Dimensions and Course of Clinical Recovery in Schizophrenia and Related Disorders

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1.1 Introduction

Since the inception of Kraepelin's point of view relating to unavoidable "deterioration" [1], schizophrenia has traditionally been viewed as a chronic condition characterized by an extremely negative outcome. Bleuler himself seemed to share a pessimistic view of the disorder; indeed, when describing patients with an apparent return to normal functioning, he referred to "recovery with defect" or "healing with scