the exposure to environmental hazards and the clinical manifestation of psychotic

disorders. As already mentioned above, recent hypotheses also put the immune system into a central role to mediate the effects of environmental damaging factors on the development of brain circuits, including delayed effects [36].

35.3 Diagnosis and Classification

Schizophrenia is defined as a mental disorder characterized by psychotic symptoms (delusions, hallucinations, thought disorder) of a certain duration occurring in the absence of other recognizable causes of psychotic disorders like several general somatic disorders, substance use or withdrawal of substances of addiction. The diagnosis of schizophrenia is therefore a clinical diagnosis. Following the limited degree of changes in clinical classification criteria for schizophrenia in DSM-5, there is now increased research interest in more robust studies of the phenomenology of psychotic disorders [37, 38]. A recent meta-analysis showed, for example, that the phenomenology of hallucinations in schizophrenia is not characterized by single unique features but largely shared with other psychotic disorders and that age at onset was a discriminative clinical feature [39]. Kendler reviewed the history of paranoia as the other defining clinical feature of schizophrenia in textbooks and DSM [40] and showed that the definition was unstable, indicating that further work is necessary to more clearly define the clinical picture of paranoia in schizophrenia. In modern classification, technical investigations like cranial neuroimaging or laboratory tests are only used to exclude other disorders as the causes of the symptoms of schizophrenia. The classification of schizophrenias and related disorders has received much attention since 2009 due to the revision process of the psychiatric classification systems ICD-10 and DSM-IV. Both major international classification systems for mental disorders, DSM-5 (published in 2013; [41]) and ICD-10, include a category "schizophrenia". The major changes in the chapter of schizophrenia implemented by DMS-5 compared to the previous version (DSM-IV) were the following [42]:

- First-rank symptoms were deemphasized.
- Dimensional assessments of the degree of severity of five classes of symptoms were introduced.
- "Catatonia" was redefined as a clinical specifier applicable to psychotic disorders
- Novel course specifiers were introduced.
- An "attenuated psychosis syndrome" was introduced as a novel diagnostic entity requiring further study.

The clinical symptoms of schizophrenia used in the classification criteria are given in Table 35.1. Due to the differences of details of the classification criteria in both systems, a person diagnosed with schizophrenia following the guidelines of one classification system may not fulfil the criteria of the other system, or vice versa. Such distinguishing differences are, for example, the different duration

Table 35.1 Comparison of the clinical symptoms of schizophrenia in the *Diagnostic and Statistical Manual of Mental Disorders* (fifth revision, DSM-5; [41]) and the *International Classification of Diseases* (tenth revision, ICD-10; [43])

DSM-5	ICD-10
Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated) At least one of these must be (1), (2) or (3) (1) Delusions (2) Hallucinations (3) Disorganized speech (e.g. frequent derailment or incoherence) (4) Grossly disorganized or catatonic behaviour (5) Negative symptoms (i.e. diminished emotional expression or avolition)	One very clear symptom (and usually two or more if less clear-cut) belonging to any one of the following groups listed as (a) to (d) or symptoms from at least two of the groups (e) to (h) (a) Thought echo, thought insertion or withdrawal and thought broadcasting (b) Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions or sensations; delusional perception; (c) Hallucinatory voices giving a running commentary on the patient's behaviour or discussing the patient among themselves or other types of hallucinatory voices coming from some part of the body (d) Persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity or superhuman powers and abilities (e.g. being able to control the weather or being in communication with aliens from another world) (e) Persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content or by persistent overvalued ideas or when occurring every day for weeks or months on end (f) Breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech or neologisms (g) Catatonic behaviour, such as excitement, posturing or waxy flexibility, negativism, mutism and stupor (h) "negative" symptoms such as marked apathy, paucity of speech and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication (i) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifested as loss of interest, aimlessness, idleness, a self-absorbed attitude and social withdrawal

criteria (6 months in DSM-5 and 1 month in ICD-10) and that ICD-10 does not require social or occupational dysfunction, as DSM-5 does, for establishing a diagnosis of schizophrenia.

The tenth revision of the ICD (ICD-10) was published in 1990, and a major revision of the classification of disorders was initiated by WHO in 2005 [44]. WHO appointed expert working groups to recommend changes to specific areas in the Mental and Behavioural Disorders chapter based on reviews of the available evidence and current practice. A "beta draft" of the new categories and definitions for the mental disorders in ICD-11 was publicly available on the Internet (http://apps.who.int/classifications/icd11/browse/f/en). More detailed draft diagnostic guidelines for Mental and Behavioural Disorders are currently under review and comment by members of WHO's Global Clinical Practice Network. Mental healthcare

professionals interested in the classification of mental disorders may become members and register for their participation in field trials [45] (http://gcp.network). The ICD-11 beta draft criteria are currently being assessed for their feasibility and inter-rater reliability in a range of field studies, both Internet- and clinic-based [46]. Proposals for revised classification criteria of schizophrenia and other primary psychotic disorders were developed and published by the WHO working group on psychotic disorders [47]. If approved following the current phase of field testing, the revised classification criteria for schizophrenia in ICD-11 may lead to a harmonization of the course criteria with DSM-5 but will retain the difference in the duration criterion. Similar to DSM-5, ICD-11 will deemphasize Schneiderian first-rank symptoms and will introduce severity/symptom specifiers. Details of the changes in diagnostic groups other than schizophrenia are detailed in Gaebel et al. [48].

35.3.1 Classification of Schizophrenia and Other Primary Psychotic Disorders

This grouping includes schizophrenia, schizoaffective disorder, schizotypal disorder, acute and transient psychotic disorder and delusional disorder. The chapter will have a range of changes from the previous ICD-10 categories with the intention to improve diagnostic clarity and utility [37, 38, 49]. In schizophrenia, the ICD-10 subtypes ("paranoid", "hebephrenic" and "catatonic") will be omitted, and the importance of the Schneiderian first-rank symptoms will be deemphasized, since there was not sufficient evidence for their clinical utility and stability over time. Newly developed symptom specifiers for the presence and severity of psychotic symptoms will be introduced to improve the characterization of the clinical picture. The specifiers will be tailored to assess the following psychopathological domains: positive symptoms, negative symptoms, depression, mania, psychomotor symptoms and cognitive symptoms. New course specifiers will also be introduced and will characterize the disease course by distinguishing between first and subsequent episodes of primary psychotic disorders and chronic (non-episodic) course types. Among the acute episodes, a clinical distinction will be made between acute psychotic symptoms which fulfil the classification criteria of the respective primary psychotic disorder, partial and complete remission. Another important new definition will be introduced for schizoaffective disorder as the simultaneous occurrence of schizophrenia and a mood disorder. This should help to clarify the clinical concept of temporal co-presence of symptoms of schizophrenia and a mood disorder, thus hopefully providing a more reliable classification and the exclusion of cases showing alternating subsequent signs of schizophrenia and mood episodes without clear clinical temporal overlap. In the group of acute and transient psychotic disorders (ATPD), clinical manifestations with and without symptoms of schizophrenia will be better differentiated. This change would be expected to help clinicians to better differentiate between cases of schizophrenia and cases of ATPD.

35.4 Treatment

Various treatment strategies and interventions have been developed for schizophrenia which have been summarized in particular over the last two decades in clinical practice guidelines (CPGs). These interventions have also been evaluated regarding efficacy (or effectiveness) and safety based on principles of evidence-based medicine to support clinicians and practitioners in their treatment decisions. As to schizophrenia, several CPGs were provided predominantly on a national level however many of them with limited quality [50]. Nevertheless, also CPGs with high-quality levels are available [1], one of them is the CPG of the UK National Institute for Health and Care Excellence [51, 52]. This description of treatment follows the [51, 52] recommendations, which correspond to those of other high-quality CPGs in core treatment decisions [1].

According to the factors involved in the aetiopathogenesis of schizophrenia, treatment is likewise multifaceted and includes biological and psychosocial interventions. In addition treatment interventions are conceptualized according to the illness course with early recognition and intervention in the premorbid prodromal phase, interventions in the acute phase and long-term treatment strategies in the post-acute stabilization and stable phase.

35.4.1 Early Recognition and Intervention in the Premorbid Prodromal Phase

It is well known that prior to the onset of a first episode in schizophrenia with manifest psychotic symptoms, many patients pass through a phase of several years with functional decline and unspecific (e.g. depressed mood, social withdrawal) or even more specific symptoms for schizophrenia (like attenuated or mild forms of psychotic symptoms). Early recognition and intervention in the premorbid prodromal phase aim at identifying persons in a state of (clinical) high risk (CHR or HR) for "psychosis" (including schizophrenia and other disorders with psychotic symptoms) and to provide interventions to prevent or postpone the psychotic onset. Besides this "indicated prevention" in the pre-psychotic phase, one has to distinguish programmes for early identification and early intervention in the (very) early psychotic phase (right after onset of psychotic symptoms) to shorten the "duration of untreated psychosis" (DUP) and thus also to improve course and outcome in schizophrenia [53, 54].

Besides early recognition based on neurobiological [55, 56] or neuropsychological [57] indicators for persons at HR, the clinical indicators range from "basic symptoms" or "cognitive disturbances" (COGDIS) in the "early at-risk psychosis state" to attenuated psychotic symptoms (APS) or brief limited intermittent psychotic symptoms (BLIPS) in the "ultrahigh risk" (UHR) or "late at-risk psychosis state" [58]. Based on two meta-analytic reviews, there seems to be no significant differences in diagnostic properties of the different clinical indicators [55, 56, 59]. Transition into psychosis rates for CHR subjects based on any clinical indicator

varies from 17.7% after 6 months up to 31.5% after 36 months [55, 56]. However a recent meta-analysis indicates an overall elevated risk in all help-seeking persons undergoing CHR assessment (CHR or non-CHR) with an overall transition rate of about 15% after 38 months [60].

The early intervention strategies in CHR subjects range from psychological interventions (mainly CBT), over neuroprotective agents (such as omega-3 fatty acids) to antipsychotic drugs. A meta-analytic review on RCTs indicates significant effects in preventing from transition into psychosis for the interventions (based on an overall comparison, mostly with standard treatment or placebo) after 12, 24 and 48 months [61]. Database for specific recommendations is too weak, but under safety considerations (low dose), antipsychotic treatment should not be the first choice [62].

35.4.2 Treatment in the Acute Phase

Antipsychotic drugs still represent the cornerstone of treatment after the full onset of psychotic symptoms in the acute phase. The initial expectations regarding the advantages of the newer second-generation antipsychotics (SGAs) compared to first-generation antipsychotics (FGAs) in efficacy and tolerability have only partly been fulfilled. SGAs also show different unwanted effects like weight gain or metabolic side effects, and their impact on negative or cognitive symptoms is not fully convincing [63]. Accordingly, SGAs are no longer preferred as first-line treatment in clinical practice guidelines in the main. Drug choice should be made in individual cases based on efficacy and tolerability considerations [64] and in shared decision with the patient whenever possible. The latter should contribute to a more favourable adherence, which is still a major problem in schizophrenia treatment. Nevertheless, drug treatment should be initiated as early as possible to shorten DUP with its negative impact on treatment course and functional outcome [65]. Antipsychotics should be administered in the recommended dose ranges, and somewhat lower doses are recommended in first-episode patients due to a better responsiveness and a higher propensity to side effects in this subpopulation in the main. Close monitoring of efficacy and especially side effects is recommended, and in case of non-response (after considering a sufficient time frame of applying the drug in the recommended dose range of about 2 weeks and also monitoring patients' adherence) or nonacceptable side effects, drug should be switched to another compound, including application of at least two SGA drugs. In case of further non-response and treatment resistance (after excluding adherence problems by drug monitoring on the serum level), a trial of clozapine treatment is recommended. In case of further non-response, the possibility of electroconvulsive therapy (ECT) could be offered and discussed with the patient.

NICE (1009, 2014) recommends offering psychosocial treatment (especially CBT) to all patients already in the acute phase; however this topic is a matter of debate [66]. Nevertheless CBT is recommended in case of treatment resistance and persisting (positive) symptoms.

35.4.3 Long-Term Treatment in the Post-acute Stabilization and Stable Phase

After sufficient response of acute symptoms, the respective antipsychotic should be maintained in the same dose to further improve symptom decline preferably to full symptom remission of positive and negative symptoms as consented by Andreasen et al. [67]. Beyond that, maintenance treatment (MT) should be continued, if applicable in a lowered dose, to prevent from relapse and improve quality of life and functioning. MT is recommended for (at least) 1 to 2 years after a first episode in schizophrenia and 2–5 years after multiple illness episodes up to lifetime in case of multiple relapses. MT with oral antipsychotics is recommended as the first choice; however MT with long-acting injectables (LAIs) or depot antipsychotics is an alternative treatment option especially in patients with adherence problems, in whom continued drug delivery is strongly indicated or if it is the preferred option by the patient. Besides continuous MT, the strategy of intermittent treatment (IT: stepwise drug discontinuation and early intervention in case of prodromal symptoms or early warning signs for an impending relapse) is available and, however, should not be (routinely) provided due do noticeably higher relapse rates (even in first-episode patients; [68]). Nevertheless based on the results of one RCT on targeted discontinuation (vs. MT, whereas drugs could be completely discontinued in only 22% in the IT-group, so authors later named it "personal dose reduction"/PDR) which shows higher social and occupational functioning after 7 years in the IT/PDR group [69], there is an actual debate about the pros and cons of (earlier) drug discontinuation or PDR after a first episode in schizophrenia [70].

In the last years, beyond the treatment goal of (full) symptom remission, the concept of recovery with obtaining a status of (almost) full social functioning and autonomy and occupational (re-)integration [71] was refueled. Especially in the USA, a nationwide initiative and research program for early and comprehensive treatment of first-episode patients was implemented [72]. Besides early initiation of drug treatment, in particular, psychosocial interventions (individual CBT, interventions to improve adherence, family interventions, elements of ACT, occupational rehabilitation/individual placement and support) are provided [73]. First results are promising (e.g. [74]) and however do also indicate that recovery in schizophrenia is further on challenging, in particular due to minor impact of available treatment options on negative and cognitive symptoms. Whether SGAs, CBT, antidepressants, brain stimulation or adjunctive glutamatergic drugs, significant effects and improvements are evident, however, they do not lead to a clinical breakthrough [75].

35.4.4 New Drug Developments

Especially regarding a more favourable impact on negative and cognitive symptoms, there are several efforts to develop and evaluate new and more effective drugs. Beyond the main neurotransmitter pathways of dopamine (targeted by FGAs) or serotonin (additional targeted by some of the SGAs), additional pathways involved

in the aethiopathogenesis of schizophrenia are targets for new drugs. The main proposed additional transmitter systems and respective mode of actions are GABA allostatic modulators, NMDA agonists (like glycine or d-serine), COMT agonists, A-7 nicotinic receptor agonists, glycine transporter inhibitors, antioxidants, and anti-inflammatory agents (for a summary, see [76]). Some of the proposed pathways have already led to new drug developments with promising first results, e.g. for celecoxib as an anti-inflammatory drug administered adjunctive to antipsychotics [77]. In addition, different new drugs for schizophrenia affecting mainly the dopamine and serotonin pathways have been developed and are already approved and available (mainly in the USA). According to a review from Citrome [78], iloperidone shows antagonistic effects at the D2/3 and 5-HT1A receptor as well as at the noradrenergic alpha 1/2 receptor, asenapine exhibits antagonistic effects on different dopamine and 5-HT receptors as well as the muscarinic M1 receptor, lurasidone has affinities to different dopamine and 5-HT receptors (with partial agonism at the 5-HT1A receptor) as well as effects on histaminic and muscarinic receptors and cariprazine shows effects on different dopamine and serotonin receptors (including also a partial agonism at dopamine and 5-HT1A receptors). Beyond that, brexpiprazole is approved in the meanwhile and shows partial agonistic effects at D2/3 and 5-HT1A receptors as well as antagonistic effects at different serotonin and noradrenergic receptors [79].

35.5 Discussion

It is becoming increasingly appreciated that the psychotic symptoms occurring in schizophrenia are not readily explained by neurobiological (neurophysiological or neurogenetic and other) mechanisms alone. While there is clearly a complex genetic underpinning leading to an increased individual risk of developing schizophrenia, current research shows that the aetiopathogenetic actors determining the transition from “at risk” to “schizophrenia” may be different from those sustaining chronic positive or negative symptoms [80], leading to the concept of stage-specific mechanisms acting in aetiopathogenesis and pathophysiology. Neuroimaging and neurophysiology data shows that schizophrenia and other mental disorders are characterized by disturbances of brain neurocircuitry and that there may be critical time windows of neurodevelopment in which preventive measures must be applied in order to prevent disorder development [81]. Therefore, the RDoC research initiative by the National Institutes of Mental Health aims to elucidate how neurobiological, psychosocial and environmental factors in a time-specific manner interact to cause mental disorders [82, 83]. New advances in “immunopsychiatry” may lead to a better characterization of the multiple aetiopathogenetic pathways into the clinical picture of schizophrenia, providing new methods to subtype patient groups and develop new immunomodulatory therapies [84]. While this search for novel diagnostic and therapeutic strategies is ongoing, the classification criteria of ICD-10/11 and DSM-5 are still useful to clinically define those in need of mental healthcare due to schizophrenia. At the same time, it is becoming evident that different criteria

may be useful for research purposes, because the DSM-5 and ICD-10/11 criteria may collect individuals with very different aetiopathological pathways under a single diagnostic term [85].

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Fighting Mental Illness-Related Stigma: What We Have Learned

36

Heather Stuart, Norman Sartorius, and Graham Thornicroft

Abstract

Negative societal responses to people with a mental illness may be the single largest barrier to the development of mental health programs worldwide. In addition to the symptoms of the illness, people with a mental illness must endure structural inequities that impinge on their health, social welfare, and civic participation. This chapter provides a narrative review of anti-stigma initiatives using selected examples from large national and international initiatives in order to draw out common (perhaps best) practices and lessons learned. Also, wherever possible, this review is based on programs that have been systematically evaluated with published results in the peer-reviewed literature.

Negative societal responses to people with a mental illness may be the single largest barrier to the development of mental health programs worldwide. In addition to the symptoms of the illness, people with a mental illness must endure structural inequities that impinge on their health, social welfare, and civic participation. Governments are increasingly aware of the heavy burden caused by stigma, and many countries now have large-scale anti-stigma programs to improve public attitudes and promote better social inclusion for people with a mental illness and their family members [1].

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This chapter provides a narrative review of anti-stigma initiatives using selected examples from large national and international initiatives in order to draw out common (perhaps best) practices and lessons learned. Also, wherever possible, this review is based on programs that have been systematically evaluated with published results in the peer-reviewed literature.

36.1 Conceptualizing Stigma

People use the term 'stigma' to mean different things. For some, it is synonymous with a negative and pejorative attitude, where 'discrimination' is reserved for the behavioural consequences of stigma. Often it is used to refer to a mark of shame that taints the bearer and reduces their social value. Social psychologists consider that stigma is a problem of knowledge, attitudes, and behaviour, where sociologists consider a much broader array of structural and social-psychological factors, including the greater power base of stigmatizing groups that allows them to marginalize and exclude those considered to be less acceptable [1]. When considering stigma in the context of a global public health problem, a definition that highlights the serious social justice and human rights inequities for people with mental illnesses is preferred, as this broader perspective aligns with the United Nations Convention on the Rights of Persons with Disabilities [2]. The Convention has reframed the notion of disability (including mental disability) from one that focuses on individual impairments, to one that emphasizes social and structural determinants of discrimination. The Convention affirms that people with disabilities have the right to be full and effective members of society and requires member states to tackle the social and structural barriers that currently exist [3]. While the focus on structural discrimination is a significant advancement in international discourse, it assumes that all mental illnesses are disabling (in itself, perhaps a consequence of stigma), ignoring the fact that there are people who have a mental illness who are not disabled.

36.2 Anti-stigma Initiatives

Given the broad array of stigma definitions, it is not surprising that considerable heterogeneity also exists in the realm of anti-stigma programming. Thus, defining what should be counted as an anti-stigma program can be challenging. As Beldie et al. point out, many programs undertake anti-stigma initiatives without ever conceptualizing them as such, including attempts to revitalize outdated laws and policies, as well as efforts to increase awareness about the availability and importance of accessing mental health treatments. For example, World Mental Health Day activities are often directed to mental health promotion, but they also have an important component of destigmatization [4]. For the purposes of this review, anti-stigma initiatives are considered to be those whose primary focus is to reduce prejudice and discrimination caused by mental illnesses and promote greater social inclusion for people who have had a mental illness and their family members. Mental health

promotion programs and advocacy programs that have stigma reduction as one among several of their goals are not included. Anti-stigma initiatives are described in chronological order (from earliest to latest) so that the evolution of anti-stigma efforts can be highlighted and better understood. Unless otherwise cited, information has been obtained from program websites, which are indicated.

36.3 Closed Ranks: Canada

Early promoters of community mental health have always assumed that there was a relationship between the environment and the occurrence of mental illnesses. Considering primary prevention of mental illnesses, they further assumed that the environment could be modified by educating the public, by fostering healthy habits in family life, and by intervening in social institutions [5]. While they were aware of stigma and talked about the need to deal with it to build community mental health, the first concerted effort to reduce stigma can be traced back to Elaine and John Cumming, described in their book, *Closed Ranks,* published in 1957 [6–8]. As the first published account of public perceptions of mental illness and as a result of their careful and critical evaluation of the effects of their anti-stigma activities, *Closed Ranks* achieved international recognition. Situated in a small prairie town in Canada, dubbed Blackfoot, the Cummings embarked on a 6-month intervention that used group interactions and personal communications, taking advantage of community events that could be platforms for stigma reduction. Given the intractable nature of stigma, the Cummings reasoned that Blackfoot residents would not be moved by the usual didactic methods or mass media interventions. Stuart et al. have since conceptualized this approach as 'enlightened opportunism' and describe it as a flexible, grass-roots process that capitalizes on community events and uses these springboards to action [9].

Their interventions followed three themes: first, that the range of behaviour that might be considered normal was broader than most would believe; second, that mental health problems have causes that can be identified and related behaviours addressed; and third, that normal and abnormal behaviours exist along a continuum with no sharp dividing point between the two. The Cummings used a quasi-experimental design to evaluate their effects. A control community, dubbed Deerville, was chosen as the basis of comparisons. The prairie towns were similar and far enough away from each other to avoid any contamination of effects.

Though initially hospitable, Blackfoot residents became increasingly hostile towards the researchers, eventually rejecting further interventions and 'closing ranks' (thus, the name of the book). The mayor of the town eventually and pointedly asked them to leave, and the evaluation data showed no evidence that Blackfoot residents had become less stigmatizing as a result of the planned interventions. Subsequent appraisal of the assumptions (or the theory of change) on which the program was based showed that they had been seriously flawed. For example, the townspeople accepted a much broader spectrum of normal behaviour than did the mental health educators who were trying to teach them to be more tolerant of

abnormality. Second, the lay population was not as ignorant of the social and biological causes of mental illnesses as the professionals believed and did not need advice in this regard. Finally, the message that there was a continuum between health and illness and that the dividing line between the two was arbitrary was entirely unacceptable. Residents saw a sharp distinction between the two and any information to the contrary caused anxiety and hostility.

The research team had not adequately understood the depth of resistance of the public's stigmatizing views nor had they involved the local community in their planning, evaluation, and program delivery. By their own admission, the Cummings had built an intervention on untested assumptions that were not evidence based or evidence informed—a mistake that has been repeated many times since. Blackfoot residents were recipients of anti-stigma interventions, rather than collaborators in the process. Key lessons were that a credible theory of change that is locally grounded and locally acceptable is needed to mount an effective anti-stigma initiative. Secondly, greater citizen engagement in the design and implantation of the program would have created better buy-in and have highlighted sooner the flawed nature of the program assumptions. The Cummings' disappointing results reverberated throughout the international community promoting a sense of nihilism with respect to stigma reduction efforts and a hiatus in dedicated anti-stigma programming that lasted four decades.

36.3.1 *Open the Doors*: Global Initiative

In 1996, the World Psychiatric Association embarked on an ambitious global program to fight the stigma associated with schizophrenia entitled *Open the Doors* under the then-president Professor Norman Sartorius [9–11]. With the exception of the Cummings' work, anti-stigma interventions had not received much academic attention so the scholarly literature provided little guidance on how to proceed. This meant that the program had to develop basic operating principles and structures including a conceptual framework to guide activities, an administrative structure, and evaluation approaches. An important challenge was the lack of data describing the scope and impact of stigma from the perspective of people who had experienced a mental illness and their family members, as well as the lack of psychometrically tested instruments that could be used to fill this gap. The lack of data made it difficult to target program activities to where they were needed most. Consequently, the program placed a high priority on the active participation of individuals with lived experience of a mental illness and on obtaining qualitative (e.g. focus group) data to help identify local priorities.

The selection of a well-defined target was one of the first key decisions made. *Open the Doors* targeted stigma associated with schizophrenia, rather than mental illnesses in general. Though a broad range of conditions might be included under the 'mental illness' umbrella, the public often thinks of symptoms and behaviours indicative of schizophrenia when they think of 'mental illness'. Also, the stigma associated with schizophrenia was thought to be more serious that that associated

with other more prevalent disorders such as depression or anxiety. The focus on schizophrenia facilitated the design and implementation of interventions and made it possible to work closely with community advocacy groups that shared this target group. Further, it was thought that any lessons learned in the fight against stigma associated with schizophrenia would translate to other conditions.

To develop community support, the program operated through Local Action Groups composed of thought leaders, policymakers, advocates, researchers, and people with lived experience of schizophrenia. Local Action Groups were keys to insuring that activities were locally relevant, and recruitment of enthusiastic volunteers enhanced the long-term sustainability and effectiveness of the program. They also had the benefit of coordinating efforts of other local groups towards a single common purpose. *Open the Doors* became active in over 20 countries and implemented more than 200 interventions. Though not all of these interventions were formally evaluated, critical reflection and formal evaluation of selected program processes and outcomes resulted in a number of key lessons. Perhaps the most important among these was that anti-stigma efforts could be launched in any country, including those with minimal resources if a devoted small group of community volunteers, including people with a mental illness and their family members, were central to the process. A number of programs continue to be active as part of the *Open the Doors* global network (e.g. Slovakia, Spain, Turkey, Romania, Poland, Italy, Greece Germany, Czech Republic) [12].

36.3.2 *Like Minds Like Mine*: New Zealand (https://www.likeminds.org.nz)

Like Minds Like Mine, in New Zealand, began in 1996 making it one of the first comprehensive national anti-stigma programs. Unlike many other anti-stigma programs, *Like Minds Like Mine* has been entirely supported by long-term government funding. Most other anti-stigma programs are funded from non-governmental sources or have received short-term government funding. The program deliberately articulates a human rights approach focusing on the social justice model of disability described above. *Like Minds Like Mine* is multilevel and multipronged. It combines national media messaging with local-level community action to change discriminatory attitudes and behaviours. Three levels of outcomes are articulated. At the societal level, the goal is a nation that is inclusive of people with a mental illness. At the organizational level, the goal is for all organizations to have anti-discriminatory policies and practices. Finally, at the individual level, the goal is that people with a mental illness will have the same opportunities as those without. The three foci are intended to align with contact, protest, and educational approaches to stigma reduction.

As knowledge about what is needed and what works has deepened, the emphasis of activities has changed from raising awareness and promoting attitude change to bringing about changes in behaviours. To assess effectiveness in creating behavioural change, a representative sample of service users was surveyed to determine if their experiences of discrimination had decreased during the previous 5 years. The

most common discrimination experiences reported were from family members (30%), followed by difficulties in making or keeping friends (28%). Sixteen percent identified healthcare staff as 'moderately' or 'a lot' discriminatory, and this was higher (26%) among those who were more frequent users. Just over half (54%) reported that there had been some improvement in prejudice and discrimination over the previous 5 years and 48% considered that the *Like Minds Like Mine* program had assisted in creating this change [13].

By 2003, the program had evolved to include structural discrimination as a key target. This meant advocacy for nondiscriminatory policies and practices both within organizations responsible for housing, education, and employment and within health services. One focus of activities was the development of a human rights training program to assist individuals with mental illnesses to use the existing protest mechanisms to eliminate mental illness-related discrimination. This resulted in an increase in human rights complaints relating to mental illnesses.

36.3.3 *See Me*: Scotland (https://www.seemescotland.org)

Scotland's *See Me* campaign was launched in 2002 after long-standing national concerns that action was needed to address prejudice and discrimination because of mental illnesses. Initially, the emphasis was on raising public awareness about the impact of stigma on people who have a mental illness and to improve public understanding of mental ill health. In addition to targeting the general public, certain specific groups were also targeted, such as youth and workers. There was also support for local activities. The model of change underlying the campaign was one that moved from awareness to attitude change to behavioural change, and this process was expected to take a generation or more.

Over time, the program adopted a more explicit human rights framework that emphasized behavioural change, and it was formally refounded in November 2013 with this explicit focus. Currently, the mission of *See Me* is to mobilize people, especially those with a mental health challenge, to work together and lead a movement to end prejudice and discrimination, work with people to change negative behaviours towards those with mental health problems, and ensure that the human rights of people with mental health problems are respected and upheld. *See Me* is committed to including people with mental health problems in all aspects of program delivery, including their participation in opportunities to influence government and other decision-makers. Their ladder of engagement describes how members of the public can interact with *See Me* to form a social movement. Initially, for example, people engage through the website and by receiving the newsletter and then through following the program on social media; participating in events and getting involved in focus groups and surveys; volunteering as a speaker or peer researcher; and becoming a community champion. Published evaluation data is not available for the refounded program, though a process evaluation has been completed showing that the program has been implemented as intended with fidelity the human rights principles and framework [14].

36.4 EU Ministers' Council Resolutions

In 2003, within the Greek Presidency of the European Union, the Greek Ministry of Health and Welfare organized a major conference focusing on stigma: *Mental Illness in Europe: Facing Up to the Challenges of Social Inclusion and Equity* [15]. The conference was organized in collaboration with the European Commission and the World Health Organization. The major issues discussed at the conference included prejudice, discrimination, social exclusion, mental health challenges in transitional Europe, care systems, the role of the media, and strategies to combat stigma, such as the global initiative *Open the Doors* and Scotland's *See Me* program. The conference provided a forum to voice deep concerns about the negative effects of stigma on the course and outcome of mental illnesses and on the quality of care and life of people with a mental illness and their family members. All parties agreed that there was a need to enhance the visibility and public awareness of the importance of mental health as well as the problems associated with stigma. Clear statements also emerged concerning the importance of accessing appropriate and effective treatment, education, and work and facilitating greater social integration. Based on these discussions, the Greek Ministry drafted a series of conclusions for endorsement to the EU Ministers' Council, which were officially endorsed in 2003. The Council's adoption of these conclusion committed the EU Ministers of Health to promote mental health issues, reduce stigma, and redress structural stigmatization at political and policy levels. More specifically, the Ministers recognized:

- That stigma contributes negatively to equality and social inclusion and has implications for health protection
- The deleterious effects of stigma on the course and outcome of mental illnesses and the standard of living and quality of life of persons affected
- The importance of promoting effective actions across all relevant policies to increase social inclusion and equity to combat stigma
- The need to enhance the public visibility and awareness of the importance of mental health and the problems associated with stigma
- The importance of access to appropriate and effective treatment, the labour market, education, and other public services to facilitate integration

In addition, they invited member states to give specific attention to the impact of stigma and ensure that these problems were recognized and that specific actions were taken to reduce the impact of stigma across all relevant policies and actions.

The European Council of Ministers' prompt adoption of the conclusions that came out of the conference is a good illustration of how structural changes at the highest policy levels have the potential to have far-reaching effects. Because it is not enough to address stigma reduction at the political level alone, however, these resolutions also underscore the importance of national anti-stigma initiatives such as those described throughout this chapter.

36.5 Stigma and Mental Illness Scientific Section, World Psychiatric Association

When Sartorius became President of the world Psychiatric Association, he proposed that the World Psychiatric Association become actively engaged in the fight against stigma. The *Open the Doors program* (described above) was one result. Members of the program came together for an inaugural *Together Against Stigma* international conference in Leipzig, Germany, in 2001, with the aim of fostering multidisciplinary interest in stigma reduction. *Open the Doors* members organized a second conference in Kingston, Canada, in 2003. Based on the success of these efforts, *Open the Doors* members developed a proposal for a scientific section on Stigma and Mental Disorders for the World Psychiatric Association. The World Psychiatric Association has more than 60 sections that are theme based and form the scientific backbone of the organization. In 2005, the Association's general assembly ratified the creation of a scientific section devoted to the prevention and reduction of stigma related to mental illnesses. Since that time, the section has coordinated international work related to stigma reduction and co-sponsored regular *Together Against Stigma* international conferences in Istanbul, Turkey (2006); London, UK (2009); Ottawa, Canada (2012); Tokyo, Japan (2013); San Francisco, USA (2015); and Copenhagen, Denmark (2017). These conferences are unique in that they deliberately bring together researchers, mental health professionals, policymakers, members of the media, and persons with lived experience of a mental illness to present results of effective anti-stigma interventions and develop collaborations between all concerned for further work in this field. The conferences have grown in size over the years, with over 800 attending the most recent meetings, indicating the section has taken a leadership role in building capacity and interest for anti-stigma measures across the world.

Current stigma section members are 41 active researchers from 22 countries who regularly contribute to the peer-reviewed academic literature. The section produces a bibliography outlining publications for a 3-year rolling window (available upon request). Publications reflect work conducted in both developing and developed countries, and the bibliography represents one of the most comprehensive lists of anti-stigma literature available. The current bibliography lists more than 150 publications (journal articles, books, and book chapters) where a stigma section member has been a lead or a co-author. Collaborations between Stigma section members have resulted in research networks such as ASPEN (http://mdac.info/en/aspen) and INDIGO (http://www.indigo-group.org) that are devoted to collecting cross-cultural data on stigma and stigma reduction (a list of publications can be found on their websites), collaborative research projects, such as the images of psychiatry project, which grew out of a leadership course for young psychiatrists organized by the Association for the Improvement of Mental Health Programs in Geneva [16, 17], and recent books examining stigma reduction from different perspectives in different parts of the world [18, 19]. Finally, section members have taken leadership roles in the creation of a new Stigma and Health peer-reviewed journal (http://www.apa.org/pubs/journals/sah) that was launched in 2016.

36.5.1 *Time to Change*: UK (https://www.time-to-change.org.uk)

Time to Change began in 2007 to improve public attitudes and behaviours towards people with mental health problems, reduce discrimination that people with mental health problems report, make sure that more people with mental health problems can take action to challenge prejudice and discrimination, and create a sustainable campaign that would contribute to communities and workplaces into the future. Activities are multipronged involving a national marketing campaign aimed at public attitude change, as well as targeted interventions to local communities, workplaces, and schools.

Time to Change has worked with researchers from the Institute of Psychiatry, Psychology and Neuroscience at King's College, London, to conduct independent evaluations of its activities. For example, changes in public attitudes were measured every year between 2008 and 2015; mental health service users were surveyed about their experiences with discrimination; a media analysis was conducted; and a return on investment economic analyses was completed. The early part of the program (2007–2011) showed a fairly consistent pattern of small, incremental, and positive changes over time (2009–2015). Initially, there was a small reduction in the discrimination reported by service users, improvements in employer recognition of common mental health problems, and improvements in medial students' attitudes (though these were short lived), but there was no improvement in the knowledge or behaviour of the general public or healthcare providers. (More detailed results can be found in a special supplement of the British Journal of Psychiatry, 2013.) In the second phase of the program (2009–2015), there were more consistent improvements in public knowledge, attitudes, social distance, and reported contact with people with a mental illness [20]. Subgroup differences were also noted. Those aged 25–45 reported greater changes than those over 65 or less than 25. Also, women reported greater improvements in contact with people who had experienced a mental illness. These findings support the effectiveness of combined local and national activities in reducing stigma, highlight the importance of long-term multipronged efforts, and suggest the need to tailor programs to specific demographic audiences, such as those based on age, ethnicity, or gender. A list of peer-reviewed publications can be found on the *Time to Change* program website.

36.5.2 *Hjämkoll*: Sweden (www.hjarnkoll.se; http://zeroproject.org/practice/handisam-nsphhjarnkoll-sweden)

The Swedish national anti-stigma campaign was carried out between 2009 and 2014 in several regions, ultimately covering approximately a half of the Swedish population [21]. The program was multipronged and multilevel, focusing on four main areas of work. A core area was the development of events that promoted social contact with people who had experienced a mental illness. Approximately 350 ambassadors were trained to take part in these activities. Media campaigns were a second focus, through television, the Internet, and newspapers. Third, the program

mobilized local-level activities in an effort to create sustained action. Finally, a fourth area was working life and the role of middle managers with staff responsibilities.

A network of Swedish researchers has evaluated the effects of the Swedish campaign using yearly population surveys (2009–2014) conducted by an external survey firm. They evaluated changes in mental health literacy, attitudes towards people with a mental illness, and intentioned behaviour. Mental health literacy, public attitudes, and intended behaviour improved significantly in the campaign regions between 2009 and 2014. Factors associated with greater improvement were female gender, higher education, and more familiarity with mental illnesses. Improvements in literacy, attitudes, and intended behaviours were also noted across the nation during the same time period. However, the timing of many of the changes in the campaign areas coincided with the roll-out of the campaign suggesting that the program was responsible for these improvements [21].

36.5.3 *Opening Minds*: Canada (http://www.mentalhealthcommission.ca)

Canada's *Opening Minds* anti-stigma initiative was established in 2009 and represented the largest systematic anti-stigma effort in Canadian history. From the beginning, the program took a targeted approach, focusing on youth, healthcare providers, the media, and workplaces. Unlike programs in other countries, *Opening Minds* did not undertake a media campaign as preliminary results showed little effect. Within each target area, *Opening Minds* partnered with university researchers and a host of community groups who were actively engaged in anti-stigma programming to create best practice networks. All programs used some form of contact-based education, where individuals who had experienced a mental illness delivered an educational intervention focusing on personal recovery and active learning.

Overall, results have been positive illustrating that contact-based education has the potential to reduce stigma across a range of target groups. (More detailed results are presented in a special supplement of the Canadian Journal of Psychiatry, 2014.)

Like *Time to Change* and *Hjämkoll*, *Opening Minds* also found that population subgroups based on gender and prior contact reacted differently to anti-stigma messages. There was also considerable heterogeneity in the implementation of like programs across the country and within specific target groups, suggesting that the creation of fidelity criteria would help maximize program outcomes across the board [22]. For example, a meta-analysis of 22 programs targeting healthcare providers showed that the most successful programs included positive social contact with people who have experienced a mental illness, personal testimonies from trained speakers with lived experience of a mental illness, multiple types of contact, a focus on behavioural change through skills-based interventions, enthusiastic facilitators who model a person centred approach, and recovery as a key message. Programs that included all six ingredients performed significantly better than those that did not [23]. The heterogeneity of program implementation has been noted elsewhere [4, 12].

36.5.4 *One of Us*: Denmark (http://www.oneofus.eu)

One of Us was initiated in Denmark in 2011, after considerable policy and planning work examining mental health literacy and stigma [24]. The first phase of the project was funded until 2015. A second phase (2016–2020) has now been funded. Work revolves around five target areas: public and the media, service users and relatives, staff in the health and social sectors, the labour market, and young people. The vision for *One of Us* was based on the *Time to Change* program in the UK: to combat discrimination and promote inclusion for people with a mental illness. This was to be accomplished by enhancing mental health literacy in the Danish population, reducing social isolation and exclusion, and creating a better understanding of mental illnesses in schools, workplaces, and everyday life situations. Activities occur at national, regional, and local levels. Social contact with people who have experienced a mental illness is a key ingredient, and a number of primary ambassadors (people with a mental illness) have been recruited to undertake program activities. In addition, secondary ambassadors—celebrities who support the campaign, some of who have experienced a mental illness—have also been recruited. Evaluation results (unpublished) have demonstrated that being an ambassador has a strong empowering impact on an individual's personal life, improves their self-esteem, instills hope for the future, improves capacity to deal with prejudice, and increases confidence. *One of Us* has also worked extensively with the media to combat prejudice, humanize people who have had a mental illness, investigate society's treatment of people with a mental illness, and make clear that a psychiatric diagnosis is not a life sentence. Population awareness for the campaign has risen from 26 to 37% over 3 years.

36.5.5 *See Change*: Ireland (http://www.seechange.ie)

See Change was initiated in 2010 to change minds about mental illnesses and end stigma. It is a partnership involving over 50 organizations. The goal is to create a disruptive, community-driven social movement in order to create an environment where people can be more open and positive in their attitudes and behaviours, have greater understanding and acceptance of people with mental health problems, have greater knowledge about mental health services, and reduce prejudice and discrimination. Rather than a top-down approach, *See Change* is a grass-roots initiative that engages people in their local communities to bring about change. Young males, people in the workplace, farmers, and rurally based communities were key target groups as they were found to be most likely to hide a diagnosis and the least likely to seek help. As with other national programs, the cornerstone of the approach is social contact theory that uses the personal stories of people who have had a mental illness to break down attitudinal and behavioural barriers. In 2005, over 80 ambassadors were involved with the program. The program also has a strong online presence through their website and social media networks.

Similar to the Canadian initiative, a partnership model drives the program's activities. In 2015, over 94 organizations had formally partnered with *See Change* to conduct local anti-stigma activities. Once a year (in May), they run a Green Ribbon campaign where they distribute green ribbons to spark a national conversation about mental health. In 2015, over 500,000 green ribbons were distributed free of charge which coincided with hundreds of local community events. A post-campaign survey conducted by a marketing firm showed that 75% of the public who responded said they felt more comfortable having a conversation about mental health (up from 71% in 2014) and 66% said the Green Ribbon campaign had encouraged them to start a conversation (up from 52% in 2013).

36.6 Discussion

Information on anti-stigma programs is difficult to acquire, as there are few of the programs that have been subjected to detailed evaluation over time. Online information may be available but only in local languages [12]. Also, at times, it is difficult to know what should be counted as an anti-stigma program, as many programs adopt a broad approach to mental health promotion and never conceptualize their work as an anti-stigma effort [4]. In addition to the programs reviewed here, scoping reviews have identified additional programs in Belgium, Croatia, Czech Republic, Hungary, the Netherlands, Norway, Portugal, Slovenia, Spain, and Switzerland [4, 12], and there are likely many more that have not yet been identified. This review focused on large (national and international) anti-stigma initiatives that had stigma reduction as their main goal with an emphasis on programs that have formally evaluated their activities, preferably with publications in the peer-reviewed scientific literature. All of the programs identified areas of success, though considerable heterogeneity was noted. Nevertheless, several common themes do emerge which can be considered to serve as a useful practice standard for the field:

- To be successful, programs need to be locally relevant. If not deemed to be locally relevant, programs may be met with community indifference or, in the case of Blackfoot, outright hostility. Most programs have addressed local relevance by adopting a grass-roots or multilevel structure that includes locally driven activities. While community engagement is an important strength of this approach, a limitation is that it is unclear which activities lead to meaningful reductions in stigma.
- A human rights, social justice framework is increasingly used as the starting point for program goals and activities. This is consistent with the United Nations Convention on the Rights of People with Disabilities [2] that focuses on improving social inclusion for people with disabilities. In the context of anti-stigma programming, it means moving away from knowledge creation or attitude change as primary outcomes, in favour of reduced discrimination at both individual and structural levels.

- Systematic review and evaluation are uncommon, though several large programs (e.g. the UK, New Zealand, Canada, Sweden) are notable in this regard. They have deliberately partnered with university researchers to undertake arms-length evaluations with the goal of publishing results in the peer-reviewed academic literature where they are available for best practice reviews. Such partnerships help to narrow the knowledge-to-action gap that has characterized much of the advocacy work in this area.
- Budgets for anti-stigma programs are not always reported, but they can be large (in the millions of dollars) or small. The *Open the Doors* network demonstrated that meaningful anti-stigma activities could be undertaken on a shoestring budget in both developing and developed countries. Partnership models, such as those used by Ireland's *See Change* or Canada's *Opening Minds*, make use of 'in-kind' resources and provide an important mechanism to promote local empowerment and sustainable action.
- Social marketing campaigns are characteristic of programs with large budgets but are typically used in conjunction with activities and regional and/or local levels. These are expensive, may be out of reach for many anti-stigma efforts, and may not be the most important ingredient needed to bring about behavioural change. Lack of ability to mount a large social marketing effort should not be a barrier to meaningful anti-stigma activity.
- All programs have used social contact theory as the basis for including people with prior experience of a mental illness as the centerpiece for anti-stigma activities. Personal stories and testimonies, offered face to face and/or via social media, have been considered to be a best practice in the field, and there is good evidence that these social contact approaches are effective in improving attitudes and reducing social distance [25]. They are also particularly well suited to local efforts and have the added benefit of promoting empowerment among those providing the interventions.
- Heterogeneous effects have been noted both across similar programs and within programs depending on participants' age, gender, or past contact with someone with a mental illness. These results suggest that anti-stigma programs need to consider even more targeted approaches that are strategically focused on the learning needs and predispositions of specific subgroups (defined, e.g., by age, gender, or ethnicity) within broader target audiences.
- Though many programs identified the general public as a target group of interest, more specifically defined groups, such as youth, workers, or healthcare staff have emerged as important targets for anti-stigma activities across most of the programs. Much program activity is now undertaken at local levels with these groups in mind.
- Finally, it is clear that to be successful, anti-stigma programs need to be sustained over many years. One off interventions or short bursts of activity do not yield meaningful or sustained change.

Stuart and Sartorius [11] have described a new paradigm in anti-stigma programming as one that recognizes that stigma is not a generic social process stemming from ignorance and misinformation but evolves along various social dimensions

that are locally and culturally specific. In the new paradigm, the ultimate goal is no longer to improve knowledge or attitudes but to create improved social inclusion and life chances for people with a mental illness. Programs that target localized needs among clearly delineated target groups will hold the best promise for success. The initiatives reviewed here provide examples of anti-stigma activities that are embracing aspects of this new paradigm. While we have learned much from these efforts, in the future, more systematic evaluations conducted at arm's length by university-based researchers are necessary to further create and disseminate best practices in the field.

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Transcultural Psychiatry: Refugee, Asylum Seeker and Immigrant Patients over the Globe

37

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Abstract

The number of refugee, asylum seeker and immigrant patients over the globe is growing dramatically, and industrialized countries are likely to receive increasing numbers of people belonging to ethnic minorities in the form of refugees and asylum seekers due to a global increase in social and political instability as well as socioeconomic conflicts. The proportion of people with a serious mental disorder such as PTSD among this population is high. Thus health-care services should prepare themselves to better serve this group of ethnic minorities. They are insufficiently prepared for this specific population of mentally ill immigrants or ethnic

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minority groups. Particularly, mental health care for refugee, asylum seeker and immigrant patients is lacking, e.g. in cultural competence, intercultural psychotherapy and ethnopharmacology as well as legislation related to access to and utilization of health services, and varies from country to country. Transcultural psychiatry is a discipline within psychiatry, which deals with refugee, asylum seeker and immigrant patients over the globe. This chapter will give an overview on transcultural psychiatry and psychotherapy and future perspectives.

37.1 Introduction

The older approaches in transcultural psychiatry were part of colonial ways of thinking, in which professionals' work was based on a universal system of knowledge grounded in science that was viewed as acultural [1]. However, the postcolonial turn in scholarship showed clearly that all knowledge systems, including science, bear traces of their social, cultural and historical origins [1].

In its homepage, the WPA-TPS describes that the discipline of transcultural psychiatry (TP) continues to pursue the comparative approach outlined by Kraepelin [2] and subsequently developed by Wittkower [3] in the achievement of its five main objectives. These are:

- Exploration of the similarities and differences in the manifestations of mental illness in different cultures
- Identification of cultural factors that predispose to mental illness and mental health
- Assessment of the effect of identified cultural factors on the frequency and nature of mental illness
- Study of the form of treatment practised or preferred in different cultural settings
- Comparison of different attitudes towards the mentally ill in different cultures

WPA-TP Section represents a global network of researchers, clinical workers and teachers in the field of cross-cultural and ethno-psychiatry. Section membership is open to psychiatrists, psychologists, anthropologists and social scientists who are committed to this field (http://www.wpa-tps.org/about-wpa-tps/transcultural-psychiatry/).

This chapter will give an overview on transcultural psychiatry and psychotherapy and future perspectives.

37.2 Statistical Data About Displaced Persons

According to the UN [18], the number of international migrants, persons living in a country other than where they were born, reached 244 million in 2015 for the world as a whole. This is an increase of 41 per cent compared to 2000. According to

UNHCR [19], there are more than 65.5 million forcefully displaced people worldwide. This figure includes almost 22 million refugees. The majority of these refugees live in neighbouring countries. Only 6 per cent of them are living in Europe. UNHCR [20] reports that the terms asylum seeker and refugee are often confused. According to their definition, an asylum seeker is someone who says he or she is a refugee, but his or her application for asylum has not yet been definitively accepted [20]. Asylum seekers are individuals who have sought international protection ([20], p. 28). "Refugees include individuals recognised under the 1951 Convention relating to the Status of Refugees; its 1967 Protocol; the 1969 OAU Convention Governing the Specific Aspects of Refugee Problems in Africa; those recognised in accordance with the UNHCR Statutes; individuals granted complementary forms of protection; or those enjoying temporary protection. The refugee population also includes people in a "refugee-like situation" ([21], p. 56). They have well-founded grounds for fear of persecution because of their race, religion, nationality or political opinions or membership in a particular social group. These groups are unable to obtain sanctuary from their home country or, because of perceived threat, are unwilling to avail themselves of the protection of that country or, in the case of those not having proof of nationality and who have left their former countries of residence, are unable or, because of perceived threat, are unwilling to return to their former countries of residence [21].

The migrant population includes persons who are forcibly displaced (notably refugees, asylum seekers, internally displaced persons (IDPs)) and those who have found a durable solution (returnees) as well as stateless persons. For reasons of persecution, armed conflict, strife, generalized violence or human rights violations, most of them have had to leave their homes. During 2014 an average of 42,500 persons per day left their homes *to* seek protection elsewhere, either within the borders of their countries or of other countries because of armed conflict and persecution [20]. Many of these displaced persons have frequently been subjected to physical, sexual and/or psychological violence and traumatic bereavement [20]. It is well known that there are significant geographical differences as the developing regions are host countries for 86 per cent of the world's refugees and the least developed countries provide asylum to 25 per cent of the global total [20].

37.3 Migration and Mental Health

Globalization and refugee migration are significant issues in transcultural mental health care. Migration is part of human life. It is well known that migration can take on different forms, although it may be difficult to differentiate between forced and voluntary migration because both elements are often involved [4, 5]. Factors such as poverty, persecution or violence may play a main role in the process of migration, in which moving from one cultural and social setting to another for an extended period of times is involved and the loss of the familiar language (especially colloquial and dialect), attitudes, values, social structures and support networks may be also involved [4, 6]. Concerning this matter, Eisenbruch [7] termed it as a loss

"cultural bereavement". Particularly, in minority groups, the loss may be serious if the available social support is not appropriate. Sometimes, the cultural bereavement may be diagnosed as a psychiatric disorder; it is misdiagnosed because of linguistic and cultural misunderstandings and because of the use of Western diagnostic criteria in non-Western people [4, 6, 8–10]. Additionally, stress-related risk factors in migrant groups may be related to three arbitrary stages: premigration, migration and post-migration. Furthermore, social factors including cultural bereavement, culture shock, social defeat, as well as a discrepancy between expectations and achievement, and acceptance by the new nation can all affect adjustment [4, 6, 10, 11]. Further risk factors in new communities can include social exclusion, stigma and discrimination. Cantor-Graae and Selten [12] put forward the hypotheses of chronic experience of social defeat related to poor mental health and risk of psychosis in immigrants. It is well known that stigma and social exclusion commonly affect a person's recovery process as well as opportunities for societal participation [13–15]. Social exclusion may especially count for migrants without a resident permit. Laban et al. [16] found, e.g. that a long asylum procedure (with very limited rights to work and education) doubled the risk for a psychiatric disorder, independently from the experienced traumas in the country of origin. Stigmatization and discrimination which is often faced by the migrant in the host country are also emphasized as strong influencing factors of the mental health consequences of migration [14].

Beyond that, Butler et al. [17] highlighted that individual psychological resources, social support, a successful acculturation process, cultural variations and time since relocation are identified as statistically significant protective factors against the development of common mental disorders among migrants. The authors found new enlightening points including the significant impact of varying patterns of psychological distress, which is the most adverse for common mental disorder [17].

37.4 Mental Health in Refugees, Asylum Seekers and Immigrant Patients

It is well known that migration is one of the risk factors for developing mental disorders and that traumatized migrants in particular may face psychological distress and even serious psychiatric illness as they have been exposed to adverse conditions before, during and after migration [4, 6, 11, 17]. Prior to migration, migrants may have been exposed to deprivation, persecution, violence, imprisonment and human rights violation, including sexual harassment and even torture [6, 11]. Particularly, it is recognized that the transition phase which often includes a temporary residence can also be perceived as very stressful as well as the post-migratory phase in the new host country. Data from studies on risk for psychosis show that stress factors in the post-migratory stage over all have more impact on mental health than those in the pre-migratory stage [22]. Several authors reported [23–26] that the loss of loved ones/caregivers and/or livelihood, the destruction of property, deprivation, persecution, insecure living conditions, war, torture, imprisonment, terrorist attacks, abuse and sexualized violence are traumatic experiences of refugees and asylum seekers.

According to Heeren et al. [27], experiences e. g., defencelessness and disorientation, conditions of cold or heat, hunger and thirst, lack of medical care, robbery, assault and discrimination during the process of flight are often. Furthermore, many women may be subjected to different kinds of sexual assaults and violations [28, 29].

Lindert et al. [5] reported that the rate of mental disorders was twice as high among refugees than among economic migrants in Europe. The authors found also that refugees and asylum seekers suffered 44 per cent from depression, 40 per cent from anxiety disorders and 36 per cent from PTSD. Accordingly, Gerritsen et al. [30] reported that among refugees and asylum seekers, 56 per cent suffered from depression, 56 per cent from anxiety disorders and 21 per cent from PTSD. Several studies have the focus on the psychiatric morbidity among different types of migrants in different countries. But findings are not all the same which is reflected in Priebe's finding published in a report for WHO that, in general, the rates of psychotic, mood and substance use disorders in groups of refugees and asylum seekers appear similar to those found in host countries. The authors found also that post-traumatic stress disorder (PTSD) is more common in refugees and asylum seekers [31].

Along this line, a Swiss study reported that illegal migrants, asylum seekers and refugees had higher psychiatric morbidity compared with native groups and that about half of the asylum seekers and refugees fulfilled PTSD criteria [27]. However, Steel et al. [32] reported in a systematic review and meta-analysis an average for PSD in refugees and asylum seekers between 13 and 25 per cent. Hassan et al. [33] underlined that some forcibly displaced people are at particularly higher risk for mental disorders: women in female-headed households, adolescents, the elderly, those lacking documentation, persons with disabilities or pre-existing health or mental health issues, survivors of various forms of violence and those in extreme poverty [33].

37.5 Resilience-Oriented Treatment of Refugees and Asylum Seekers

As shown above the prevalence rates of psychopathology among asylum seekers and refugees are high and next to the traumatic experiences in their country of origin, they face many challenges, disappointments and adversities in the host country. These day to day stressors interfere heavily with the treatment. The debate of what kind of treatment should be given to asylum seekers and refugees is still going on. Nickerson et al. [34] observe two approaches, namely, trauma-focused therapy and multimodal intervention. The trauma-focused approach is grounded in the contemporary cognitive behavioural framework, while the multimodal intervention tries to address not only the psychological reactions that may occur after traumas as well as subsequent psychological stressors, physical health problems and resettlement and acculturation challenges.

A new approach in this seemingly contrasting treatment interventions is based on the concept of resilience. A resilience-oriented approach encompasses both

trauma-focused therapies and multimodal interventions: trauma-focused therapies (e.g. narrative exposure therapy or EMDR) can be added to a resilience-focused treatment programme, when needed, acceptable and possible. The resources of resilience can be classified according to the biopsychosocial model: *biological* (physical exercise, understanding the body, relaxation, treatment of medical illnesses), *psychological* (positive emotions and humour, acceptance, cognitive flexibility, empowering self-esteem, active coping) and *social* (social relatedness, reconnecting the family, creating and enhancing social support). For the asylum seekers and refugee population, two kinds of resources should be added: *cultural* (cultural identity, acculturation, language skills) and *religious/spiritual* resources. (The Cultural Formulation Interview (see later) is a perfect tool to investigate these last two resources.) Southwick and Charney [35] interviewed a variety of groups of trauma survivors and found ten what they call "resilience factors": realistic optimism, facing fear, moral compass, religion and spirituality, social support, resilient role models, physical fitness, brain fitness, cognitive and emotional flexibility and meaning and purpose. This new knowledge is important in the prevention of psychopathology, but it is also helping to shape treatment programmes [36, 37].

37.6 Religion, Spirituality and Migration

Forced migration results in crises of meaning, and refugees commonly resort to religious/spiritual beliefs and practices to help them cope. For forced migrants, there are multiple transitions, from their original homeland, community and family to a place of different faith, culture, language and climate. Being forcefully displaced is traumatic and is associated with multiple stresses including torture, loss, bereavement and suffering. Religion is important to asylum seekers and refugees, and it is notable that many migrants classify themselves by religion or nationality, as opposed to ethnicity [38]. One study of a UK reception centre indicated only 9% declared no faith and 75% declared themselves to be Christian or Muslim [39]. Additionally many organizations who assist asylum seekers are faith based and utilize religious frameworks [40]. But as Summerfield [41] notes, trauma work in humanitarian operations occurs in such a way that medicine and psychology have largely displaced religion in Western culture.

While much of the research on the experiences of dislocation and integration of asylum seekers and refugees focuses on external factors including housing, welfare and education, there is limited work conducted on the subjective experiences, attributions, beliefs, intentions and emotions elicited by a forced migration including spirituality. However, migrants are forced to produce meaning in some way. One study on Kosovar Albanian refugees in the United States found that migrants viewed their suffering as a spiritual experience deploying emotional and cognitive support deriving from their spiritual and religious frameworks [42]. Tweed [43], highlighting the dynamics of religion across time and space, developed a diasporic theory of religions among Cuban catholic exiles in Miami. He argued that forced migrants could deal with suffering by utilizing human and superhuman forces to make homes and cross boundaries. He examines the Nuestra Señora de la Caridad del Cobre

shrine as a site for contested religious meanings, a hallowed centre where Cubans are able to construct their national identity in exile. Raghallaigh [44] found religious coping to be especially important for unaccompanied young asylum seekers in Ireland. Overall the literature suggests that religion is central to the coping strategies of forced migrants, and we argue that significantly more attention should be devoted to this area.

37.7 Cultural Competence

Every psychiatrist should see his/her patients in the context of his/her culture as well as their own cultural values and prejudices [4, 6, 8, 11, 45–47]. In such cases the psychiatrists are experts in biomedicine, while patients are experts in their own experience of distress. Therefore, cultural competence should be a main issue in the daily work of the psychiatrists [10, 48, 49]. Cultural competence is one of several concepts used with the ambition of grasping the need of knowledge, skills and efforts to work with culture and context in clinical care. Alternative concepts are cultural sensitivity, humility and responsiveness. Even though the concepts have different historical backgrounds, they all try to capture the need of clinicians to remain open and be willing to seek clarification when presented with unusual or unfamiliar complaints. Psychiatrists should also be aware of their own cultural biases and knowledge on the use of interpreters or culture brokers, culturally different family structures, the effects of discrimination, exclusion, unemployment, intergenerational differences in acculturation, different explanations of illness, symptom presentations and treatment expectations and idioms of distress [50]. They should also be knowledgeable of the training in the use of cultural mediation, culture brokers or other models, including interpreters, working with family members or relatives. Additionally, they should be trained in intercultural psychotherapy, including issues of transference and countertransference and somatization [50]. There must be knowledge on how the professional's own cultural background and limitations could influence working relationships with and the effectiveness of treatment they provide for people from other cultural backgrounds. The context of cultural competence should be a part implemented both at the individual/clinical level and at the institutional level [10, 49, 51].

Cultural competence requires knowledge, skills and attitudes which can improve the effectiveness of psychiatric treatment [52–54]. It represents a comprehensive response to the mental health-care needs of refugee, asylum seeker and immigrant patients. Cultural knowledge means cognitive cultural competence, which is known as "knowledge" about the various ways in which culture, immigration status and race influence psychosocial development, psychopathology and therapeutic transactions. Therefore, it is important to be mindful of the risks of stereotyping [10]. Cultural skills and technical competence are essential in applying the knowledge in the clinical context. There are three main skills: intercultural communication, the capacity to develop a therapeutic relationship with a culturally different patient and the ability to adapt diagnosis and treatment in response to cultural differences between the psychiatrist and the patient [10, 46–49]. These skills explore the awareness of differences and similarities between cultures and their role in the expression

and explanation of mental distress. Cultural attitudes and beliefs which include personal prejudices will be affected by knowledge and will also impact behaviours [55, 56]. Intercultural work requires psychiatrists to challenge their own perceptions of "reality"; to explore their own cultural identity, prejudices and biases; and to be willing to adapt to distinct cultural practices [10]. It should be stressed that cultural competence is not an end product, a kind of technical expertise that confers on the individual a resolved accreditation which will enable them to work with patients from all cultures [49, 57, 58]. Cultural competence is an ongoing process of learning by training. The WPA guidance on mental health and mental health care in migrants [4], the EPA guidance on mental health care of migrants [6] and the EPA guidance on cultural competence [10] offer recommendations to policymakers, service providers and clinicians.

37.8 Cultural Formulation Interview

An important novel approach for awareness of culture and context in clinical psychiatric assessment is the inclusion of a Cultural Formulation Interview (CFI) in DSM-5. With 16 open questions, clinicians can explore cultural aspects of the current illness episode. Patients are encouraged to give narrative responses. Distress is acknowledged in relation to four main domains, cultural definition of the problem, perceptions of cause, context and support and cultural factors affecting self-coping and past help seeking and cultural factors affecting current help seeking [59]. In addition to the core CFI, there are 12 supplementary modules and an an informant version that can be used when additional information is needed [60]. One of the supplementary modules is specifically targeted towards the experiences of immigrants and refugees [61]. The core CFI and the additional interviews are helpful support for including an awareness for cultural verity in illness expressions, explanatory models, hardships and resilience factors in an individualized and non-stereotyping way.

The CFI in DSM-5 was developed from experiences of the Outline for a Cultural Formulation in DSM-IV. Lewis-Fernández et al. [60] discussed the results of research based on the operationalizing cultural formulation (OCF). For each domain of the OCF, the authors summarized findings from the cross-cultural issue subgroup (DCCIS) that was the base for the revision and operationalization in the CFI [60]. For assessment of psychopathology and treatment needs of refugees in the Netherlands, Rohlof et al. [62] had applied the cultural formulation in DSM-IV. They worked out that it was a useful method in mental health care and produced information that challenges the stereotypes of both clinicians and patients.

In the long run, the chapter on cultural formulation of the DSM-5 incorporates the CFI, which makes it possible to find a way of understanding the cultural context of a patient's experience of illness, which is essential for effective diagnostic assessment and clinical management. Using the Cultural Formulation Interview (CFI) of the DSM-5, psychiatrists may obtain information during the mental health assessment about the impact of culture on key aspects of the patient's clinical presentation

and care. The CFI in DSM-5 is helpful for use also in assessment situations where the diagnostic system of ICD is used.

Learning to work with the CFI in the clinical practice of psychiatrists can substantially increase the competence in working with cultural variety. Therefore, understanding psychopathology and formulating psychiatric diagnosis in refugees, asylum seekers and migrants could be facilitated by a dimensional approach, more then by a categorical approach [63–65]. On an individual level, the Cultural Formulation Interview (CFI) can be usefully employed during a mental health assessment to obtain information about the impact of culture on key aspects of a patient's clinical presentation and care, including their concepts of health and disease, expectations of treatment and the stress factors they are confronted with [64]. Training at undergraduate level, postgraduate level, further education or continuing professional development could benefit greatly from the inclusion of teaching on the factors influencing the clinical assessment, treatment and cultural integration of migrants [66].

37.9 Ethnopharmacology

Until recently variations in treatment response across diverse cultural groups, including effectiveness, dosing strategies and adverse effect profiles, have attracted relatively little attention. It is important to be aware that migrants may respond differently to psychotropic medication compared to the host majority. Different pharmacokinetics and pharmacodynamics may render some groups more vulnerable to side effects [67]. For instance, one study found that Asians experienced more extrapyramidal side effects than whites [68]. African Americans have been found to be at greater risk of lithium toxicity than their white counterparts [69].

Cultural attitudes may influence adherence to medication, the interpretation of side effects, enzyme induction as a result of diet and the use of traditional healing, complimentary and herbal medicines. Furthermore, there may be cultural differences in the placebo response. Placebo effects are dependent upon cultural expectations and beliefs; these are responsible both for the therapeutic effects of treatment and also for adverse effects. Mismatches in beliefs and expectations between clinicians and their patients may result in a breakdown of clinician-patient communication with subsequent treatment discontinuation and nonadherence [70]. Thus, it is important to assess attitudes towards medication, folk remedies and the use of tobacco and alcohol [4].

37.10 Intercultural Psychotherapy

Intercultural psychotherapy describes a setting, in which the psychotherapist and the patient have different cultural backgrounds [6]. The communication of distress in the face of language barriers can be a significant reason for nonengagement, increased levels of dissatisfaction as well as of break-off. Sue and Morishima [71] underlined that the greater the similarity between psychotherapist's and the patient's

ethnic and racial backgrounds, the more effective the therapeutic relationship. Accordingly, a culture match between psychotherapist and the patient is expected to facilitate a common understanding of symptom attribution and treatment, self-disclosure and expressive styles and the importance of the family in states of illness and treatment [72]. According to Atkinson [73] and Atkinson et al. [74], cultural matching can minimize problems in assessment, avoid group stereotypes and enhance rapport. These earlier studies are challenged by later studies pointing to that therapist; multicultural training/experience and use of culturally adapted treatments are significantly more important than ethnic matching [75]. Ethnic mismatch between patients and therapists does not have to be a significant barrier to treatment engagement and session attendance [76]. A meta-analysis of 52 studies indicated almost no benefit to treatment outcomes from racial/ethnic matching of clients with therapists [77].

Kirmayer [78] pointed out that the intercultural work challenges the shared "assumptive world" which might result in problems of translation and positioning, working across and between systems of meaning and structures of power that underline the therapeutic alliance and the process of change. He points out that the encounter of psychotherapist and patient from two different cultures is not simply a matter of confrontation or exchange between static systems of beliefs and values. In his concept of "potential space", Winnicott [79] described a space that is not fantasy and not reality, where imagination, symbolization and creativity are possible. In this space, transitional objects and phenomena, as well as play, can exist, and meaningful communication is enabled treatment [72]. Transferring this concept to the setting of intercultural therapy, the creation of a mutual creative space allows both psychotherapist and patient to play with the idea of being the other. This mutual creative space can also help to address the phase in the lives of refugee, asylum seekers and immigrant patients in society facing transitions in which aspects of their existence must be addressed [72]. According to Kirmayer [80], every system of psychotherapy thus depends on implicit models of the self, which, in turn, are based on cultural concepts of the person. Kirmayer [80] underlined that most forms of psychotherapy are based on Euro-American values of individualism. He highlighted that individualistic and egocentric concepts of the person can be contrasted with more sociocentric, ecocentric or cosmocentric views, so that the person could be understood in relation to the social world, the environment and the cosmos. Furthermore for him intercultural psychotherapy must consider the cultural concept of the person implicit in therapeutic discourse and practice to determine how well it fits or conflicts with the concepts, values and way of life of the patient. There are ongoing efforts to adapt psychotherapeutic methods to cultural variety. One example of this cultural adaption is CBT for mental illness [81]. This compromise is making individual case formulations including the background and perspective of the patient and the community. Additionally, it attempts to pass beyond the therapy dyad and if appropriate involve the family, religious leaders and the community [82].

In the setting of intercultural psychotherapy, language plays an important role. Additionally, idioms of distress in which patients communicate with psychotherapists can vary considerably from culture to culture. It is well known that many

languages do not have equivalent words to describe various mental disorders [6]. For example, the word and notion of "depression" do not exist in all cultures, even though sadness, unhappiness and other symptoms can be described and verified [6]. It is therefore necessary for psychotherapists and psychiatrists to be sensitive to cultural and contextual aspects of communication [83]. Without the help of interpreters or culture brokers, effective communication between professionals and patients from different cultural origins and with differing language capacities is sometimes impossible [84]. In relation to that, psychotherapists and psychiatrists had developed conceptual models, skills and experience in conducting cross-language concepts of psychotherapy using interpreters or culture brokers [85]. Particularly with regard to psychotherapy, language ability plays an essential role. Language ability is a main meter for psychiatry and psychotherapy [6, 10] in immigrants' utilization of health-care services, particularly, of psychotherapy. Language challenges can heighten systemic and sociocultural barriers to accessing health information and resources.

Trust and confidence are central to good quality cross-cultural communication. A trustful relation in which the patient and the clinician want to convey and understand the meaning of the other is the basis for overcoming communication barriers. At the same time, trust and confidence are central to good quality cross-cultural communication [83]. According to Bäärnhielm and Mösko [83], a trusting relationship in which the patient and the clinician want to convey and understand the meaning of the other is the basis for overcoming communication barriers. Non-professional translators (family members, hospital staff members, etc.) can have a negative influence on trust and confidence. Non-professional translators can also have negative impact on medical treatment due to erroneous translation in the form of omissions, additions or indeed changes to the initial message [86]. Therefore, the use of professional interpreters or culture brokers is obligatory. Bauer and Alegría [87] highlighted that professional translation improves the quality of treatment and patients' satisfaction with treatment.

While patients and psychotherapist and psychiatrists preferred simultaneous interpretation, interpreters or culture brokers used more often the consecutive method [88]. During intercultural psychotherapy, it is very important to be aware of the model of interpreting which is used. Beside the psychotherapeutic or constructionist mode, there are three more modes of interpreting described. These are linguistic (word for word), psychotherapeutic or constructionist, health advocate/community interpreter or the bicultural work modes [89].

37.11 Education and Transcultural Psychiatry and Psychotherapy

The Lancet commissions on culture and health [90] highlight the importance of remodelling medical practices by stressing the importance of culture and its effect on well-being. They argue that medical practice needs to account for how cultural values and related heritage can be better understood and nourished in the interests

of health. In line with growing globalization and an increasing number of people on the move across national and international boundaries, it has become vast important that psychiatry and psychotherapy are aware of the different needs of the patients they are responsible for including cultural [66]. Therefore, during times of global migration and an increasing number of ethnic minority migrants including refugees and asylum seekers, psychiatrists and psychotherapists may have a different cultural background than their patients. Thus, cultural psychiatry and psychotherapy are a matter of primary relevance. The onset of illness may occur soon after migration, or mental health problems may develop over time as results of the impact of social factors and changes related to the host society [6, 66]. According to Laban et al. [91], post-migration factors have a high impact on the development of psychiatric disorders. Furthermore, it is well known that the process of migration can lead to a whole spectrum of mental health disorders including psychoses, post-traumatic stress disorder (PTSD), common mental disorders (CMDs), eating disorders and suicidal behaviour [6, 17, 31]. However, there is still a need for further studies to collect more information on the prevalence rates of mental disorders in migrant groups as compared to the host culture. Therefore, cultural psychiatry and psychotherapy must be included as an integral part of educational curricula, from the undergraduate level through continuing professional development. As mentioned in the action plan for the triennium 2014–2017, the WPA should recommend that WPA member societies create national branches or sections of social/cultural psychiatry and psychotherapy if they do not already exist, thereby pushing forward the awareness and knowledge of immigrants, ethnic minority groups, refugees and asylum seekers [50]. Related to cultural psychiatry and psychotherapy, the WPA outlines some of the key issues on what undergraduates and postgraduates need to know as well as what is required for CME/CPD (continuing professional development). Furthermore, WPA summarized in this action plan what service providers, policymakers and mental health professionals should do [50].

37.12 Future Perspectives

Kirmayer and Ban [92] assert that methodological strategies for unpacking the concept of culture and studying the impact of cultural variables, processes and contexts are needed. Quantitative and observational methods of clinical epidemiology and experimental science as well as qualitative ethnographic methods should be used to capture crucial aspects of culture as systems of meaning and practice. According to them, these methods are important to bridge the gap in cultural psychiatric research on cultural variations in illness experience and expression. Additionally, the authors argued that there is more research needed on the situated nature of cognition and emotion as well as on cultural configurations of self and personhood, on concepts of mental disorder and mental health literacy and on the prospect of ecosocial models of health and culturally based interventions. The authors considered the implications of the emerging perspectives from cultural neuroscience for psychiatric theory and practice [92].

According to Laban and Dijk [93], quantitative epidemiological studies still dominate. Little anthropological research with qualitative methodologies and an "experience near" approach has been conducted [93], in which the main topics related to psychiatry were perceptions of illness and disease, use of nonbiomedical health care, health-seeking behaviour, cultural identity and mental health and patient-therapist interaction, especially the effects of ethnic matching of therapists and patients. The authors asserted that the core transcultural psychiatric concepts of idioms of distress and explanatory models have been also topics of anthropological research [93]. Laban and Dijk [93] summarized that the research findings have not yet had much impact on political decisions. Furthermore, the authors pointed out that in a complex world with a multitude of scientific findings, chaotic and incident-focused behaviour of politicians and media and increasing "fact-free politics", researchers have a hard time getting their message through. They considered that perhaps greater cooperative efforts with relevant nongovernmental organizations could increase the chances of the translation of scientific findings into political decisions [93]. In line with that, the authors established a list of research questions, which should be relevant to policy and practice for future consideration: "1. What factors can keep immigrants, refugees, and asylum seekers healthy and make them resilient, and what interventions could improve their mental health and well-being? 2. What is the effectiveness of standard therapeutic interventions in the mental health care of immigrants, refugees, and asylum seekers? And what other interventions could be equally or more effective? 3. Which combination of characteristics—among others, SES, ethnicity, culture, personal life situation—increases the risk for mental health problems in ethnic minority groups, and contributes to underutilization of mental health services and dropout from treatment? 4. Which combination of elements—such as country of birth and upbringing, ethnicity, race, religion, age, gender—in matching patients and therapists contributes most to effective treatment?" ([93], p. 809).

Another author, Wintrob [94], maintains that psychiatry has been fundamentally concerned with pathology and its diagnosis and treatment. Factors of individual perseverance in the face of adversity and illness, of spiritual strength and purpose, of family support and of community belonging that contribute to coping ability, recovery and an overall sense of well-being are less in focus [94]. The author also underlined that cultural psychiatry has recognized the importance of each of these factors in coping with the stress of rapid culture change, migration, acculturative stress, the social burden of discrimination and unequal access [94]. He underlined that, culturally, psychiatry needs to expand research into "cultural resilience" as it applies to individuals, families and communities across generations. Additionally, Wintrob [94] favoured the person-centred care within the conceptual framework of cultural psychiatry, which then would emphasize the personal and cultural identity of each individual, their conceptions of illness and its appropriate treatment, personal resilience and family support, religious and spiritual orientation and capacity for long-term restoration and maintenance of individual and family well-being [94].

An upcoming field is cultural neuroscience, an interdisciplinary field that investigates the relationship between culture (e.g. value and belief systems and practices

shared by groups) and human brain functioning. Main focuses of cultural psychiatry for the future should be the implications of cultural neuroscience findings for understanding human brain function in sociocultural contexts [95–98]. Beyond that cultural psychiatry should address questions to cultural neuroscience research for the future.

Further clarification is needed to gain deeper understanding of the relationship between migration and common mental disorder to address contradictions in the literature and health inequalities among migrants [17].

Conclusion

As pointed out in the introduction, in the early phase of our field of interest, the transcultural psychiatry, the focus was on "the people out there". In a later phase, it was recognized that culture is present in every human experience and that all knowledge system bear traces of social, cultural and historical origins [1]. We have the strong feeling that we are moving into another phase of transcultural psychiatry. The mass migration and even more the staggering amount of forced migrants as asylum seekers, refugees and undocumented migrants in all our societies make it clear that people from different cultural backgrounds are interconnected in everyday life. Moreover, the growing inequality in resources between people within and between countries; the policies to build walls and to increase border controls; and the concentration on "our one people", "our own country" is sharpening human relationships and increases the risks of extreme poverty and marginalization. There is an increasing level of public antagonism towards migrants in recent years—whether they be immigrants, refugees or asylum seekers—and a concomitant increase in public policy of non-acceptance and rejection of migrants in countries of the industrialized world that had been the main humanitarian receiving countries for migrants for generations. That is, there are profound negative implications of current cultural stereotyping and, in particular, the fear of terrorism that adversely affects the mental health of the citizens of those receiving countries, as well as the mental health of all migrants. The consequence is, undoubtedly, that the process of acculturation and integration of migrants and refugees will be disturbed; asylum seekers and undocumented migrant will face hard measurements, like imprisonment and exportation.

More obvious than ever before, transcultural psychiatry is connected to human rights issues, social inequalities, discrimination, social exclusion and (threats of) violence and terror. The many risk factors, discussed in this chapter, affect millions of people and will lead to mental health problems in high proportions. Psychiatry as a whole has put a lot of emphasis (and spend a lot of money) on—research on—biology and genes as causal factors of psychiatric disorder. It has to be noted here that in a short time social factors will be the leading cause of the majority of common mental disorders.

The responsibility of psychiatrists, and maybe especially of transcultural psychiatrists, in this era is huge. The knowledge of the negative implications of the present amount and characteristics of risk factors on mental health cannot be ignored. This also applies to the existing knowledge of the "healing factors":

restoration of human rights, safety, social connections, provision of basic needs, an approach of respect and dignity, transparency and promises that are kept and (access to) cultural sensitive treatment, among others. For the millions of people on the move, it is essential that they have the opportunity to bounce back from all adversities they have experienced.

Psychiatrists, together with other health professionals, therefore, have a special duty to raise awareness among the general populations and among policymakers of the dangers we encounter. Equal opportunities to obtain equal levels of mental health and equal access to mental health facilities should go together with opportunities to maintain and achieve resources of resilience. Access to the housing market, education and the labour market is an essential aspect of these resources. Fired by basic facts, ethical considerations and human empathic advocacy activities are necessary on a large scale.

An era has begun in which transcultural psychiatrist should not only closely ally with psychologists, anthropologists and social scientist. They have to widen their scope and search cooperation and affiliation with human rights specialists, employers' organizations, nongovernmental organization migrant/refugee interest groups, common citizens/volunteers and, not in the last place, politicians and (local and national) governments.

Conflict of Interest None.

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Urban Mental Health in the Twenty-First Century

38

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38.1 Introduction

N. Sartorius

The contribution of the WPA Section on Urban Mental Health to the volume describing the work of the WPA sections describes three facets of the work on the promotion of mental health in urban settings. The first, that of Professor Shinfuku, deals with the consequences of a disaster on people living in towns; the second, that by Professor Kua, describes the issues related to getting old in an urban setting; and the third describes hikikomori, a syndrome of isolation and withdrawal from social contacts—apparently growing in parallel with urbanization—that has recently gained prominence. All three contributions are placed in the setting of Asia, in two of the most urbanized countries in the world, Japan and Singapore.

The selection of these examples among many others could be criticized as being restricted to a small section of the whole world currently reeling under the impact of urbanization which has never been so rapid and massive as it is now; yet, such a criticism would not be justified because the choice of Professor Shinfuku clearly serves two important purposes. First, the decision to present two of the many facets of urbanization in a single country—weakening of the social fabric in towns and the epidemic dimensions of misery when disaster strikes in a densely populated urban area—clearly illustrates the endless variety of mental health issues arising on the background of urbanization. Second, the selection of a paper dealing with the fate of the elderly in an urban setting demonstrates the matrix within which those interested in resolving or preventing mental health problems must work. The victims of the earthquake in Japan also included, perhaps preferentially, those aged. The hikikomori stricken youth seek isolation and reject contacts with others in stark contrast to the elderly which in many parts of the world place loneliness, isolation, and lack of contact with other people as their first problem, a problem more important than their health condition.

Professor Shinfuku's three cameos also demonstrate that work in the field of urban mental health requires a systematic examination of most principles of public health which have in times past been formulated on the basis of data and experience gained, to a large degree in rural and small town settings. The Alma Ata conference expressed the consensus of the majority of the world's countries about the importance of primary health care which was seen as the main line of the governments'

action to improve the health of their citizens. The principles and methods of primary health care are very well applicable and useful in rural settings: the promotion of health in the huge towns—those now existent and the many which will be in existence soon—requires different ways of action, different priorities, and different ways of organizing health care. The formulation of an effective strategy of health care in urban settings is a major task before health authorities dealing with mental health and with health in general: this is a task which can be approached by a systematic examination of the examples and urban situations of the type presented in this chapter. The WPA Urban Mental Health section has a huge task before it: it is reassuring to see that it has become very active and that it has started its work by the analysis of specific situations, an analysis which may produce the basis for the formulation of principles not only for mental health but for urban health care in general.

38.2 Mental Health in the City of Kobe, Japan: Two Decades After the Great Hanshin Awaji Earthquake

Naotaka Shinfuku

Abstract
A number of cities in the world have experienced the destruction by natural and manmade disasters. The author lived in Kobe city and experienced Hanshin Awaji earthquake in 1995. The disaster killed more than 5500 population on the spot and destructed the major part of the city. I also observed reconstruction process of the city. Disaster caused a wide range of psychological, physical, and social distress. These symptoms changed from the time of a disaster until present over 20 years. Volunteers came from all over the world soon after the disaster. The victims suffered for long during recovery, reconstruction, and preparation phases. For the affected population, long-term and comprehensive programs were needed to cover a wide range of social structures. This included housing, safe water, electricity, transportation, safety, minimum financial support, medical, and health care. Mental health recovery of victims requires a systematic and comprehensive approach. Knowledges gained from a disaster in Kobe will be useful to plan mental health care for the peoples damaged by an urban disaster.

Keywords
Kobe city, Urban disaster, Disaster psychiatry, PTSD, Recovery process.

38.2.1 Introduction

38.2.1.1 Kobe City

Kobe is the capital of Hyogo Prefecture and one of Japan's ten largest cities. Kobe is a city on Osaka Bay in central Japan close to Osaka and Kyoto located between

the sea and the Rokko mountain range. Kobe is well known for its signature marbled beef and scenic setting of mountains framing the harbor. Kobe is considered one of Japan's most attractive cities.

Kobe has been an important port city for many centuries. Its port was among the first to be opened to foreign trade in the nineteenth century alongside the ports of Yokohama, Nagasaki, Hakodate, and Niigata.

I experienced the Great Hanshin Awaji earthquake as the resident of Kobe on the spot and lived in the city as victim [1].

38.2.1.2 Hanshin Awaji Earthquake

The Great Hanshin Awaji earthquake, with a magnitude of 7.2 on the Richter scale, hit the southern part of Hyogo Prefecture and neighboring areas at 5:46 a.m. on January 17, 1995. In Kobe, where most of the damage occurred, houses, buildings, and railways collapsed, where "lifeline" services such as water, gas, electricity, and telephone were interrupted for a long period. The great quake killed an estimated 5500 people on the spot and left about 310,000 people homeless.

38.2.1.3 Mortality and Morbidity Immediate After the Disaster

The number of the population affected by the earthquake was estimated as 2.4 million. The number of the death immediately after the earthquake was counted as 5502 in January 1995. It was reported that more than 95% of death occurred within 24 h. The fact suggests the difficulty for outside medical team to rescue the human lives at the disaster [2].

The official number of death due to the earthquake was once again revised to more than 6500 in August 1995 because some of the delayed death causes such as pneumonia and suicide were certified as resulting from the earthquake.

38.2.2 Psychological Reaction at the Disaster

I personally experienced the Great Hanshin Awaji earthquake on the spot at that time. I have also been witnessing the recovery process of victims in the Kobe area over 20 years. As a psychiatrist, I have also been observing the changes of psychiatric problems of the earthquake victims over the time [3].

38.2.2.1 Psychological Vacuum at the Disaster

Many people could not understand what had happened soon after the Hanshin Awaji earthquake. Also, it took a long time for many people in Kobe to realize that the epicenter of the Earthquake was near Kobe.

Nobody expected an earthquake in the Kobe area. Kobe University was the center of the hard hit area. Many victims in the Kobe area could realize the magnitude of the earthquake only after watching the burning scene of nearby Nagata district on television. It is important to know that the population affected by the disaster is sometimes the least informed on the magnitude and nature of the disaster.

38.2.2.2 Emergency Medical Care at the Disaster

Immediate medical needs were the service of emergency medicine. At Kobe University Medical School, many victims being brought to emergency services were found to be "dead on arrival (DOA)." The forensic department of our medical school was extremely busy for administrative autopsy and certification of death.

38.2.2.3 Emotional Numbness and Panic Reaction

Soon after the earthquake, most of victims experienced emotional numbness. One of my friends who lost his parents said that he felt out of touch with reality, that he could not feel sad, and that a shaking feeling continued due to frequent aftershocks. This could be a psychological protection from the disaster [4].

38.2.2.4 Joy of Survival and Hypomanic Reaction

A couple of days after the earthquake, many victims became talkative and joyful. Some people even became hypomanic and showed signs of psychomotor excitement, which might be caused by the biological joy of survival. I also observed memory loss and disorientation among the victims particularly the elderly. In general, patients with bipolar disorder became manic.

38.2.3 Mental Health of the Population Soon After the Disaster

38.2.3.1 Battlefield Friendship and Survivor's Guilt

For the first week, everybody was anxious to secure food, water, and information. A kind of a battlefield friendship existed for a certain period. Those phenomena resulted in mental excitement and friendship among victims. The feeling of survivor's guilt was strong for those who lost family members.

38.2.3.2 Anxieties and Insomnia

A week later, the focus of medical service was shifted from the care of emergency medical service to that of the chronically ill. Treatments of the chronic patients including those with hypertension, diabetes mellitus, and mental diseases were resumed. Care for the demented elderly and mentally handicapped in shelters posed difficult problems for managers of shelters. Residents in the crowded shelters commonly suffered from insomnia, acute stress responses, and nightmare.

38.2.3.3 Acute Stress Reactions

Ten days after the earthquake, the life in shelters became stressful for many victims.

Increase of acute stress response including serious stress ulcer was reported. The staff at medical clinics at Kobe University Medical School were busy in treating of many cases of extremely serious bleeding ulcers. Anxiety reaction and sleep disorder were also common. Increased cases of pneumonia and bronchitis were observed among the elderly since the earthquake took place in January, which was winter in Japan.

38.2.4 Devastated Mind of the Affected Population

38.2.4.1 Facing the Loss and the Hardship

After 2 weeks, victims started facing the reality of the loss including family members, housing, and jobs. Depression became manifested among them.

The victims continued to have acute stress disorder (ASD) with the symptoms of flashback [5].

38.2.4.2 Various Health Problems Due to Continuing Stress Situation

After 2 months, most victims had been transferred from shelters to temporary housing. At one time, more than 320,000 people lived in shelters such as schools and public buildings. The government officials started to build temporary houses which were similar to those often seen in military barracks. In total, 47,000 temporary houses were constructed using public fund, and almost 80,000 people lived in temporary housing.

Long-lasting stress of the population after the disaster decreases the activity of natural killer cell. This caused stress-related ion physical problems as well as psychological weakness.

It was difficult to differentiate the problems of body and mind after the disaster. The various health problems both physical and mental should be considered as a whole. The disaster impacted both body and mind. Lowering of the immunity triggered pneumonia and other infectious diseases among the dwellers of temporary houses. Also, victims with physical problems such as hypertension were accompanied by depression.

Acute stress disorder and post-traumatic stress disorders are not adequate to cover the full range of trauma-related psychological problems. But a complete form of PTSD so far has been rather rare among the victims in Kobe [6].

38.2.4.3 Crimes After the Disaster in Kobe

One of the characteristic scenes after the disaster was the orderly behavior of the population waiting in long line for water and food. No crime was reported during the confusion period after the earthquake. Kobe was a hometown of the big "yakuza" clan. News media reported even members of yakuza provided food and other needed materials to the victims as volunteers. During the Hurricane Katrina in Florida which damaged the city of New Orleans with massive flood, the stealing of shops and violence were frequently reported taking the advantage of the confusion. After the Hurricane Katrina, an American media surveyed the crime during the Hanshin Awaji earthquake from the police record; he found only two cases of the thefts at convenience stores. But the thefts of both cases were done by foreigners. The traditional moral standards of Japanese people prevented the crimes and violence to happen during the Hanshin Awaji earthquake.

38.2.5 The Recovery Process

38.2.5.1 Recovery of the Kobe City

The damage of the Great Hanshin Awaji earthquake was not limited to human lives. The earthquake brought a tremendous damage to the Kobe city and its residents. The city lost about 100,000 population after the disaster, as many had to leave the city due to the closure of factories and workplaces. But, the population has gradually recovered and returned to the same level before the earthquake after 5 years [7].

The port of Kobe was Japan's busiest port and one of Asia's top ports until the Great Hanshin Awaji earthquake. Kobe has since dropped to fourth in Japan.

The Kobe city built several memorials. Several UN and governmental agencies for disaster prevention were set up in the Kobe area. To commemorate Kobe's recovery from the disaster, the city holds an event on every December called the Luminarie, where the city center is decorated with illuminated metal archways.

38.2.5.2 Opening of Era of Disaster Medicine in Japan

It was important for the victims to become supporters to victims of the disasters. Through this process, the Kobe city and its residents are trying to recover from their traumas. Also, Hanshin Awaji earthquake provided the opportunity for Japanese medical professionals to establish "disaster medical assistance team."

38.2.5.3 Kobe City: 20 Years After the Disaster

In Japan, January 17 has been officially designated as the "day of disaster prevention."

In January 2011, many anniversary events were held to commemorate the victims of Hanshin Awaji earthquake. A sum of 10,000 lanterns was lit in memory of the victims.

People who visit Kobe now can hardly recognize the damages caused by the Hanshin Awaji earthquake. The Kobe city gives an impression of a busy, affluent, and modern Japanese city. Museum and memorial park for the earthquake and a few newly built research and training centers for the mitigation of the earthquakes are some of the buildings which remind of the earthquake.

38.2.6 Conclusion

Asian countries are constantly menaced by violent natural disasters to cause a wide range of psychological, physical, and social distress. Little attention has been paid to the impact of disasters on mental health following disasters throughout Asia. But in the past decade, disaster mental health gained an increased attention resulting from having major disasters in Asia. In Japan, the Hanshin Awaji earthquake marked the turning point to popularize PTSD and the need for mental health care for

survivors. This recognition has spread to mental health professional in China [8] and Taiwan [9] after major disasters in their respective countries. The Hanshin Awaji earthquake was tragic. But the lessons learned in Kobe is being shared by mental health experts in Asia and in other developing countries [10]. This transfer of experiences has constituted a continuous process in Japanese recovery from the Great Hanshin Awaji earthquake. One could say that sharing is the source of our recovery from the disaster.

38.3 Elderly in the City: Mental Health Promotion and Preventive Psychiatry in Singapore

Heok Eee Kua

38.3.1 Introduction

Mental health of elderly people living in the city should be a major policy priority because of the aging of the population in urban communities in developed and less developed countries [11]. Common mental disorders in old age, for example, depression, anxiety, and dementia, are associated with physical illnesses such as stroke, heart diseases, hypertension, and diabetes mellitus (Kua and Mahendran 2017). In many cities around the world, caring for the frail elderly has become more challenging especially when the elderly lives alone and needs assistance. Living alone and a sense of loneliness are risk factors for depression and poorer quality of life [12]. The rising tide of dementia is a global concern and will be a major public health issue because it exacts a heavy toll on not just health services and family life but also the national economy. In the Western Pacific and South Asian countries, there is a phenomenal increase in the number of dementia cases [13].

From a public health perspective, it is crucial to focus on preventive psychiatry. Most research on the epidemiology of mental disorders in old age do not include those elderly with subclinical or subsyndromal depression, anxiety, or dementia. A study on elderly Chinese, Indian, and Malay in Singapore [14] adds valuable information on the epidemiology of subsyndromal depression. The data were from a cohort of 1092 subjects from a nationally representative multiethnic stratified random sample of older adults aged 60 and above. The prevalence of subsyndromal depression was 9.6% (Chinese 10.1%, Malay 8.2%, Indian 12.6%). In the multivariate analyses, controlling for age, gender, education, ethnicity, and socioeconomic factors, both syndromal and subsyndromal depression, were significantly associated with medical comorbidities, comorbid dementia, and functional disabilities.

Mental health promotion to enhance well-being or quality of life is important to prevent the occurrence of depression, anxiety, and even dementia. Because the physical health of elderly people is linked to mental health, any program for

preventive psychiatry should also control for the common chronic disorders like hypertension, diabetes mellitus, and obesity.

38.3.2 Dementia and Depression Prevention Program in Singapore

The Jurong Ageing Study (JAS) in Singapore is a project to ascertain whether psychosocial interventions through group activities together with health education on lifestyle, diabetes mellitus, and hypertension can prevent or delay the onset of depression and dementia. In this study in western Singapore, we delineated a catchment area with about 1000 elderly living around the Jurong Point Shopping Mall where we have established a research base at TaRA (Training and Research Academy).

In March 2013, a community mental health program for the elderly was launched with the participation of nongovernmental organizations (NGOs), the private sector, and volunteers. Every elderly person had a thorough physical, mental, and social assessment, including blood examination and neuropsychological tests—MRI brain scans will be carried out for those with mild cognitive impairment or dementia. This cohort of elderly people will be followed up for 10 years.

The first study group comprised 110 Chinese elderly with mild depressive symptoms and mild impairment of cognition. This was a naturalistic study, and all of the elderly attended group meetings once a week for 3 months, fortnightly for 6 months, and monthly thereafter. Each meeting began with a 20-min talk in Chinese on health issues, including controlling diabetes mellitus and hypertension with medication, diet, and exercise. After the talk, participants were divided into four groups for art activities, tai-chi exercise, mindfulness practice, and music reminiscence—this session lasted 30 min. The groups were assessed at the beginning, after a month, at the end of the third month and after a year. The scores for depression on the self-rating Zung depression scale showed significant improvement in mood after 3 months. After the first month, there was a significant improvement in the groups on music reminiscence and art activities. However, by the third month, there was no significant difference among the four modalities.

In cognition, after a year only 57% continued to decline, 24% remained stable and 19% improved. The results are very encouraging because they indicate that health education and psychosocial interventions can improve the mood and cognition of elderly people. More importantly, they enjoyed the art activities, music reminiscence, and mindfulness practice [15–17].

There are now four randomized controlled trials (RCTs) for the prevention of depression and dementia using mindful awareness practice (MAP), art activities and music reminiscence, choral singing, and horticultural therapy. Besides neuropsychological tests and rating scales for mood, we have biological markers like brain scans (MRI), telomere length, oxidative stress tests, immunological studies, and assessment of gut bacteria. The head-to-head RCT on art and music reminiscence

and RCT on choral singing and health education are in progress—the studies will conclude in mid-2017 [18].

38.3.3 Green City and Mental Health Promotion

Densely populated megacities with the inadequate provision of green spaces are associated with poorer mental health. Several research studies have shown that exposure to green spaces can be psychologically and physiologically restorative by promoting mental health, reducing blood pressure and stress levels, as well as promoting physical activity [19, 20].

Green urbanism is of vital importance for sustainable and livable cities. Several other studies have also demonstrated that interacting with natural environments can have beneficial effects on attention and memory for healthy individuals and for patient populations. There is now a growing interest and research on horticultural therapy which taps on nature's benefits for human health. Horticultural therapy involves a planned program that uses plants as a therapeutic medium by a trained professional to achieve a clinically defined goal. It has been noted to promote the social functioning and self-esteem of patients with psychiatric illness especially those with chronic schizophrenia [21]. There was also a paucity of data from Asia, Africa, or Latin America.

The National Parks Board of Singapore, in collaboration with the National University Health System, conducted a randomized controlled trial [22]. The study aimed to investigate the efficacy of horticultural therapy in improving the mental health and cognitive functioning of elderly people aged 65 years or older living in public housing in the community. There were 69 elderly divided into two groups—treatment (horticultural therapy) and control (wait list). To assess the psychological well-being of participants, the Zung Self-Rating Depression Scale [23] and Zung Self-Rating Anxiety Scale [24] were used. Blood samples were taken to check the levels of biomarkers like cytokines.

In the preliminary results after 3 months, the elderly who received horticultural therapy did better than the control group in terms of their scores for life satisfaction, memory, and psychological well-being, but the differences were not significant. The only significant finding ($p < 0.05$) was for positive relation, which refers to social connectedness and trusting relationships. During the assessment of the biomarkers, it was found that in the sixth month of the program, the level of cytokine interleukin-6 (IL-6), a pro-inflammatory protein, was significantly reduced when compared to that in the third month for the horticultural therapy group, as opposed to the control group.

The outcomes of the research study on horticultural therapy mentioned earlier provide empirical evidence for the effectiveness of horticultural therapy in improving the psychosocial and cognitive well-being of the elderly and reducing healthcare costs. With its clinical implications, this initiative could potentially persuade policymakers and health-care providers of the need to support cost-effective horticultural therapy as a strategy to engage older adults in a more active and healthier lifestyle. To promote green urbanism, community participation is important, and

there are programs to encourage the public to be part of the green movement and adopt responsible practices and healthy lifestyles [25].

38.3.4 Future Challenges

Preventive measures should include maintaining a healthy lifestyle, including regular exercises, a well-balanced diet, and periodic medical checkup. Social adjustment means a need to disengage or relinquish responsibilities—new role in the family and seeking other roles in volunteerism. All these strategies could be preventive for depression and dementia [15].

The mental health of the elderly is linked to their social needs such as community and home support. Public education from talks, books, and mass media on prevention is important to decrease morbidity. Using the internet for information on illness and services should be encouraged. A key feature in the provision of health care of the elderly will be the involvement of the community and community-based organizations. The family and the community will need to be given the necessary support, resources, and knowledge to care for the elderly at home.

38.4 Hikikomori: Japan's Social Shut-Ins from a Culture-Bound Phenomenon to a Globalized Boundless Syndrome

Takahiro A. Kato, Alan R. Teo, Masaru Tateno, Tae Young Choi, Yatan Pal Singh Balhara, Naotaka Shinfuku, Norman Sartorius, and Shigenobu Kanba

Abstract

In recent years, cases of "hikikomori" (a social withdrawal syndrome originally introduced as a Japanese culture/society-bound syndrome) have been reported not only in Japan, but overseas as well, and this phenomenon is receiving international attention. We have conducted international collaborative research to understand the underlying biopsychosocial pathophysiology of hikikomori and develop therapeutic approaches in international settings. In this review paper, we will introduce recent findings regarding hikikomori. We have developed a pilot diagnostic and evaluation tool to better understand hikikomori based on interviews by psychiatrists. We have identified hikikomori cases in four countries (Japan, the United States, South Korea, and India), and based on self-administered questionnaires, we revealed that most cases of hikikomori involved feelings of isolation, functional disability, and a desire for direct treatment (particularly psychiatric treatment). Through the Structured Clinical Interview for DSM Disorders (SCID)-I and SCID-II administered to cases of hikikomori in Japan and the United States, we discovered that there is frequent comorbidity of mental illnesses such as avoidant personality disorder, major depressive disorder, and social anxiety disorder. These recent findings will play an important role in future investigations of treatment strategies for hikikomori in Japan and overseas. In this review paper, we discuss

that the reasons for the internationalization of the hikikomori phenomenon are globalization, urbanization, and the spread of the Internet, and we propose that it is important to engage with these facets of contemporary society to further our understanding of hikikomori.

Keywords
Hikikomori, Culture-bound syndrome, Internet, Social network, Urbanization, Globalization, Boundless syndrome.

38.4.1 Introduction

Japan's social phenomenon of "hikikomori," began to attract greater attention in the late 1990s as "*Shakaiteki hikikomori* (or social withdrawal)" [26]. An epidemiological study in Japan has reported that 1.2% of the population has been identified with a hikikomori status for 6 months or longer [27]. A variety of interventional approaches against hikikomori have been attempted; however, the affliction remains resistant to improvement and new strategies are needed [28–30].

In the twenty-first century, hikikomori-like cases have been reported in France, Hong Kong, South Korea, Oman, and Spain [31–38], and the word "hikikomori" was added to the Oxford Dictionary in 2010 as "(in Japan) the abnormal avoidance of social contact, typically by adolescent males/a person who avoids social contact [Origins] Japanese, literally 'staying indoors, (social) withdrawal'."

Does this affliction, which was once seen as a culture-bound syndrome particular to Japan, now truly exist in differing overseas sociocultural environments? If it does, what is the cause, and what treatment methods are available? Is there a common cause? In this review paper, we will present our research results [30, 39, 40], which attempt to answer these questions.

38.4.1.1 First International Survey of Hikikomori Using Case Vignettes

As a first step toward shedding light on the above questions and developing a new, effective approach toward hikikomori, we administered a self-rated vignette survey which was published in Social Psychiatry and Psychiatric Epidemiology [30]. This was the first international, collaborative survey targeting psychiatrists in Australia, Bangladesh, Iran, India, Japan, South Korea, Taiwan, Thailand, and the United States, and reported the possibility that the hikikomori phenomenon occurs in all these countries. In this survey, we presented two typical cases of hikikomori (modified from the original case vignettes in Social Psychiatry and Psychiatric Epidemiology [30]).

A Typical Case of Teen Hikikomori

> Case: Mr. A, a 15-year-old junior high school student.
> (His parents say) "He obstinately refuses to see us and never comes out of his own room."

Social history: He is the first son, with a younger brother. He is brought up by his father who is a company employee, and his mother who works part-time. His father, a salesman, has been transferred every 2–3 years and moved with his whole family, but when he entered junior high school, his father moved by himself, so he now lives with his mother and a brother 4 years his junior. There was nothing particularly problematic during his development and his school grades were medium, but not bad. He naturally found it hard to make friends, and he would prefer reading books and playing PC games by himself rather than sports with others. Half a year after entering junior high school, he suddenly stopped going to school. At home, he is absorbed in PC games and the Internet, he hardly ever leaves his room, and his day and night are reversed.
Past psychiatric history: None.
Family history: None.
History of present illness: After 2 years of school absenteeism, when his entrance exams for senior high school were near at hand, his father returned home and warned him: "Why don't you go to school once in a while? Can't you be serious about your future?", to which he yelled "I don't need you tell me that!" and he suddenly used violence on his father. While his father was dumbfounded, he headed back to his room. A few days later, his parents made up their mind to force him to come with them to the nearby psychiatric faculty where he is examined by you.
Drug history: None.
Mental status exam on first interview:
Mr. A, just standing between his parents, kept silent, with his head hung down. His parents bowed and described his life history and problematic situations. From beginning to end, he just kept looking downward. His attitude does not imply any psychotic experience, such as delusion/hallucination. He just seems to be withdrawn into his own shell. Even when you addressed him, "Mr. A," he did not reply at all.

A Typical Case of Young Adult Hikikomori

Case: Mr. B, a 24-year-old male living with his parents.
(His parents say) "He never comes out of his own room." (Mr. B) just keeps saying "I don't know."
Social history: He is an only child. He is brought up by his parents in a two-bedroom urban apartment. There was nothing particularly problematic during his development until elementary school. In junior high school, he often skipped school and avoided mingling with peers, which he linked to experiences such as being bullied by classmates in elementary school. His academic performance was good, and he directly entered a middle-class university of engineering faculty, but 3 years ago (third grade, 21 years old) Mr. B dropped out of university for lack of motivation.
Family history: None.
History of present illness: For the last 3 years, he has hardly ever left his room, spending 23 h a day behind its closed door. He eats food prepared by his mother

who leaves trays outside his bedroom. He sleeps all day, then awakes in the evening to spend his time surfing the Internet, chatting on online bulletin boards, reading manga (comic books), and playing video games. Despite parental encouragement, he has repeatedly resisted going to vocational school or taking a job.
Psychiatric history: Since last year, his parents have taken him to several local hospitals where he was variously diagnosed with "mild depression" and "latent schizophrenia." On a mental status exam, he had a flat affect, denied depressed mood or anxiety, and answered most questions by saying "I don't know." Neuropsychological testing revealed no cognitive abnormalities. Brain imaging and standard screening laboratory studies for altered mental status were unremarkable. He failed trials of psychotropic medications including antidepressants and antipsychotics.
Mental status exam on first interview:
Expecting a possible solution of his social withdrawal, his parents brought him to the psychiatric faculty where he is examined by you. Mr. B, just standing between his parents, kept politely silent. His attitude does not imply any psychotic experience, such as delusion/hallucination. He just seems to be a quiet person. Even when you addressed him, he just replied "I don't know."

Such hikikomori case vignettes were sent to psychiatrists in Australia, Bangladesh, India, Iran, Japan, Korea, Taiwan, Thailand, and the United States. Psychiatrists rated the syndrome's prevalence in their country, etiology, diagnosis, suicide risk, and treatment. Out of 247 responses to the questionnaire (123 from Japan and 124 from other countries), 239 were enrolled in the analysis [30]. Psychiatrists felt the hikikomori syndrome is seen in all countries examined and especially in urban areas. Biopsychosocial, cultural, and environmental factors were all listed as probable causes of hikikomori, and differences among countries were not significant. Japanese psychiatrists suggested treatment in outpatient wards, and some did not think that psychiatric treatment was necessary. Psychiatrists in other countries opted for more active treatment such as hospitalization. This first international survey has proposed that persons with the hikikomori syndrome are perceived as occurring across a variety of cultures by psychiatrists in multiple countries [30]. These pilot results provide a rational basis for study of the existence and epidemiology of hikikomori in clinical or community populations in international settings.

38.4.2 International Clinical Research Focusing on Hikikomori

38.4.2.1 Development of an Evaluation Tool for Hikikomori

Herein, we introduce our ongoing international collaborative research with the ultimate goal of better understanding hikikomori and developing diagnosis and treatment methods [39]. Firstly, we developed a new hikikomori diagnosis and

evaluation tool (tentative version) for use in international collaborative research based on the newest "social hikikomori" diagnosis standards in Japan [41] as well as suggestions from Teo and Gaw [42]. The standard for a diagnosis of social hikikomori was fulfillment of the following four criteria for 6 months or more: (1) the patient stays at home almost all day, almost every day; (2) the patient avoids nearly all social situations such as school, work, etc.; (3) the patient avoids direct social interaction with family or acquaintances; and (4) the above hinders the individual's social life. Individuals who fulfill all four of these criteria will be defined as "hikikomori."

38.4.2.2 Identification of Hikikomori

Next, we have conducted the first international clinical survey focusing on people with hikikomori in Japan, the United States, South Korea, and India using the above evaluation tool for hikikomori [39]. Psychiatrists in each country recruited individuals who might have hikikomori. In India, the survey focused on psychiatric outpatients; in Japan and Korea, it focused on outpatients at mental health institutions and mental health welfare centers (or equivalent facilities in the case of South Korea); in the United States, it focused on individuals who responded to online advertisements. Individuals between the ages of 18 and 39 who were able to speak their native languages fluently (English in the case of India) were recruited. Individuals who had been diagnosed with schizophrenia, dementia, autism, or autism spectrum disorder, as well as individuals who had withdrawn from society due to physical illnesses or injuries (as reported by the individuals themselves), were excluded at the time of recruitment. There were 108 entries from four countries. After excluding individuals who did not meet the standards for hikikomori (indicated below), individuals who had been diagnosed with schizophrenia, autism spectrum disorder, etc., and individuals whose consent was not obtained, 36 individuals who met the standards of a diagnosis for hikikomori were included for analysis. The majority of the people with hikikomori identified were highly educated males (university level or above), and their average time in hikikomori status was 2.1 years. The majority lived with their families; however, a small number lived alone (11%).

38.4.2.3 Psychosocial Characteristics of Hikikomori

In addition to the interview evaluation described above, the participants answered the following self-administered questionnaires: the UCLA Loneliness Scale [43, 44], the Lubben Social Network Scale-6 (LSNS-6) [45, 46], and the Sheehan Disability Scale (SDISS) [47, 48]. On the SDISS questionnaire form, the word "symptoms" was replaced by "hikikomori." Based on the scores of the UCLA Loneliness Scale and LSNS-6, we revealed that people with hikikomori have extremely limited social networks and suffer from a high level of loneliness. On the SDISS, which measures the extent of functional disability, people with hikikomori in this survey obtained an average score of 16.5 (SD = 7.9), which was more than three times higher than those who do not suffer from a

mental disorder [47]. A multivariate linear regression analysis of the correlation between the psychosocial characteristics of hikikomori and their countries has shown that, in comparison to people with hikikomori in Japan, respondents in the United States feel intense loneliness and suffer from a higher degree of dysfunction at home. The functioning of the social network is relatively well preserved among people with hikikomori in India; however, their level of functional disability is high overall. Korean respondents feel intense loneliness, have little interaction with acquaintances, and suffer from a high degree of functional disability.

38.4.2.4 Comorbidity of Psychiatric Disorders

During the course of the international survey among four countries, a structured interview using one of the most reliable psychiatric diagnostic tools available today, the Structured Clinical Interview for DSM Disorders (SCID)-I and SCID-II, was administered to Japanese and American people with hikikomori [40]. Among the subjects, there was a high degree of comorbidity with five psychiatric disorders: avoidant personality disorder, major depressive disorder, paranoid personality disorder, post-traumatic stress disorder, and social anxiety disorder. More than half of hikikomori persons fulfilled the diagnostic criteria for two or more mental illnesses. Five Japanese hikikomori persons did not fulfill the criteria for any of the mental illnesses evaluated by the SCID-I and SCID-II. Relative to Japanese subjects with hikikomori, a significantly higher number of American subjects with hikikomori had been diagnosed with mood disorders, substance abuse disorders, and anxiety disorders.

Another report from a recent clinical survey in Japan indicates that in almost all cases, hikikomori status was comorbid with some types of psychiatric disorders [49], and the results of the structured diagnostic interviews using the SCID conducted by us with Japanese and American people with hikikomori support these results. According to one point of view, hikikomori status should be categorized as an independent disorder known as "primary hikikomori," and interestingly, the fact that a certain number of individuals (though few) did not fulfill the criteria for any mental illness under the SCID also suggests the existence of a "primary hikikomori" [42]. Interestingly, only Japanese hikikomori subjects met the criteria for primary hikikomori, and it is likely that Japanese sociocultural factors contribute to this phenomenon, which is worthy of further consideration [30, 40].

Some researchers have regarded hikikomori as a culture-bound syndrome and have previously proposed including it in the DSM-5 [42]. Unfortunately, the disorder was not included in the updated DSM, but based on the fact that hikikomori exists not only in Japan but in other countries as well, perhaps hikikomori should be included in some form of the international diagnostic standards such as the International Classification of Disease (ICD)-11, which are currently being formulated.

38.4.2.5 Implications for Future International Research

The survey introduced here involved only a very small number of hikikomori cases and may not accurately reflect the status of hikikomori in each country; therefore, we must be cautious when interpreting the results. However, the significance of this research is in the application of a novel international evaluation tool which will assist in deepening out understanding of hikikomori and the establishment of a defined method. Prior Japanese epidemiological studies of hikikomori have been limited by the fact that structured interviews were not used to determine hikikomori status and were based only on responses to one or two limited questions [27]. Using the tools we have developed, future epidemiological studies should help overcome the limitations of previous epidemiological studies.

Autism-related disorders were excluded through self-reported screening; however, because it is not possible to diagnose autism or autism spectrum disorder using the SCID, the possibility that the subjects with hikikomori in the study also suffered from autism-related disorders cannot be ruled out. A possible link has been proposed between hikikomori status and developmental disorders [50], and in the future, it will be necessary to conduct a clinical survey using evaluation tools for autism and its related disorders at the same time.

38.4.3 The International Hikikomori Phenomenon as a Contemporary Society-Related Boundless Syndrome

Mental illnesses, in particular those referred to as "syndromes," are strongly influenced by culture, society, and historical period. From the end of the nineteenth century to the beginning of the twentieth century, a social upheaval took place in Europe, and hysteria was extremely widespread during this time. There is no doubt that Freud's studies with Charcot, a major figure in the study of hysteria, as well as Freud's own clinical experiences with hysteria patients, played a significant role in Freud's invention of psychoanalysis. In the 1950s, eating disorders appeared in the United States and elsewhere, and in the 1970s they began to appear in Japan as well. At the same time, borderline personality disorder appeared, and it became extremely widespread in Japan in the 1980s and in the 1990s; however, currently it is rare to encounter borderline personality disorder patients who drastically act out. In addition, hikikomori began to receive attention in the late 1990s, and currently a new type of depressive syndrome has appeared, mainly among the young (note: this is referred to by informal names such as "modern depression," "new type depression," etc.; however, there is no uniform point of view on the issue among psychiatrists), and we are considering that both phenomena have a common pathological links based on the psycho-bio-social aspects [29, 51]. In just 100 years, manifestations of mental illness have changed drastically; however, human evolution could not possibly have changed in a

corresponding fashion in such a brief time. This transformation in manifestations of mental illness appears to have been strongly influenced by various unique forms of stress present in modern society, in particular childhood environments. It is likely that these varied temporal, social, and cultural factors bring about epigenetic changes and changes in the brain, for instance neuron-glia interaction, manifesting in particular forms according to particular temporal and social conditions [52–55].

A variety of psychosocial factors, from the early stages of life through to adolescence, have been suggested to contribute to the onset of hikikomori (Fig. 38.1). Especially important are childrearing, school, and later workplace environments. Within this, parent-child relationships and how/whether good-enough relationships between peers and friends have been established are vital components. The establishment of these bonds can facilitate smooth relationships with workplace colleagues and superiors later in life. However in hikikomori, the establishment of such fundamental interpersonal skills during the early stages of life may be insufficient, which can induce vulnerability to stress meaning that mental dysfunctions are more likely to develop. In other words, lower resilience and the greater possibility of experiencing stress traumatically. Regarding the sociocultural impact in Japan, along with modernization and globalization, there has been a continuing shift away from a hitherto respected and venerated "group mentality" to an "individualism" in which individual achievements are pursued and this shift has resulted in rapid changes in school and work environments. In addition, we suppose that such sociocultural factors are occurring along with an interrelated biological basis, and it is important not to ignore underlying biological factors (Fig. 38.1). With regards to diagnosis and evaluation of hikikomori, we are in a transitional period and a differential method to distinguish from existing psychiatric diagnoses is warranted.

Conclusion

It may be that environments that favor the emergence of the hikikomori phenomenon are spreading worldwide. Psychiatrists and mental health professionals tend to overlook the fact that contemporary society itself is transforming manifestations of mental illness; however, we must attempt to confront this important theme consistently. Multifaceted research in fields ranging from psychology to biology will shed new light on the unknown pathophysiology of hikikomori. In order to verify the presenting hikikomori pilot data and to deepen it further, it will be necessary to carry out a large-scale epidemiological study using novel tools such as the hikikomori diagnostic tools we developed. In the future, consideration should be given to including these tools in international diagnostic standards such as the ICD-11.

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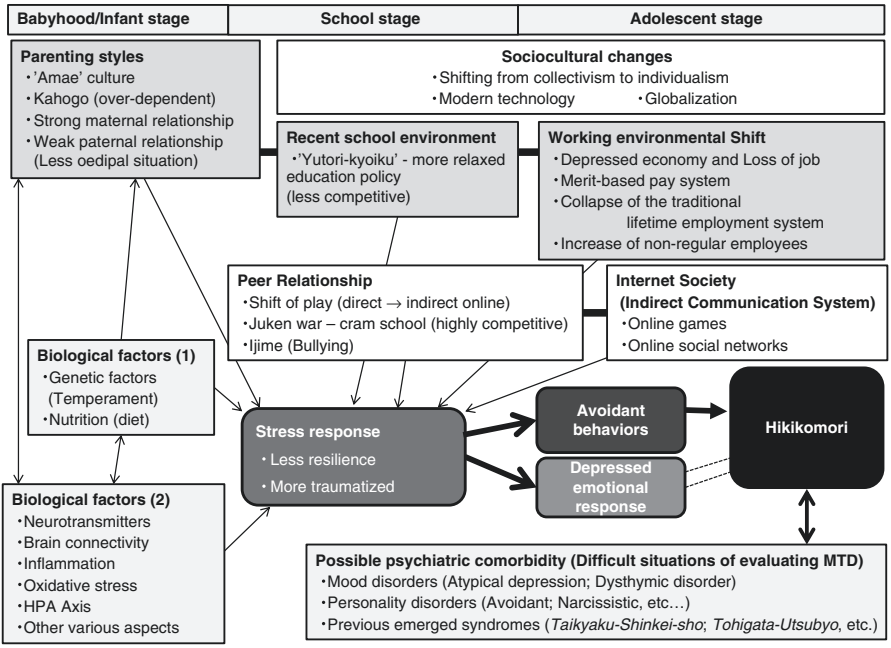

Fig. 38.1 Multidimensional understandings of hikikomori (Modified from [28, 51])

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Economic Recession and Mental Health: An Analysis

39

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Abstract

This chapter looks at the interrelationship between economic recession and mental health. The world has been fraught with many economic recessions, and this chapter provides an overview of various effects that economic recession may have on mental health at an individual, family, and epidemiological level. Various economic recessions that have affected humanity across the world are outlined. Suicide, depression, and various mental health problems resulting from an economic recession are discussed. There is also a discussion of management strategies for the same at an individual, group, and policy level. There is also a need for mental health services to be easily available at the time of economic recessions to reduce that negative outcomes that may ensue due to the same.

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39.1 Introduction

Positive mental health is the basis for an overall well-being for an individual where he or she is able to function effectively, work productively, handle normal stressors in day to day life, and contribute to the society. Positive mental health helps ensure effective functioning of an individual at a personal, professional, and societal level [1]. As demonstrated across studies, mental health is affected by various psychosocial factors, and one such factor from the nation's standpoint is the economic domain [2]. Several dynamics of the economy such as recession, unemployment, and slumping stock markets are among the various factors that are known to affect the mental health negatively across various countries [3]. Historically, economic recessions are known to have mental health casualties as demonstrated by the great depression, the economic recession in the Gulf and in Asia [4].

39.2 What Is an Economic Recession

An economic recession is understood as a fall in the nation's gross domestic product (GDP) or, simply, the national output. A typical recession is characterized by high unemployment, falling average incomes, increased inequality, and higher government borrowing. Thus, effects of a recession include a slump in the stock market, an increase in unemployment rate, and an increase in the overall national debt [5]. The impact of a recession depends on how long it lasts and the depth of the fall in output. Unemployment rates tend to increase with economic recessions [6]. The visibility of the impact is seen specifically more in younger adults, as they are more prone to experiencing the prolonged negative outcomes due to low wages and difficulties in finding employment [7]. Some indicators may improve during crises, but a diversity of mortality and morbidity outcomes has shown to be affected making a ripple effect on the individual's mental health and consequently the nation's happiness index [8].

39.3 Economic Recession and Mental Health

The potential of impact of economic recession on the global population's mental health has been on an increasing trend. Mental illnesses are interlinked with the trends of the national economic situation, both in the short-term and long-term period [9]. Numerous negative effects of economic downturns have been recorded in literature. It is essential to consider that there are a certain category of populations that tend to be more vulnerable to the negative impacts of recession (and unemployment) that includes younger people, children and adolescents, those who are least educated, low-income individuals/families, those at risk for poverty before downturn, single parent families, precarious workers, people with a history of mental illness, ethnic minorities, and migrants [10].

Mental health and economic recession have an interdependent relationship and impact on individuals. As easily understood, sound mental health provides the fundamental base for optimal operations and functionality, greater productivity at workplace, better decision-making capacities, opportunities to take up challenges, and niche for excellence and promotion; on the contrary, mental illnesses may disrupt the aforementioned [11]. Economic recession has the potential to create a negative impact on an individual's mental health. Work changes due to economic turndowns can lead onto an increase in the cognitive and emotional demands of work. This, therefore, leads onto absenteeism and withdrawal from the labor market because of stress-, anxiety-, and depression-related disorders, thereby leading to potential unemployment [12]. It has also been seen that the unemployment rate is a measure of economic well-being of population [13].

Chances of becoming ill, specifically those who become unemployed, are twice as likely to develop a "limiting illness" (i.e., a health condition or disability that limits one's ability to work) and are 60% less likely to recover. The risk of developing mental illness increases as the duration of unemployment increases, especially among young adult males [14].

39.4 The Major Economic Crises of the Twentieth Century

To understand the magnitude of impact on mental health that economic recessions and downturns have had, it is prudent that we understand the five most befalling economic crises that the world economies faced [15]:

1. *Great Depression of 1929*: This was a worldwide depression that lasted for 10 years. Its kickoff in the US economy was "Black Thursday," October 24, 1929, when 12.9 million shares of stock were sold in 1 day, which were triple the usual amount. Over the next 4 days, stock prices fell 23% leading to crash of the stock market. It had a worldwide impact leading to a fall in international trade of more than 50%; rapid rise in unemployment across the industrialized world; hyperinflation in a few countries, with profound political consequences; and lastly, it paved the way for the emergence of fascism in Germany and Italy that lead onto World War II.
2. *Post-Communist Depression of 1990s*: Gorbachev's attempt to reform the Soviet Union was brought to an abrupt halt by an attempted coup in August 1991. Within a few days, the Soviet Union broke apart as its constituent republics successively declared independence. Each republic had been part of a complex and interlinked trading system in which a single truck emerging from a factory in Kiev might contain components from ten other republics, with the whole process controlled through a system of central planning that was only possible when the state owned all the factories. Many of the political leaders in the newly independent republics made a seamless transition from party apparatchiks to some form of democracy and capitalism. In some countries, however, the economic changes

were profound. Economic collapse ensued, unemployment rose, and savings were wiped-out by inflation.

3. *South-East Asian Financial Crisis of 1997*: The Thai government had tied the Baht to the US Dollar but was no longer able to defend its currency against intense speculative pressure. Careless lending by banks created an unsustainable bubble. Once international investors realized the true state of the economy, the Baht was forced to devalue by 50%. Problems spread rapidly to Thailand's neighbors, leading to mass withdrawal of capital and rapidly rising unemployment across the region.
4. *European Recession in 2008*: It began in January 2008, primarily due to nearly 15 years of bad mortgaging deals by banks worldwide. It led onto bankruptcy of the automobile industry (GM, Chrysler), along with housing and real estate problems. This mainly affected the USA, Britain, and Europe (among other parts of the world). The economy of Europe shrank by 4% in 2009, and unemployment reached 10%. Britain, Ireland, Iceland, and Eastern Europe were most affected. The European Union (EU) countries reduced their health budget and introduced structural changes and austerity measures. However, the endpoint has not yet been perceived to be reached in the short term. Significant impact has been seen in the form of increase in national debt levels, decreased gross domestic product (GDP), worsened unemployment rates, challenging of the basic European assumptions of welfare state, and principles of solidarity.
5. *Demonetization and the Indian Economic Crisis in 2016*: On November 8, 2016, the Indian Prime Minister made a sudden announcement about both demonetization and scrapping of high denomination currency, that is, INR 500 and INR 1000 with immediate effect; both these denominations comprised nearly 86% of circulating cash of the Indian economy. Apart from the widespread economic impact and other hardships faced by the people, this decision has received both plaudits and criticism alike at political, economic, and common man level. An immediate concern was its impact on the healthcare system and concerns related to its potential impact on the mental health of the individuals. Deaths have been linked to demonetization and denial of healthcare services, especially in the private sector, were reported in the initial few weeks when the cash crunch was severe.

39.5 Economic Recession and Psychiatric Comorbidities

39.5.1 Effects on Health and Well-Being

The health effects of economic recessions and crises have been studied for decades, as long as in 1959. Economic recession hits hard to those who are employed as well as unemployed. Though those who are unemployed are in a worse condition, the consequences faced by the employed individuals include—loss of income, loss of investments, and job insecurity. Economic crises bring national and international concern in the domain of public mental health [16].

Emile Durkheim's seminal work on *Le Suicide* in 1897 is the historical landmark to where the origin of the work on economic recession and mental health can be traced down to [17]. Durkheim proposed that changes in the economy could increase psychiatric pathology, even leading to suicide, and noted that macroeconomic phenomena could have significant psychological effects on individuals. It was Durkheim's research that persuaded sociologists to study the rates of suicide within and across societies, based on sociodemographic characteristics by conducting research [18].

After almost two decades, Brenner conducted empirical studies linking societal economic change to increased psychiatric hospital admissions. He argued that economic instability was the major factor influencing rates of mental hospitalization [19]. He found that individuals who had lost employment were at a greater risk than individuals who had not lost employment. Those who worked in organizations and lost many employees (causing fear and stress to those who remained) could also experience negative mental health outcomes [20].

39.5.2 Psychiatric Morbidity

It is well known that a link with increased mental health problems with poorer psychological well-being is reported. The main common mental disorders reported include depression, anxiety, sleep problems, marital dissatisfaction, family conflicts, and cognitive decline. Psychiatric comorbidities have been studied through various methods, viz., cross-sectional assessment, longitudinal assessment, and assessment of self-help behaviors as surrogate markers [21].

39.5.3 Alcohol Abuse and Addictive Behaviors

Alcohol abuse (sometimes leading to alcohol dependence or binge drinking), smoking cigarettes, chewing tobacco, and, more recently, the intake of cannabis have been one of the most studied health behaviors among employees, as outcomes of macroeconomic fluctuations [22]. With the prevailing economic recession, drinking usually decreases (most likely due to pricing effects); however, a subsample increase in binge drinking, harm, and dependence and the same has been reported [23]. Various factors mediating this risk entail male gender, duration of unemployment, severity of economic loss, pre-existing individual vulnerability, quality of social and family support, and pre-existing economic disparity. For illicit substances, a consistent pattern has been seen with low socioeconomic strata, but an inconsistent pattern has been observed with periods of economic crises due to flexibility of the illegal market [24]. For nicotine, a consistent increase is seen in adolescents, younger adults, and adults. Overall, a complex relation between substance use patterns and consequence and economic downfall is seen [25].

39.5.4 Suicide

The largest number of studies has focused on the association between suicide and the rates of unemployment, deliberating on a positive correlation between the rates of unemployment and the rates of suicide [26]. Numerous studies have shown an increase in suicide rates in the first 5 years following economic recessions (after 2008). Though rates of suicide may subside with time, they can continue to remain high for up to 16 years after a recession [27].

39.5.5 Healthcare Utilization

There is an increase in the inpatient cost per discharge, and changes in utilization patterns and resource use or the increased willingness from providers to treat medical patients (due to providers facing reduced demand for their services) are a documented trend [28]. An increase in the number of admissions among elderly with increased mortality rates is also seen. Contrastingly, therapy client have also seen to increase significantly when economic crises have struck nations. The same has been reported by studies and mental healthcare professionals [29]. The further study in related demographic details is required to understand the complete pattern; however, economic recession is likely to impact the mental health of the individuals; a study in New Delhi reported a 30% hike in the patients at therapy clinics as a result of the economic crunch [30]. Economic recession does contribute to a markedly lesser willingness to ask for healthcare due to costs involved; however, on the contrary a rise in the number of patients for mental health help has been reported [30].

39.5.6 Emotional Distress

An upheaval in the emotional well-being of individuals who have been struck with economic recession is one of the first problems that surface. In situations where increased stress levels are unaided by adequate family and social support, the consequences may be dire. Emotional distresses have the potential to scale up to a full-blown depression, panic attack, or any other mood or anxiety disorder that needs clinical attention. In the absence of any scaffolding and added stressors, emotional distress may even lead to suicidal ideation and suicidal attempts [31].

39.5.7 Interpersonal Distress

The financial strain that results from retiring or losing a job can affect marital satisfaction and further reduce mental well-being [32]. Financial strain can result in the loss of personal control which further inhibits emotional functioning and physical health [33]. Financial strain can lead to reduced social support and negative relationships with family [34]. Finally, workplaces are often a source of social support;

therefore, job loss can negatively affect psychological well-being [35]. However, research findings elucidate contradictory findings. A review of studies published between 1990 and 2009 found strong evidence supporting adverse effects of job loss on depressive symptoms, suicide, and substance abuse and a moderate positive association between economic contraction and antisocial behavior [36].

39.6 Psychological Theories Explaining the Links Between Economic Recession and Mental Health

Durkheim and Brenner's research highlighted one of the theoretical explanations for explaining the importance of public policy implications and the impact of macro-level social conditions on population mental health [37]. Their work thus suggests the need for policymakers to consider the psychological implications of economic decisions given that the economic environment influences the incidence of symptoms of mental disorders in populations [37].

Other theoretical models explain how macroeconomic conditions might influence mental disorders. Brenner's "Economic Change Model of Pathology" examined the complex relationship between the economic environment and changes in physical, social, and mental well-being [38]. Catalano and Dooley proposed that macroeconomic indicators influence the use of mental health facilities based on the "provocation" and "uncovering" hypotheses. During economic downturns, family members and society have decreased tolerance for disordered behavior, hence "uncovering" behavior resulting in more manifest psychiatric disorder seen by health providers. Alternately, economic change can cause new disorders by eliciting or "provoking" maladaptive behavior. Their work suggests more evidence for the uncovering hypothesis, but the provocation hypothesis was also maintained [39].

Yet other relevant theories include the "shift hypothesis" which suggested that economic contractions may deprive certain populations of private treatment, thereby increasing use of public mental health facilities, and the "stress hypothesis" that community economic change is related to mental disorders via individual life changes and elevated symptoms of depression and stress [40]. It has been suggested that the relationship between the economy and mental health can be evaluated on the continuum between the "unfettered enterprise" hypothesis and the "social protection" hypothesis [37]. Unfettered enterprise suggests that the human costs of economic change are negligible and that "normal" people can adapt to such change, whereas social protection identifies high human costs of economic change that may be inequitably distributed over the population. Research identifies results more consistent with the social protection hypothesis, and it is suggested that the policymakers should seek to prevent harm and provide support for those who are most vulnerable during economic downturns [41].

While these theoretical perspectives and existing research have offered reasons why there may be a link between economic processes and population mental health, the empirical literature must evaluate whether such a link exists.

39.7 Research on Economic Recession and Mental Health

There have been several researches conducted to study the relationship between economic recession and mental health; however, the studies largely pertain to Europe, the USA, and the UK. Empirical research studies have described three primary mental health indicators with respect to understanding the influence of economy: (1) mental disorders, (2) admissions to mental health facilities, and (3) suicide.

Studies of the relationship between macroeconomic decline and mental disorders were primarily conducted in the 1970s and observed that people in the workforce were more likely to be negatively affected by the economic downturn than people not in the workforce [37]. These studies reported that people of lower socioeconomic status were more likely to be negatively affected than middle- or upper-status groups [42].

Most research on the impact of unemployment on mental health focuses on studies of suicide. Findings differ by demographic characteristics (such as sex and age) as well as based on occupational status. Findings regarding suicide rates were often more nuanced than simply a negative or nonsignificant relationship between economic downturn and suicide [43]. Many studies explored the impact of a variety of different economic factors on suicide rate in the USA and Canada. In a study, it was calculated that there were 4750 excess suicides in the USA from 2008 to 2010, drawing from results of previous studies, while other researchers calculated a 2309 excess suicides from the baseline rate in 2009 [44, 45].

Furthermore, they identified an 8.7% rise in suicide rate in men in the USA, and women in the USA also experienced a significant rise in suicide rate of a smaller magnitude (2.4%). Phillips and Nugent [46] identified a higher percentage of males, a higher percentage of elderly, a higher divorce rate, and a lower percentage of foreign born with a greater variation in suicide rates across states and within states over time. They reported that lower average suicide rates were found in states with a higher per capita income, a higher percentage of manufacturing jobs, and a higher percentage of foreign born. In other words, wealthier states had lower suicide rates. This also highlighted the impact that manufacturing jobs have on suicide rates, as these jobs offer a good income for individuals of lower socioeconomic status; the risk of suicide likeably reduces. Results also showed that cultural differences can impact suicide rates as lower average suicide rates were found in states with a higher percentage of foreign born were found [46]. They found that during the recession, higher average levels of state unemployment were correlated with higher suicide rates, while other articles refuted this.

Researchers also explored the modulating effects of various economic factors (maximum state unemployment benefits and female labor force participation) on the impact of rising unemployment levels on suicide rates. They found that after adjusting for confounders, every percentage point increase in state unemployment rate associated with 0.16 more suicide-related deaths per 100,000. While the impact of maximum state unemployment benefits on suicide rates was nonsignificant, there was a negative interaction between unemployment rate and maximum state

unemployment benefits. This highlights the impact of a social safety net on modulating the impact of rising unemployment levels during a recession on mental health [47]. They found that rising unemployment was associated with higher levels of suicide overall and that these levels were higher for male suicide. Phillips and Nugent also reported a positive interaction between elevated female labor force participation (females accounting for a larger percentage of the labor force) and rising unemployment levels on suicide rates, i.e., a higher female labor force exacerbated the effects of rising unemployment levels; the magnitude of this interaction was of questionable significance [48].

Researchers explored the impact of rising foreclosure rates on rising suicide rates. They found that eviction-/foreclosure-related (any action taken to evict someone living on the property, either as tenant or owner) suicides accounted for 1–2% of all suicides and accounted for 10–16% of financial suicides from 2005 to 2010 [49]. The US housing bubble was a real estate bubble affecting over half of the US states. Housing prices peaked in early 2006, started to decline in 2006 and 2007 from 2006 to 2007. Furthermore, relative to all other suicides, eviction-/foreclosure-related suicides increased in frequency from 2006 to 2007 and decreased in frequency from 2009 to 2010, reaching a further low till 2012 [49]. Real estate owned housing foreclosures can occur in severe situations where the owner's home has to be repossessed due to financial difficulties. These foreclosures can have a significant psychological impact on the owner. An increase in real estate owned housing foreclosure rate of 1% was associated with an increase of within-state suicide rate of 0.16, even when sociodemographic factors were taken into account. An increase in real estate owned foreclosure rate from 0 to 5% was associated with a 25% increase in suicide rate for the 46–64-year age group, from 18.5 to 23 per 100,000 [50].

In another study, researchers 242 excess suicides in Canada from 2008 to 2009 relative to the baseline levels, which they confirmed to be statistically significant. Chang et al. similarly found a significant rise in suicide rates in 2009 relative to baseline for Canadian men (8.9%) but not for Canadian women [44].

Juan Antonio and others [51] carried out a research in Andalusia, the most populated region of Spain, and which has a high level of unemployment. Information on suicide attempts attended by emergency services was extracted from the Health Emergencies Public Enterprise Information System (SIEPES). Suicide attempts occurring between 2003 and 2012 were included, in order to cover 5 years prior to the crisis (2003–2007) and 5 years after its onset (2008–2012). Information was retrieved from 24,380 cases (11,494 men and 12,886 women) on sex, age, address, and type of attention provided. Age-adjusted suicide attempt rates were calculated. Excess numbers of attempts from 2008 to 2012 were estimated for each sex using historical trends of the 5 previous years, through time regression models using negative binomial regression analysis. To assess the association between unemployment and suicide attempts rates, linear regression models with fixed effects were performed [51].

Suicides, as discussed have generally found to increase during times of economic troubles, and according to experts, Asians are likely to be particularly susceptible as the region has among the world's highest suicide rates. Studies have claimed that

the suicide rate in South Korea nearly doubled during the Asian financial crisis 10 years ago, with experts blaming the increase on stress caused by job and income losses [52].

India is particularly vulnerable because economic crunches in the past 15 years had raised expectations enormously, and many people have consequently faced severe problems accepting their loss of income and status. Several recent suicides resulting from job losses have highlighted the increased need for mental health services in the country. Debt and distress has also driven tens of thousands of Indian farmers to commit suicide in the past two decades, and farmer suicides have become a roaring problem in the face of mental health issues in India in the last decades [53].

39.8 Gender and Economic Recession-Mental Health

Studies examining the impact of macroeconomic conditions on mental health have yielded mixed findings with respect to gender. Put in a historical context, economic recessions and periods of high unemployment have been shown to have greater effects on men than women [54]. For example, in the UK, men experienced poorer mental health in 2009 and 2010 than in 2008, while women had no significant changes in their mental health during these years. In the USA, men have experienced disproportionately more job losses than women in this economic recession, partly because of the greater loss of jobs in the construction and manufacturing sectors than in the service sector; thus, their mental health may be impacted more negatively than women. Moreover, men have lower rates of mental healthcare utilization than women in general [55]. In fact, research in the USA showed that physician visits for treatment of anxiety and/or depression decreased by 7–8% among females and by 25% among males during the economic recession. Thus, authors expected differences by gender in the relationship between indicators of the economic recession and mental health outcomes [56].

One study showed that suicide and unemployment rates were positively correlated in employed males and negatively correlated in employed females, but no significant correlations were found between suicide and the unemployment rate among unemployed people of either sex [57]. Studies have shown mixed results regarding whether men [58, 59] or women [60] have increased rates of suicide during economic downturns.

A cross-sectional, descriptive study of two periods, before the recession (2006) and after the recession (2011–2012), was carried out in Spain [61]. The study comprised of 25,234 subjects (2006) and 20,754 subjects (2012). Independent variables, (1) sociodemographic (age, socio-professional class, level of education, nationality, employment situation, marital status), (2) psychosocial (social support), and (3) financial (GDP per capita, risk of poverty, income per capita per household), public welfare services (health spending per capita), labor market (employment and unemployment rates, percentage of temporary workers), were studied to find out the psychic morbidity (dependent variable). Multilevel logistic regression models with mixed effects were constructed to determine change in psychic morbidity according to the variables studied. The macroeconomic variables associated with worse

mental health for both males and females were lower health spending per capita and percentage of temporary workers. Among women, the risk of poor mental health increased 6% for each 100€ decrease in healthcare spending per capita. Among men, the risk of poor mental health decreased 8% for each 5 percentage point increase in temporary workers [61].

Dagher and others [62] examined gender differences in mental health outcomes during and post-recession versus pre-recession in the USA. The years 2005–2006, 2008–2009, and 2010–2011 were utilized for data from the Medical Expenditure Panel Survey. Females were found to have lower odds of depression diagnoses during and post-recession and better mental health during the recession, but higher odds of anxiety diagnoses post-recession. Males were found to have lower odds of depression diagnoses and better mental health during and post-recession and lower psychological distress post-recession. Importantly, it was found that the higher odds of anxiety diagnoses among females after the recession were mainly prominent among specific subgroups of females, i.e., those who lived in the Northeast or the Midwest, the unemployed, and those with low household income. This study examined the relationship between recession indicators (during and after recession versus before) and population mental health separately by gender. It was hypothesized that in comparison to the period preceding the recession, (1) mental health may decline during the recession and slightly improve after the recession and (2) the recession will be associated with worse mental health among males than among females and that these gender differences in mental health will be ameliorated in the aftermath of the recession. Results demonstrated a differential association of the recession with mental health outcomes in males and females [62].

The dimension of gender needs further careful analysis in order to reveal a concrete pattern of impact on mental health as a result of economic recession at a national and international level. However, gender differences in mental health in association with the economic recession highlight the importance of policymakers taking these differences into consideration when designing economic and social policies to address economic downturns [63].

39.9 Practical Applications of Various Studies Cited

The practical applicability of the results of the studies is another issue. Though many economic factors like unemployment benefits may impact suicide rates, most of the annual variation in suicide rates is not explained by these factors. Furthermore, increasing, for example, unemployment benefits would have a minimal impact on suicide rates and would not be cost effective. Targeted screening might be a more feasible option, for example, depression screening in patients who have had recent home foreclosures might help save lives [64]. An interesting pattern emerges when the results of the various studies are taken together, which can have a significant impact on screening measures and the direction of future work. The economy is a complex, interconnected system with many components. If one component fails, it can have a significant impact on many other components, but it takes the failure of

multiple components to send the economy into recession. It can be a lengthy process from the first component failure to the full-blown recession [65].

Similarly, there must have been many other markets that were particularly impacted over the course of the economic recession, collapsing and recovering at different times. During such drastic recessions, it might be beneficial to identify which markets are being affected and implement depression and suicide screening programs for individuals who are impacted by these markets (e.g., as part of corporate employee wellness programs). This might be a more efficient way of targeting help to those who need it the most. The impact of these specific market collapses on suicide rates in affected individuals can be a fruitful area of future study [66].

The role of mental health in the association between unemployment and suicidal behavior needs to be explored further. Does unemployment increase the risk of serious psychiatric problems that in turn increase the risk of suicidal behavior or, alternatively, are those with psychiatric problems more likely to become unemployed and also more likely to engage in suicidal behavior?

39.10 Mental Health Management and Prevention (See Box)

The management of mental health problems with respect to mental health disorders and rate of suicide requires for a holistic team approach. Various stakeholders hold a responsibility in the effective prevention and management of mental health problems at the workplace. The various pillars of mental health management in the face of economic recession would involve mental health professionals, workplace management, family, employees and co-workers, and policymakers [67].

39.10.1 Role of Mental Health Professionals

Mental health professionals from all sectors including psychiatrists and psychotherapists can work in tandem in order to promote positive mental health among employees and workers. The medical care of psychiatrists and counseling services offered by psychologists can provide for supportive care for employees during the time of crises helping them cope with stress and emotional distress. Mental health professionals play a role in building resilience and providing support that reduces the vulnerability to crawl into full-blown episodes of mental illnesses such as depression, anxiety attacks, or (possibly) psychotic episodes. Group therapy may also be conducted along with various programs such as stress reduction and corporate counseling in order to promote well-being within the company [68].

39.10.2 Role of Workplace Management

The management staff at workplaces can play a crucial role in providing of a grievance cell within companies along with an active HR department where employees can discuss conflicts, challenges, and stresses that employees face in times of

recessions. Economic crises have a magnifying impact on employees, and addressing their issues can help manage well-being at an individual level and productivity at the workplace. Efficient management, team building, and stress reduction among employees can maintain the flow of work in times of crunch [69].

39.10.3 Role of Employees and Co-workers

A support group within the company can help employees identify with each other's problems. Such a process helps build belongingness and sense of healthy dependence among the workers, especially in a crisis situation where all can share the burden. An emotional understanding and empathic approach among working fellows promotes for mental health of everyone in the work space, providing for healthier and more competent working atmospheres in times of crises such as recessions [70].

39.10.4 Role of Family

Job redundancy and unemployment rates are crucial phases when the family provides the much required social support and emotional backbone for the employees who get affected by such crises. A healthy family support offers for lesser chance for developing mental illnesses as the emotional cushioning is present [71].

39.10.5 Role of Policymakers

Policymakers must ensure to make a provision for quality care and rightful provision in the face of economic adversities keeping in mind the employees on board. Policymakers play a crucial role in determining the layout of rules and regulations that have a crucial, indirect impact on the lives of employees. Policymakers can promote for better mental health by keeping in mind the adversities faced during an economic recession and providing guidelines for care in advance so as to control for negative mental health [72].

39.11 Take Home Points

- Economic recessions and downturns are common in the modern era especially with the fluctuations in the economy and global financial markets. Large mental health implications surround these economic recessions.
- Following an economic recession there is a marked increase in suicides, depression, and alcohol dependence in the population. This has been noted across all the recessions that have happened in the world.
- The increase in mental health problems is coupled with a decrease in healthcare utilization as financial power to use healthcare reduces in times of economic recession.

- Gender differences in the mental health problems seen after an economic recession have been noted and well elucidated.
- Prevention and management of mental health problems after an economic recession needs an integrated approach at an individual, community, family, and policy level.

Mental Health Promotion Endeavors in Times of Economic Recession
Suggestions for Mental Health Professionals, Companies, and Policy Workers

1. Policy workers may consider providing employees with a day off when they may find it difficult to cope with the work or related stress at the workplace as it affects their mental health and daily functioning, and in-house mental health support may be provided. This helps offer acknowledgment of the problem that the working professional is suffering from.
2. A full-time psychologist on board the HR department to address the personal grievances of the employees that may interfere with work.
3. Policymakers may keep in mind the varied impacts of economic recession on males and females in order to draft for better prevention and management programs.
4. Better organizational behavior promotion techniques which are in line with the mental health status of employees.
5. Application of motivational theories, art of leadership, and skill of redesigning jobs and modification to organizational structure.
6. Mental health problems being brought under general health insurance shall help ease the burden on the employees.

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Psychiatry Residency Education in Countries with Low- and Middle-Income Economies

40

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Abstract

Utilizing scarce resources creatively becomes challenging for psychiatrists in impoverished countries. Balancing academic duties with public health needs compounds economic hardship, having to face concomitant problems of low wages, personnel shortages, large-volume practices, societal stigma, and discrimination. This chapter reviews how economic disparities in most of Asia, Africa,

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and Latin America, combined with psychiatric workforce inequities, create resource deficiencies having to culturally adapt educational initiatives. We recommend a learning inclusive approach that incorporates meeting public health needs and highest standards of care educational models. Specific examples will be given of collaborative didactic programs that connect mentors and institutions from high-income countries with trainees and faculty in underserved areas.

40.1 Introduction

Psychiatrists in countries with low- and middle-income economies encounter obstacles that interfere with the provision of high-quality evidence-based treatments to persons with mental disorders. Having to utilize scarce resources in creative ways becomes challenging for psychiatrists in impoverished countries. Balancing academic and clinical duties with public health needs further compounds economic hardship, having to face concomitant problems of low wages, personnel shortages, large-volume practices, societal stigma, and discrimination.

This chapter will review how economic disparities, particularly in most of Asia, Africa, and Latin America, combined with psychiatric workforce inequities, create what has been referred to as public health mental health resource deficiencies with implications of having to adjust and culturally adapt educational initiatives [1]. Teaching skills and knowledge to psychiatric residents who will work in a fragmented and underfunded system pose questions as to how to revise curricula and supervise clinical training experiences. Finally, incorporating relevant cultural psychiatry in the education of residents becomes imperative, given the important differences in beliefs, values, and cultural norms that will determine treatment adherence, therapeutic alliance, and clinical and public health outcomes.

We will propose in this chapter possible ways to equalize educational disparities in countries with low- and middle-income economies that occupy two-thirds of the world, in order to bridge curricular and clinical experiential learning through collaborative didactic endeavors. We will recommend a learning inclusive approach that incorporates meeting public health needs and highest standards of care educational models. Specific examples will be given of successfully implemented or piloted local and transcontinental collaborative didactic programs that connect academic mentors and institutions from high-income countries with psychiatric trainees and faculty in underserved areas.

40.2 Geographic Economic Disparities and the Psychiatric Workforce

The World Bank defines low-income economies as those with a GNI per capita, calculated using the World Bank Atlas method, of $1025 or less; lower middle-income economies are those with a gross national income (GNI) per capita between

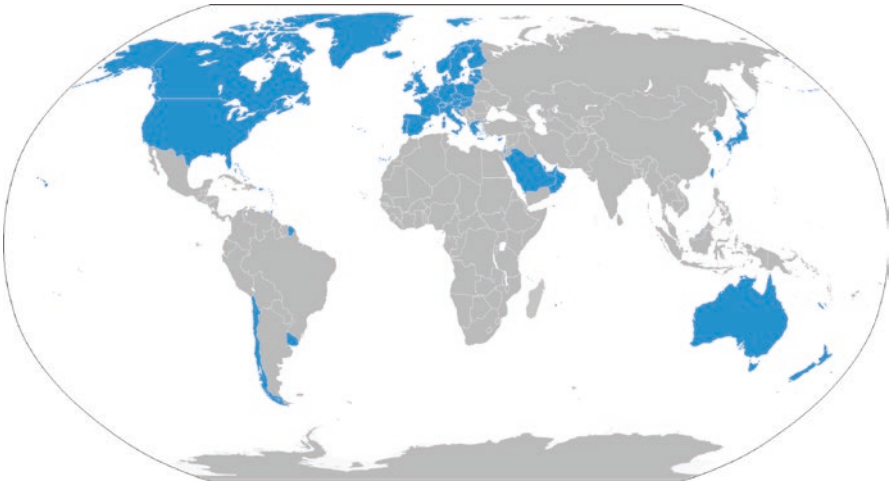

Fig. 40.1 Countries with high-income economies (highlighted in blue) and low- and middle-income economies (highlighted in gray)

$1026 and $4035; upper middle-income economies are those with a GNI per capita between $4036 and $12,475; high-income economies are those with a GNI per capita of $12,476 or more. For the purpose of this chapter, we are combining and focusing on countries with low- and middle-income economies, as these geographical areas and populations face psychiatric training and clinical workforce challenges that place them at a disadvantage when compared to countries with high-income economies. While roughly one-third of countries in the world have high-income economies (Fig. 40.1), 149 countries are currently classified as having low- and middle-income economies (see Table 40.1).

Human resources and reasonable psychiatric staffing are crucial in order to provide adequate clinical services. Additionally, countries with acceptable numbers of doctors are better able to release time to comfortably balance clinical care with academic duties. Although the median distribution of psychiatrists worldwide per 100,000 population is 1.2 (SD 6.07), a continent like Africa has 0.04/100,000, while Europe has 9.8/100,000. There are approximately 1800 psychiatrists in the African continent caring for a population of over 700 million. Estimates of the psychiatric workforce worldwide are frequently updated in the WHO Global Health Observatory data repository [2].

Countries with high-income economies have psychiatric workforce rates reported by the WHO as the following: the USA with 12.4/100,000, Australia 12.76/100,000, Uruguay 16.9/100,000, Sweden 18.3/100,000, the Netherlands 20.1/100,000, and Norway 29.60/100,000. The accuracy of these numbers has been questioned, as the WHO GHO 2015 does not seem to capture the entire psychiatric workforce in certain countries. For example, there are near 50,000 psychiatrists in the USA, and a more accurate rate for a population of 330 million would be 15.2/100,000. The authors caution readers to question the precision of WHO GHO psychiatric work force estimates, which may be skewed to under report.

Table 40.1 Countries with low- and middle-income economies classified using the World Atlas method

Low-income economies (31 countries)		
Afghanistan	Guinea	Rwanda
Benin	Guinea-Bissau	Senegal
Burkina Faso	Haiti	Sierra Leone
Burundi	Korea, Dem. People's Rep.	Somalia
Central African Republic	Liberia	South Sudan
Chad	Madagascar	Tanzania
Comoros	Malawi	Togo
Congo, Dem. Rep	Mali	Uganda
Eritrea	Mozambique	Zimbabwe
Ethiopia	Nepal	
Gambia, The	Niger	

Lower middle-income economies (52 countries)		
Armenia	Kiribati	Solomon Islands
Bangladesh	Kosovo	Sri Lanka
Bhutan	Kyrgyz Republic	Sudan
Bolivia	Lao PDR	Swaziland
Cabo Verde	Lesotho	Syrian Arab Republic
Cambodia	Mauritania	Tajikistan
Cameroon	Micronesia, Fed. Sts.	Timor-Leste
Congo, Rep.	Moldova	Tonga
Côte d'Ivoire	Mongolia	Tunisia
Djibouti	Morocco	Ukraine
Egypt, Arab Rep.	Myanmar	Uzbekistan
El Salvador	Nicaragua	Vanuatu
Ghana	Nigeria	Vietnam
Guatemala	Pakistan	West Bank and Gaza
Honduras	Papua New Guinea	Yemen, Rep.
India	Philippines	Zambia
Indonesia	Samoa	
Kenya	São Tomé and Principe	

Upper middle-income economies (56 countries)		
Albania	Ecuador	Montenegro
Algeria	Fiji	Namibia
American Samoa	Gabon	Palau
Angola	Georgia	Panama
Argentina	Grenada	Paraguay
Azerbaijan	Guyana	Peru
Belarus	Iran, Islamic Rep.	Romania
Belize	Iraq	Russian Federation
Bosnia and Herzegovina	Jamaica	Serbia

Table 40.1 (continued)

Upper middle-income economies (56 countries)		
Botswana	Jordan	South Africa
Brazil	Kazakhstan	St. Lucia
Bulgaria	Lebanon	St. Vincent and the Grenadines
China	Libya	Suriname
Colombia	Macedonia, FYR	Thailand
Costa Rica	Malaysia	Turkey
Cuba	Maldives	Turkmenistan
Dominica	Marshall Islands	Tuvalu
Dominican Republic	Mauritius	Venezuela, RB
Equatorial Guinea	Mexico	

Geographical areas are at times consolidated as cultural zones with economic or other indicators, such as the ASEAN countries or Latin America. These conglomerates of nations are quite diverse, and the clinical reality encountered by psychiatrists locally is far from assuming that there is cultural homogeneity. In the ASEAN conglomerate of ten Southeast Asian nations, psychiatric workforce disparities exist in spite of close geographic proximity, economic agreements, and some cultural parallels, with Singapore on one end with psychiatrists at an estimated rate of 3.48/100,000, Brunei Darussalam 3.31/100,000, Vietnam 0.91/100,000, Thailand 0.87/100,000, Malaysia 0.76/100,000, the Philippines 0.46/100,000, Indonesia 0.29/100,000, Myanmar 0.29/100,000, Cambodia 0.23/100,000, and Lao PDR 0.03/100,000. Latin America is equally diverse, with high-income countries like Uruguay and Chile having adequate numbers of psychiatrists, while poor countries like Bolivia and Ecuador have a psychiatric workforce of 1.06 and 1.09 per 100,000, respectively.

The most populous countries in the world, China and India, have estimated psychiatric workforce rates of 1.53/100,000 and 0.3/100,000, respectively. To put these statistics into a different perspective, approximately 10% of psychiatrists provide clinical care to two-thirds of the world population while also having to fulfill teaching and training responsibilities in their countries with low- and middle-income economies [2].

40.3 Survey Results and Comparison of Residency Training Across the World

The WHO and WPA Atlas Project [3] examined psychiatric education and training across the world by surveying eminent academics in over 100 countries. The survey response rate of 73 nations, or 38% of countries in the world, was lower than expected, but when supplemented with additional investigative outreach, it allows us to construct a partial picture of similarities and differences in psychiatric education worldwide. Although we know that 68% of countries in the world have psychiatry residency training programs, areas with low- and middle-income economies

have lower access to on-site training nationwide and sometimes even regionally. Less than half (47%) of African countries have psychiatry residency programs compared to almost all (94%) in the continent of Europe. Patel [4] underscores how the scarcity of psychiatrists is exacerbated by professional migratory practices, including relocation to wealthier countries and consolidation of services in megalopolises or metropolitan areas away from rural zones in great need. It is estimated that 90% of persons in need of mental health treatment in countries with low- and middle-income economies do not access psychiatric care [5].

Assessing quality of psychiatric training through questionnaires can be subjective, and the WHO Atlas survey methodology can be challenged as reductionist. Some findings, however, can be generalized when combing survey results with authors' personal experiences. For instance, it is well known that training in teaching and managerial skills and public health psychiatric education are virtually absent in underserved countries. Although many countries have a research requirement for psychiatry residents, this usually takes the form of or is substituted by a publication requirement (most of the time generating case reports, case series, or review articles), while virtually no formal training in research methodology takes place.

A descriptive comparison of psychiatry residency education in 10 countries with diverse economies in North and South America (the USA, Canada, Chile, Brazil), Europe (Sweden, Czech Republic, and the UK), and Asia (Korea, China, and India) found more similarities than differences in terms of duration of training, structure of clinical experiences, level of responsibility, autonomy of trainees, amount of classroom teaching, type of clinical supervision, and credentialing processes [6]. The WHO/WPA Atlas Project is the only extensive global report, but its conclusions need to be carefully examined not to over generalize. Psychiatry residency programs range from 1 to 4 years in duration in different parts of the world. Many are 3–4 years in duration. However, these numbers need to be examined in the context of prerequisites and post-residency field placement requirements. In India, for example, 4.5 years of medical school could be followed by 1 year of internship, 3 years of psychiatry, and 3 years of "senior residency," the latter necessary in order to qualify for an academic post. China, in comparison, in some locations, offers psychiatrists training of 1-year duration, while other formal academic centers have 5-year residency programs after 5 years of medical school. In both countries residents may continue on to complete lengthy PhD programs in areas such as psychotherapy or clinical research in order to qualify for academic positions or to balance their educational experience to attain clinical proficiency.

Most countries have accrediting organizations that are either independent or affiliated with the national component psychiatric societies. Examples of independent accrediting bodies include the Accreditation Council of Graduate Medical Education (www.acgme.org) [7] and the American Board of Psychiatry and Neurology (www.abpn.com) in the USA. The vast majority of countries in the world, and in particular those with low- and middle-income economies, rely on accreditation via the national ministry of health or the component psychiatric societies. Such is the case, for example, of the Indian Medical Association

(www.mciindia.org), the Chinese Society of Psychiatry, and the Royal College of Psychiatrists of Thailand (www.rcpsycht.org), to name just a few. The same national associations that conduct certification examinations and arrange continuing medical education seminars do accreditation of qualifications in virtually all of low- and middle-income countries. While most psychiatrists become licensed or certified by their national organizations, many countries lack an accrediting body responsible to unify and overview curricular quality and adequacy of clinical teaching and supervision. Generally, requirements for completion of psychiatry residency in most countries include oral and written examinations, submission of a thesis, formal extensive case protocol write-ups, and/or engaging in clinical research projects or coauthoring scientific publications.

Individual supervision occurs with lesser frequency and in a more haphazard way in countries or geographical zones where psychiatric residents face a high volume of cases. Supervision in this scenario takes on a case management, as needed approach rather than formally setting time aside to discuss pathogenesis, phenomenology, nosology, neurophysiology, genetic and molecular factors, diagnostic and pretreatment work-up, somatic treatment management, and psychotherapy theory and technique with clinical correlations, in a structured way, with regularly scheduled protected time for psychiatric residents and their supervisors.

Quality and frequency of classroom teaching is highly variable worldwide, even in countries with high-income economies. In order to bridge this educational gap that usually results from problems with inadequate faculty to student ratios, institutions in underserved areas are beginning to incorporate distance and computer-assisted technology to rethink and redesign classrooms better suited for the twenty-first century. Orchestration of this sort will be delineated later in this chapter when describing successful distance learning computer-assisted pilot programs.

Most psychiatry residents in the world have ample and varied clinical experiences. Those in countries with high-income economies learn at a pace that is less frenzied allowing for "elective" time during the last year of residency training usually resulting in strategic placement toward subspecialization. The apprenticeship didactic model seems to be favored universally over classroom teaching, regardless of location or resources, perhaps because it may be more conducive to effective learning.

Although the WPA has made efforts to standardize postgraduate education in psychiatry (in this chapter referred to as psychiatry residency education), disparities remain even within continents and culturally consonant geographical zones of the world. Countries challenged by low- and middle-income economies face the greatest difficulties. Core training curricula for psychiatry are widely available in extensive documents through the WPA website section on Education. The official WPA policy on undergraduate and residency education was approved in the 2011 general assembly meeting (to access documents, see: http://www.wpanet.org/detail.php?section_id=8&content_id=1003). These multi-authored documents/collaborations synthesize and incorporate directives from standards of training as delineated in documents from the Accreditation Council of Graduate Medical Education (ACGME) in the USA and the European framework for competencies in psychiatry,

Union Européenne des Médecins Specialistes (UEMS) [8]. The 2011 undergraduate and graduate education template is currently being revised and updated by a subcommittee of the WPA Education in Psychiatry Section.

40.4 Psychiatry and Culture: Implications for Educating Residents

Residency training in psychiatry in different parts of the world may vary in length and content, but often fails to focus on areas of knowledge that will be particularly important in the work of psychiatrists in underserved areas. Psychiatric education is influenced not only by resource availability but also substantially by culture. Psychiatry education is commonly devoid of content regarding the application of the cultural and transcultural psychiatric knowledge base in the design of models of healthcare delivery [1].

In order to reduce the burden of disease caused by mental disorders in low- and middle-income countries [9], educators need to think beyond the paradigm of expansion of services and subspecialization and pay close attention to cultural determinants of disease onset, course, and treatment outcomes as they may relate to community psychiatry and public health. The biopsychosocial model [10] postulated that the inadequacy of psychiatry as a specialty stems from a problem that affects all of medicine, that is, that the biomedical paradigm is not sufficient to properly care for patients. For over 40 years since the biopsychosocial model was proposed, psychosocial determinants have been expanded to include diverse cultural aspects [11, 12] such as understanding of illness, willingness to seek treatment, shared attributes, learned attitudes, belief and value systems, and the impact that these have on the therapeutic alliance ultimately determining treatment adherence [13] and affecting illness course.

Cultural diversity needs to be understood and taught beyond the rogue memorization of relatively rare and exotic "culture-bound syndromes" or mechanically constructed generic cultural formulations. Residents need to learn that language affinity between clinician and patient is just the beginning of the process of cultural attunement. Nuances such as symbolic meaning that may be alien to the clinicians' way of thinking, idiosyncratic ways of communicating distress, and identifying idioms of distress through detailed inquiry and neutral curiosity need to be addressed in the clinical supervision of psychiatric residents. Every clinical interaction could be construed as a transcultural exchange, even when cultural similarities seem to outweigh differences.

Finally, educational efforts in residency training should reflect the importance of incorporating cultural aspects of religion and spirituality in the individual care of patients worldwide. Psychiatric residents should learn how to form treatment alliances with spiritual advisers, elders, and community religious leaders. Although all training is implicitly culturally based, guidance on making liaisons with community religious organizations and advisers should be made explicit as part of the psychiatric residents' formative experiences. As an example, consider the following elective

rotation for fourth year psychiatry residents at the Metropolitan AIDS Program offered by a consultation and liaison service aiming to improve both competency and public health aspects of HIV psychiatric care.

40.5 The Metropolitan AIDS Program Liaison with Religious Community Leaders

When the AIDS epidemic decimated East Harlem in New York City in the 1980s, religious leaders were instrumental in the care of affected families. East Harlem is a large low-income community within an even larger high-income city, with mortality rates and poverty related multimorbidities greater to that of Bangladesh [14]. A liaison between a consultation psychiatry teaching service, the Metropolitan AIDS Program [15], and St. Cecilia's Catholic Church under the leadership of Sister Regina Burns mobilized the creation of the East Harlem Interfaith, a conglomerate of over 100 religious institutions of different denominations organized as an NGO to serve this large segment of disenfranchised individuals who were almost all recent immigrants from the Caribbean, Central America, and Africa. Psychiatric residents on the HIV Psychiatry elective rotation had the opportunity to co-lead psychotherapy support groups and train religious leaders on the psychiatric aspects of HIV infection, thus providing much needed care for the grieving families and patients without access to conventional mental healthcare. One of the interventions included encouraging young adult AIDS orphans and parents of the deceased to volunteer in hospitals, nursing homes, and hospice services to comfort those affected by the pandemic. No more than a few psychiatrists were, in this fashion, able to care for thousands of individuals and effectively combat stigma and discrimination by sharing and delegating care to religious leaders and community members.

40.6 Psychiatry Residency Education: A Competency-Based Approach

Competency-based learning has dominated the academic climate of residency training in countries with high-income economies with top-ranked university medical centers. Using the highest training standards is a way to ensure that the mental health system develops psychiatrists with the highest expertise. This educational model assumes that psychiatrists will be skilled to treat most persons with mental disorders. This would include expertise in the treatment of mood disorders, anxiety disorders, schizophrenia, neurocognitive disorders, and substance use disorders. Additionally, competency is achieved targeting comorbid psychiatric illnesses that compound disability in persons with medical disorders such as heart disease, diabetes, infectious diseases, and cancer. The competency-based model assumes that the psychiatric workforce will have expertise in treating all mental disorders and that sufficient time will be allocated by psychiatrists to research, administrative, and didactic activities in addition to their broad clinical duties.

The competency-based model "promotes learner centredness and focuses on outcomes and abilities" [16]. Standards for high-quality healthcare practices are important to stimulate and encourage academic development. As pedagogic thinking continues to evolve, the ACGME Milestones Project [17] adjusted competency-based training into a phase-specific developmental framework. The project, a joint initiative of the ACGME and the ABPN, provides a framework for assessment of the development of residents in key dimensions of the elements of 22 psychiatric competencies. Milestones are "knowledge, skills, attitudes, and other attributes for each of the competencies, organized in a developmental framework from less to more advanced. They are descriptors and targets for resident performance as residents progress from entry into residency through graduation" [17].

Applying a competency-based learning model in countries with low- and middle-income economies can be challenging and often encounters resistance. Competency in one country is not the same as in any other country. Competencies should be targeted to system and clinical needs rather than overall general global approaches.

Pedagogic accountability needs to be a flexible and contained within a fluid state not to overwhelm teachers and residents in underserved areas. Patient care comes first, often at the expense of conscientious teaching methods, as residents struggle to balance ethical principles of beneficence and nonmaleficence with attending to their educational needs. Skillful faculty members in busy hospitals and clinics teach best through clinical demonstrations, where teamwork is presented as a way to enhance clinical care, with patients feeling empowered when realizing they are contributing to the educational formation of psychiatric residents while capitalizing on being cared for by a group of experts rather than by an individual doctor.

Kigozi and Ssebunnya [18] refer to the "multiplier role of psychiatrists" in challenged geographical areas. The multiplier effect includes, in addition to clinical management and consultation, influencing mobilization of resources, generating service utilization demands, operating as an active liaison with primary care providers, and taking on public health leadership responsibilities. We may add to this construct of multiplicity of tasks the duty to adequately train in a socially responsible way the next generation of psychiatric clinicians. A public health emphasis may be more prudent in the clinical care of persons in countries with low- and middle-income economies. An educational model that expands care from the individual to the community would be ethically appropriate to match resources with high burden of disease.

40.7 Psychiatric Education in Low- and Middle-Income Countries: A Public Health Approach

A public health emphasis, which assumes that psychiatrists will spend a significant amount of time in overseeing the mental health services with only a minimal amount of direct clinical service, is the model proposed by Patel [4] when pondering about how to address the global burden of disease. Patel states: "a psychiatrist (in countries with low and middle income economies) must be primarily a public health practitioner rather than a clinician." Relinquishing the traditional role of a

psychiatrist means to renounce spending most of the work effort from providing direct clinical care to a selected few to engage in task-shifting of resources and a redistribution of care among health workforce teams. These health teams are to be composed of diverse workers who could deliver specific tasks under the guidance of or in collaboration with psychiatrists.

While traditional liaison psychiatry education includes teaching residents how to navigate through complex hospital systems and collaborate with fellow physicians, the public health educational model must include guiding residents to learn how to interact with community healthcare workers and policymakers.

Integration of mental health care within primary care has been proven to be an effective way to streamline clinical services, lowering cost and increasing treatment adherence [19]. Although this model is usually taught in psychiatry residency within the constraints of consultation and liaison psychiatry rotations and educational experiences in the psychosomatic medicine service, more time should be dedicated to demonstrate its relevance and allow residents to experience firsthand how to operationalize provision of outpatient care in a collaborative way. It would be sensible for psychiatry residents in countries with low- and middle-income economies, for example, to spend ideally an entire year providing supervised outpatient mental health services on-site in primary care clinics or community health centers.

Take as a clinical and academic collaborative example the challenge of provision of care for diabetic patients with multisystem organ failure resulting from treatment nonadherence. A psychiatric consultation for such patients may demonstrate psychosocial determinants of nonadherence, such as comorbid depression, substance use disorders, a history of adverse childhood experiences with adult retraumatization, avoidant attachments with a tendency toward excessive self-reliance, inability to engage in trusting alliances with healthcare providers, and inadequate understanding of illness processes. Such patients would resist a referral to a mental health clinic but accept being seen by a psychiatrist in consultation in a primary care setting. The consultation process could help the primary care provider understand the multiple determinants of nonadherence and shift the therapeutic alliance in ways that would promote engagement of the patient in adequate medical care while also minimizing psychological distress. The primary care doctor could be supervised to prescribe psychotropic medications and conduct supportive psychotherapy, behavioral or motivational interviewing interventions. The psychiatric resident, under supervision, could take on the role of diagnostician, educator, and collaborator, while the primary care doctor retains the responsibility of clinical care. Teaching residents how to orchestrate care in this fashion could maximize the utilization of resources effectively balancing ethical principles of beneficence and social justice.

40.8 The Interface of Psychiatry Education with NGOs and the Media

Another opportunity for task-shifting interventions as part of the public health approach to psychiatry education would be to encourage residency programs to work with government officials and NGOs to combat stigma and raise awareness of

mental health. The work of Amer Siddiq Bin Amer Nordin at the University of Malaya Center of Addiction Sciences (UMCAS) could be used as an example. Almost single-handedly, this early career psychiatrist and educator took on the challenge of promoting smoking cessation and combating addiction to opioids as top public health priorities in Malaysia and neighboring countries. Lobbying to establish opioid agonist treatment centers against conservative attitudes, and teaching harm reduction and motivational interviewing to psychiatric residents, is having a positive transformative impact on reducing the burden of addiction in Malaysian society since UMCAS was established in 2009. Using social media effectively and frequent appearances in pree ss conferences in national television helped his team transform antiquated government policies of prohibitionism and fatalistic societal attitudes reframing addiction as an illness and providing access to proper care. This is being accomplished by cementing collaborations with physicians of all specialties locally in Malaysia and under the senior mentorship of psychiatrists from New Zealand, with university support, and through aggressive grant writing and fundraising while maintaining focus on tailoring interventions according to public health needs. Although addiction psychiatry is not formally established as a subspecialty in Malaysia, a small number of faculty members, mostly at the University of Malaya (UM) and Universiti Kebangsaan Malaysia (UKM), have inspired residents to liaise with appropriate agencies as a way to facilitate awareness and access to treatmene t, creating an impactful and innovative educational intervention of community involvement beyond classrooms, clinics, and hospital ward.

Ruiz and Bhugra [20] accurately observed that cultural syncretism and globalization may facilitate easier exchanges of information resulting in more educated societies that place demands on their governments and policymakers to improve mental health services. Similarly, globalization can unify the world psychiatric community via media expansion and information exchange across borde ers.

40.9 A Combined Educational Approach for New Models of Healthcare Delivery

The authors take the position that both the compete ency-based and public health pedagogical approaches are not mutually exclusive and can inform curricular revisions and design and improve clinical supervision of psychiatric residents in countries with low- and middle-income economies. A combined competency and public health model builds on a pyramidal approach in which psychiatrists still are quite active clinically, but focus their attention only on the most complex cases, with primary care and other mental health clinicians carrying the burden of care. In this regard it would be similar to a disease management program that might be implemented for a medical disorder, with only the most complicated cases going to the subspecialist, in this case a psychiatrist directly managing complex patients that require additional clinical expertise.

This cost-effective model proposed by Saraceno et al. [21] integrates mental health services within primary care, also dissipating stigma and minimizing human

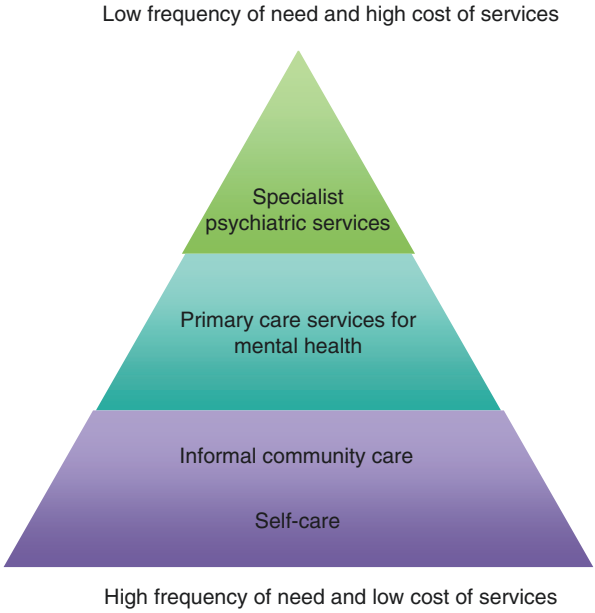

Fig. 40.2 WHO service organization pyramid for maximizing mental health services

rights violations that may occur in psychiatric hospitals by providing most care in clinics and day treatment centers. The implications for psychiatric education include teaching residents to collaborate with joint consultations, intervention, and liaisons with primary care clinicians, NGOs, community members, and non-clinician healthcare workers. The pyramidal system of the WHO model of provision of mental health services takes into account not only coordination of care with the appropriate service providers but also factors such as cost and frequency and the type of services provided, with low cost/high frequency at one end of the spectrum and high cost/low frequency at the other (see Fig. 40.2).

In the following sections, the authors will describe zonal and continental clinical and didactic practices and provide regional examples of successful ongoing educational initiatives in diverse areas of the world, applying diverse models of collaborative care and competency-based approaches.

40.10 Psychiatry Education in Asia

The most populous continent in the world may face the worst socioeconomic and mental health challenges [20]. Unique disadvantages in Asia include the radical marginalization of rural areas, as city-states and megalopolises thrive and proliferate while the rural majority struggles in poverty creating major national cultural disparities that challenge the healthcare system and academic medicine.

A comparison of residency training across the Asia-Pacific region [22] details how these populous and diverse countries structure psychiatric education.

Regionally, most programs have adequate curricular content. However, the paucity of programs reflects how underserved psychiatry is as a profession in Asia. For example, there are 9 training programs in Thailand, 12 in the Philippines, 9 in Indonesia, 2 in Malaysia and 16 in China [22, 23]. While there is an international perception that many Asian psychiatrists defect after seeking subspecialty training in countries with high-income economies, most actually return to or remain in their countries of origin to become the de facto subspecialists in academic medical centers. This is not the case with psychiatrists from the Philippines, India, and Pakistan [24] who are more frequently recruited to work and stay in high-income countries.

Perceived academic deficiencies in countries with low- and middle-income economies in Asia include the scarcity of subspecialty training opportunities and a general shortage of staff, making harmonizing clinical care with education onerous. Specifically, while most aspects of general psychiatric practice are adequately covered by most curricula, psychotherapy training is not. Most programs provide basic training in cognitive-behavioral therapy, but few formally address training in other psychotherapy treatment modalities such as supportive, interpersonal, dialectic behavioral, group, marital, family, and psychodynamic psychotherapies.

A recent curricular review of all psychiatry training sites in Malaysia [25] concluded with the following recommendations:

1. Minimize paperwork, time spent doing transcription of sessions, and psychotherapy process notes. A consensus was reached that too much valuable time is spent having trainees submit extensive written reports of their cases and going over transcripts of sessions in individual supervision.
2. Consider group supervision and supervision in tandem with more than one trainee at the same time. When there is a scarcity of supervisors, supervision can be effectively conducted when more than one trainee meet in psychotherapy supervision and present cases in tandem. Mutual learning is encouraged, and trainees benefit from participating in intensive supervision with their peers.
3. Use video recordings for self-assessment and supervision. Audio recording of sessions could be easily substituted by video recording. After proper informed consent is obtained from patients, reviewing videos in supervision could be more conducive to learning.
4. Integrate theory with technique in all treatment settings. Psychological clinical theories (in particular psychodynamic) can be obtuse and verbose. Effort should be made to have supervisors help trainees conduct brief formulations at the bedside in the general hospital and in clinical rounds in all treatment settings, to make formulations logical and purposeful.
5. Expand training to include family, couple, marital, and group psychotherapy modalities. Trainees should have exposure to implementation of CBT, supportive and uncovering-psychodynamic technique not only for individual psychotherapy but also to treat dyads and family units. Group psychotherapy with the medically ill is an effective way to provide services, and trainees should have this supervised experience.
6. Create a targeted annotated bibliography of core psychotherapy technique readings to help both trainees and supervisors do theory and practice clinical correlations.

International academic partnering using videoconferencing has been widely used in Asia to bridge training gaps of psychiatric residents [26]. Examples include collaboration between the University of Colorado School of Medicine and the University of Health Sciences in Cambodia [27, 28] in the form of monthly case conferences and 2- and 4-year training programs offering certification in psychoanalytic psychotherapy through the China American Psychoanalytic Alliance (CAPA). CAPA, started by Elise Snyder and Ubaldo Leli in the USA after academic exchanges in Chengdu, formally established training for qualified mental health professionals in China including psychiatrists [29]. Training currently spans over 25 Chinese cities, with a faculty of over 150 volunteer psychoanalysts and psychodynamic psychotherapists teaching using videoconference technologies. Forty students were accepted for the 2015 incoming class, and hundreds have graduated from the programs since 2008.

A one-semester advanced psychodynamic psychotherapy training course was specifically tailored for psychiatric residents and early career psychiatrists in ASEAN countries. This collaboration between the USA and Thailand and Malaysia and Indonesia combines on-site with videoconferencing and computer-assisted learning. It is sponsored by the WPA sections on education, psychotherapy, and psychoanalysis in psychiatry and orchestrated with the national psychiatric societies of these countries. This initiative will be described in some detail next in this chapter and may be considered in other regions of the world as a model to help alleviate psychotherapy training educational deficiencies of psychiatric residents [25, 30].

40.11 WPA Intersectional Educational Liaison with ASEAN Countries

Globally, psychiatrists and psychiatric residents advance their knowledge and supplement training through continuing medical education activities at scientific congresses. Unfortunately, few international and national conferences allocate protected time and space for residents and early career psychiatrists. The WPA makes an effort to be inclusive of trainees promoting mentorship and career development in regional, zonal, and international and world congresses. When offered, full-day or half-day psychotherapy training workshops fill to capacity. Even in countries with high-income economies with rigorous curricular guidelines that require residents to become knowledgeable and proficient of psychotherapy treatments, a desire exists to supplement training with additional educational activities. While over two-third of residents in the USA express the wish to obtain additional psychotherapy training, fewer than 5% pursue formal advanced psychotherapy postgraduate training [31]. It could well be that a 4-year residency curriculum, even under optimal conditions, is not sufficient to provide residents with a secure knowledge base and practical skills set, given the complex nature and variety of psychotherapy modalities. But even in countries with high-income economies, existing psychotherapy training seems insufficient to psychiatry residents. In an effort to address this knowledge and skills set gap in psychiatry education in countries with low- and middle-income

economies, where deficient psychotherapy training is accentuated, a WPA intersectional pilot project was designed in consultation with prominent psychiatrists from ASEAN countries.

One of the authors (C.A.) conducted a series of full-day advanced psychodynamic psychotherapy workshops on-site at meetings sponsored by the Indonesian Psychiatric Association Psychotherapy Section in Jakarta and Surabaya, the Malaysian Psychiatric Association in Kuala Lumpur, and the Royal College of Psychiatrists in Bangkok, between 2012 and 2014. These workshops were designed to be inclusive, collaborative, and interactive. The host psychiatric societies selected senior local prominent psychiatrists to run the workshop sections or modules according to the experts' areas of interest and experience. Table 40.2 describes a typical full-day workshop structure. The workshops were designed to emphasize clinical correlations and applicability of psychodynamic thinking in ordinary psychiatric practice in a variety of settings. Attendance ranged from 35 to 50 participants, a manageable number to maintain didactic group cohesion. At the conclusion of the process of planning, design, and implementation of the workshops, the workshop co-leaders were invited to join the WPA sections on psychoanalysis in psychiatry and psychotherapy. To stimulate continuity, a one-semester follow-up

Table 40.2 Advanced psychodynamic psychotherapy workshop model

Clinical workshop: basic principles and applications of psychodynamic psychotherapy—a clinical workshop for the general psychiatrist[a]	
Time	Activity
08:00–09:00	Introduction, meeting and greeting
09:00–09:45	Overview Lecture: *Basic principles of psychodynamic psychotherapy-international perspectives*
09:45–10:00	Q&A
10:00–10:15	Break
10:15–11:00	Clinical Module 1: *The psychodynamics of psychopharmacology-how psychoanalytic theory informs brief medication management visits*
11:00–12:00	Clinical Correlations; Q&A
12:00–13:00	Lunch with small group discussions
13:00–13:30	Clinical Module 2: *Psychotherapy with persons with self-injurious behaviors*
13:30–14:00	Clinical Correlations; Q&A
14:00–14:30	Clinical Module 3: *Psychotherapy challenges in addiction psychiatry*
14:30–15:00	Clinical Correlations; Q&A
15:00–15:15	Break
15:15–15:45	Clinical Module 4: *Psychotherapy challenges in the treatment of personality disorders*
15:45–16:15	Clinical Correlations; Q&A
16:15–16:45	Clinical Module 5: *Countertransference in psychosomatic medicine clinical settings*
16:45–17:00	Clinical Correlations; Q&A; Summation

[a]Each module is co-facilitated by a WPA scholar and a local prominent expert in the relevant field

advanced online course was designed and conducted during the same academic year for each of the three countries.

The 6-month advanced psychodynamic psychotherapy courses created a virtual classroom for peer and thematic supervision, with a core curriculum of 40 selected articles and textbook chapters, a moderated email list serve discussion forum in combination with on-site learning. Classes took place every other week for 90 min over videoconference, and the 10th and last class for each group took place in person in the capital city of the host country at the same time and place of the meetings of the national psychiatric societies. Courses were conducted in Thailand in 2014, Malaysia in 2015, and Indonesia in 2016. Each course had two or three co-teachers and eight students. Co-teachers were César Alfonso (USA), Rasmon Kalayasiri (Thailand), Hazli Zakaria and Aida Adlan (Malaysia), and Petrin Redayani Lukman and Sylvia Detri Elvira (Indonesia). The local co-teachers selected one student-coordinator for each group: Natchanan Charatcharungkiat (Thailand), Najwa Hanim Rosli (Malaysia), and Rizky Aniza Winanda (Indonesia). Each course was limited to eight students, and the national psychiatric societies monitored the competitive application and selection process.

Classes were clinically focused (case-conference style), each student being responsible to present a psychotherapy case concisely in writing and orally, with appropriate formulations and questions for discussion. Readings were matched and assigned according to the clinical relevance to each case, and students were required to comment on theory and technique. Classes were conducted bilingually in English and Thai, Bahasa Indonesian, and Bahasa Malay, with the student-coordinator serving as translator while trying to maintain English as the common language. Requesting informed consent, disguising identifying information, using secure videoconferencing technologies, and encrypting files protected patient confidentiality.

The aims of the intersectional WPA courses were to specifically develop the psychotherapy skills of a core group of young academic psychiatrists to improve not only practice, but more importantly, supervisory skills. Follow-up workshops are being developed to further train the graduates to embrace their supervision responsibilities with mastery. The first WPA intersectional workshop on psychotherapy supervision in 2017 in Malang, East Java will include program graduates and participants from Malaysia and Indonesia involved in psychiatric education.

Two of the graduates from the Thailand course, Warut Aunjitsakul and Kanthee Anantapong, now early career psychiatrists at Prince of Songhkla University, are organizing a 1-year-long psychotherapy journal club over a list serve, for an in-depth review of 12 recent articles published in *Psychodynamic Psychiatry*. Aunjitsakul and Anantapong have coordinated a list serve inclusive of all graduates from the three countries. In addition, they have invited the journal articles authors and the journal editors to mentor and participate in the list serve discussion along with the students throughout the year. The core group of approximately 30 graduates and co-teachers are becoming, in essence, the next generation of psychodynamic psychotherapy supervisors in Southeast Asia, a region where conventional psychotherapy training institutes do not exist.

Innovations based on international collaborations and inclusiveness, emphasizing cultural adaptations, mentoring, and continuity, are far more effective than merely inviting guest speakers from countries with high-income economies to lecture at conferences in countries with low- and middle-income economies. The educational aim, rather than impress a star-struck audience that passively reacts with awe and reverence, empowers and inspires instead the local talent to polish existing skills and mobilize courage to create time to educate eager and willing residents and teach them how to teach and supervise. The long-term impact of these initiatives is yet to be examined. So far, approximately a dozen psychiatrists from ASEAN countries have become active in WPA psychotherapy and PIP sections and participated in workshops and symposia in WPA and meetings of affiliated societies in Hong Kong, Taipei, Florence, and Berlin.

40.12 Psychiatry Education and Advanced Psychotherapy Training in the Islamic Republic of Iran

The Islamic Republic of Iran is a West Asian country with a population close to 80 million. With millennia of important medical contributions and a strong organized psychiatric community, Persia/Iran has a psychotherapy tradition that dates back to the contributions of Avicenna and Zakariyya al-Razi, who professed speech medicine and soul treatment as a complement to somatic treatments. Sanctions against Iran from 1979 to 2016 caused international discord and marginalization of academic medicine from other countries, with only recently reconnecting with the mainstream through outreach over videoconferencing and participation in few congresses (Sanati and Tavakoli, personal communication, 2016). We would like to highlight one educational program that could serve as a model in other countries.

Most of the country's 1700 psychiatrists practice in Tehran, with 110 in Isfahan, 110 in Mashhad, and 100 in Shiraz (Moinalghorabai, personal communication, 2016). There are 14 university-based psychiatry residency training programs. Tehran University of Medical Sciences (TUMS) currently has 65 residents and 6 psychotherapy fellows. It is the TUMS psychotherapy fellowship offered as an extension of psychiatry residency that merits special attention, as it could be easily replicated in other countries.

The TUMS psychotherapy fellowship is quite competitive and rigorous. An effort is made to accept psychiatric trainees from diverse parts of Iran with the intention of grooming them as the next generation of psychotherapy residency training supervisors. The course runs for 18 consecutive months and allows psychiatric residents to move along the spectrum of observation, assistance, and independent practice of psychodynamic psychotherapy, cognitive-behavioral therapy, group psychotherapy, family therapy, spiritual psychotherapy (including 12-step programs), and supportive psychotherapy. The treatment settings include inpatient and psychiatric clinics (for 17 months), concurrent with psychosomatic medicine service (100 h), child and adolescent psychiatry clinic (200 h), and addiction study center (100 h), followed by other elective settings (one full-time month).

At the completion of the fellowship, the residents participate in 400 individual psychodynamic sessions, 220 CBT sessions, 70 schema therapy sessions, 70 psychodynamic group psychotherapy sessions, 42 CBT group psychotherapy sessions, 60 family therapy sessions, 1-month equivalency of spiritual therapies/12-step groups, 24 sex therapy sessions, and 30 psychoeducation sessions.

The didactic component uses core readings from 12 books (10 in English and 2 in Farsi) and 3 main journals: *International Journal of Psychoanalysis, American Journal of Psychotherapy, and International Journal of Psychotherapy*. Individual teachers have the freedom to assign additional readings, and the amount of material covered is extraordinary considering the 18-month duration of the fellowship. Trainees read primary sources beyond textbook descriptions. For example, when learning psychodynamic psychotherapy, they study papers and books by Freud, Klein, Fairbairn, Winnicott, Balint, Hartmann, Mahler, Jacobson, Spitz, Kernberg, Sandler, Mitchell, Lacan, Bowlby, and Adler, among others. The psychotherapy fellows are also expected to teach psychiatry residents, psychology students, and medical students. Rooms with one-way mirror or video cameras are used to observe and supervise in vivo. The program assessment method incorporates trainee satisfaction and feedback, level of satisfaction of the psychiatry departments in universities that employ the graduates and standardized faculty evaluations.

The TUMS psychotherapy fellowship serves as an international model for rigorous training of psychiatry residents who are expected to take on teaching and supervisory responsibilities. Some of the senior faculty members who trained in the UK, such as Mohammad Sanati and Mahdieh Moinalghorabai, are now mentoring the next generation of Iranian psychiatrists to become psychotherapy experts and educators, emphasizing the delivery of combined psychotherapy treatments as the highest standard of clinical care.

40.13 Psychiatry Education in Arab League Countries

The Arab league is an international consortium of 22 countries with a total population of over 400 million covering the regional zone of Arabia, North Africa, and the Horn of Africa. As with the case of ASEAN countries previously discussed in this chapter, while economic and political factors unify the region, other cultural aspects may be more relevant to the clinical and educational needs of psychiatrists in these diverse countries, as educational efforts may need to be refocused from zonal to national factors to fulfill the public health needs of the individual nations. Six of the 22 countries in the region have high-income economies averaging two to five psychiatrists per 100,000 population rate (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and UAE). In contrast, countries like Djibouti and Comoros have no psychiatrists, and the majority of countries in the Arab league—Egypt, Iraq, Jordan, Lebanon, Libya, Mauritania, Morocco, Palestine, Somalia, Sudan, Syria, and Yemen—have less than 1/100,000 psychiatrists. Algeria and Tunisia have a larger psychiatric healthcare force with a rate of 2.29 and 2.58/100,000, respectively. In most Arab league countries, general practitioners and non-physician clinicians with some

mental health training provide the majority of care for persons with mental disorders. Skills enhancement training programs for non-physicians in primary care constitute the main public health initiatives in this geographical zone. In most Arab countries, physicians do not interact with traditional healers. Some interaction exists in Jordan, and only in Saudi Arabia have they become part of the clinical management healthcare team [32].

Egypt has 17 departments of psychiatry and within these 7 neuropsychiatry divisions. Psychiatry residents complete a thesis and written, oral, and clinical examinations as requirements for certification [33]. Professor Ahmed Okasha, who led the WPA as President from 2002–2005, has inspired Egyptian psychiatric residents to apply the biopsychosocial model in their cultural formulations and specialize in treating persons with complex disorders who would not receive adequate care by nonpsychiatric clinicians while collaborating with primary care doctors to optimize care of the mentally ill.

In the Kingdom of Saudi Arabia, there are three 4-year programs in Riyadh, Jeddah, and Dammam. Each of these programs graduates six to ten residents per year. Although there are eight formal departments of psychiatry at universities in Saudi Arabia, only three have psychiatry residency programs. Subspecialty training for Saudi psychiatrists only happens abroad, usually in the UK, the USA, and Canada. There are two child and adolescent psychiatry fellowship programs in Riyadh. Efforts exist to develop consultation and liaison and addiction specialty training in Saudi Arabia, taking into account the unique cultural experiences of this country of contrasts [34].

The Arab league countries face psychosocial stressors and a high allostatic load related to political unrest, war, terrorism, and religious conflicts [32, 35]. The WPA should continue to be attentive to facilitate educational collaborations with this large underserved region of the world.

One bright spot in the region is the state of Qatar. Qatar is a rapidly transforming economy with one of the highest GNI per capita in the world (data.worldbank.org). Healthcare is highly centralized with Hamad Medical City (HMC) providing more than 90% of healthcare delivery in the nation. The Department of Psychiatry at HMC has the only Psychiatry Residency Training Program in the country, with six to seven psychiatrists graduating every year. The Accreditation Council for Graduate Medical Education-International (ACGME-I) has recently accredited this program, the second program to receive such accreditation after Duke-National University of Singapore. The HMC Program also provides specialization in two subspecialties: consultation/liaison and geriatric psychiatry. HMC attracts applicants not only from the state of Qatar, but several other countries in the region. Residents enrolled in 2016 included physicians from Qatar, Bahrain, Saudi Arabia, Egypt, Libya, Sudan, Lebanon, Syria, Jordan, Palestine, Iraq, and Pakistan. The HMC Program takes advantage of faculty affiliated with Weill Cornell Medicine in Qatar and Sidra Medical and Research Center in Doha. In addition to excellence in mental healthcare delivery, the Program provides training both in psychiatry education and research. The Arab Board of Psychiatry approved the HMC Program. Negotiations are also underway for approval by the American Board of Psychiatry and Neurology-International ABPN-I.

40.14 A Psychoanalytic Psychotherapy Program Integrated Within the University of Marrakech

Psychoanalysis in North Africa is linked to the history of Morocco and that of France. Jalil Bennani, co-chair of the WPA psychoanalysis in psychiatry section, has been at the forefront of the interdisciplinary cross-fertilization between psychoanalysis and psychiatry within the Moroccan cultural context. Bennani and colleagues [36, 37] implemented a university-based psychoanalysis certification course at The Université Cadi Ayyad Medical School in Marrakech. This program offers a 2-year, 10-module, and 200-h course for psychiatrists, psychologists, and trainees in psychiatry and child psychiatry. After participating in a comprehensive theoretical and practical psychoanalytic curriculum, students are able to improve their overall skills as psychotherapists.

Psychiatrists in Morocco, Bennani proposes, should derive depth in understanding the psychosocial and developmental antecedents of psychopathology and maladaptive behaviors, a necessary skill to achieve competence and comfort as physicians caring for persons with mental disorders in underserved areas. The course uses classroom teaching, video technology, and individual and group supervision to enhance the didactic pedagogic practice. The implementation of a university-based brief psychoanalytic curriculum adapted for the clinical needs of Moroccan patients is well suited to advance the education of psychiatry residents in that country.

40.15 Psychiatry Education in Africa

Africa, carrying one quarter of the global burden of disease [38], faces a public mental health crisis, where burden of disease, morbidity, and mortality are the highest of any continent in the world. Psychiatry education in this context is particularly challenging as more than half of the continent lacks postgraduate educational programs, while undergraduate education in psychiatry is geared toward primary care medicine. Task-sharing of mental health services includes collaborating with community health workers, traditional healers, and nursing professionals [39]. e-learning is currently available for non-physician clinicians in Zambia and Ghana [40].

Sub-Saharan Africa is a world region where physicians frequently relocate migrating to other continents, usually because of compromised social conditions including lack of personal freedom and safety [41, 42]. Currently, 28% of African-born physicians live outside the continent. In a survey of close to a thousand medical students from South Africa, the Democratic Republic of Congo, Kenya, Nigeria, Tanzania, and Uganda, 40% stated plans to train and stay abroad. 5% of medical students in Africa wish to pursue psychiatry training, but given that many African countries do not have residency programs, forced migration may become inevitable to them [43].

Understanding the cultural diversity of African countries is a major task. Cultural overgeneralizations and oversights create obstacles that clash with the agendas of

designers of core competencies for mental healthcare in Africa. Nevertheless, experts generally agree that community-based services in partnerships with centers of excellence yield the best results [44]. International partnerships with countries with high-income economies can be effective in lowering the global burden of disease in Africa and improving psychiatric education.

Malawi is a small country with an estimated population of 17 million. Felix Kauye is the only Malawian psychiatrist serving the nation [45]. An NGO with teaching support from Edinburgh, the Scotland-Malawi Mental Health Education Project (http://www.smmhep.org.uk/), helped establish a master's course in clinical psychiatry at the University of Malawi College of Medicine, with three residents currently enrolled in training. Psychiatry training consists of 2 years in Malawi followed by 2 years at the University of Cape Town in South Africa under the supervision of Peter Milligan. The entire country of Malawi is served by three tertiary mental health facilities staffed by a handful of medical officers and 20 psychiatric nurses. Psychiatrists from Scotland and Norway have been visiting Malawi since 2007 to train and teach medical students in the classroom and at Zomba Mental Hospital [46]. Michigan State University in the USA offers their residents the opportunity to spend elective time on rotation in Malawi and Uganda as part of an emphasis on public sector psychiatry.

Ethiopia is a populous country with over 90 million people. Beginning in 2003 an international collaboration with Canada resulted in the creation of a psychiatry residency training program at the Addis Ababa University. The University of Toronto sends faculty and residents to spend 1-month blocks of time in Addis Ababa with education and sustainability as primary goals together with curricular and clinical development. Between 2003 and 2009, the psychiatric workforce in Ethiopia grew from 11 to 34, and a model was created to integrate mental health services within primary care [47]. The Addis Ababa residency program carefully avoided exporting Canadian curricula and ways of teaching in toto with the collaboration favoring cultural adaptation with particular emphasis on psychosocial determinants of health and illness as it pertains to the complex and diverse population of East Africa.

The University of Pennsylvania has maintained a close collaboration with the Government of Botswana and the University of Botswana, beginning in 2001. The Botswana University of Pennsylvania Partnership began focusing on HIV clinical care, education, and research and developed into an extensive program supporting medical student rotations and internal medicine resident rotations. The partnership now comprises 80 physicians and staff in Botswana. Most recently, the program expanded to include psychiatry because of the need to support University of Botswana Psychiatry faculty in educating medical students as their first cohort of students began the psychiatry clerkship. A group of University of Pennsylvania Psychiatry faculty rotated through the University of Botswana, teaching medical students and helping to support curriculum planning and long-range planning for graduate medical education in psychiatry. Simultaneously, a variety of psychiatry research projects were initiated and are ongoing.

40.16 Psychiatry Education in Latin America

Latin America is composed of 20 countries and many other smaller territories with over 600 million inhabitants, served by 20,000 psychiatrists. Latin America spans the largest area of income inequality in the world [48], with three countries with high-income economies: Uruguay, Chile, and Trinidad and Tobago. Argentina and Venezuela had high-income economies until 2014, having faced economic crises thereafter. Other commonwealth and non-sovereign states and territories in the Caribbean, such as Puerto Rico, the Cayman Islands, the Turks and Caicos, St. Maarten, Aruba, and the US Virgin Islands, also have high-income economies. Psychiatry in Latin America has a strong tradition of emphasizing the importance of psychotherapy training, in particular psychoanalysis and psychodynamic psychotherapy [49] and cultural dimensions of health and illness [50].

In Brazil where there are 4.8 psychiatrists per 100,000 population, some psychiatry and neurology residency programs are closely integrated, an example being cross specialty collaborations at the University of Sao Paulo in areas such as epilepsy and its comorbidities and degenerative dementias [51]. Psychiatry residency in Brazil increased from 2 to 3 years after 2006. Psychiatric supervision weighs heavily on senior or chief residents teaching first and second year residents. Supervision, like in many underserved areas, tends to be clinical case management based rather than occurring at protected designated educational time slots [6]. Unfortunately, in Brazil over a quarter of all psychiatry residency positions remain unfilled [52], underscoring the difficulty of meeting the country's mental health demands.

Although Argentina has the highest per capita number of psychologists in the world, most trained psychoanalytically, the country has approximately 5000 psychiatrists, that is, a psychiatrist per capita rate similar to that of the USA. The psychoanalytic tradition (especially Freudian, Lacanian, and Kleinian) in Argentina remains quite prominent, as well as emphasis on consultation and liaison psychiatry services, giving residents a balanced educational experience with clinical applicability across diverse socioeconomic settings [53].

Subspecialty training in Argentina is available in child psychiatry, consultation and liaison psychiatry, addiction psychiatry, forensic psychiatry, geriatric psychiatry, neuropsychiatry, neuropsychoendocrinology, neuropsychopharmacology, and disaster psychiatry [3].

Psychiatric residency training began in Mexico in 1953; additional 2-year fellowship training in child and adolescent psychiatry was introduced in 1971. General adult psychiatry residency training is completed over a period of 4 years, and approximately 130 positions are offered annually across 22 institutions themselves supported by 16 different universities [54]. Although Mexico has an underserved mental health system like most of Latin America, it possesses a psychiatry training infrastructure that far surpasses that found in Central American and Caribbean countries and thus provides training for a number of physicians from neighboring nations as well as its own.

The Latin American Psychiatric Association (Asociación Psiquiátrica de América Latina, APAL), an affiliate organization of the WPA that meets yearly in Central and South America, attracting close to 2000 participants at high-quality congresses, is working toward a unified psychiatry residency training curriculum for this region of the world [16].

Conclusion

Creative pedagogic methods that enrich psychiatry education in underserved areas include the use of computer-assisted technologies, in particular e-learning, in combination with international academic exchanges and visiting professorships. In this chapter we described programs that incorporate videoconferencing with on-site postgraduate courses and clinical rotations in China, ASEAN countries (Thailand, Malaysia, Indonesia, Cambodia), Iran, Ethiopia, Botswana, Malawi, and Morocco, in collaboration with WPA section leaders via organized liaisons with university medical centers throughout the world.

Educating psychiatric residents in countries with low- and middle-income economies should include the competency-based didactic models favored in countries with high-income economies, in combination with public health models that better address the burden of disease caused by mental disorders in underserved areas of the world. The professional identity and sense of self of psychiatrists facing a large volume of complex work incorporates clinical expertise, task-shifting skills, and leadership roles as public health practitioners. Facilitating liaisons with primary care doctors, community members, religious leaders, NGOs, and nonclinical healthcare workers are skills that should be taught to psychiatric residents in countries with low- and middle-income economies.

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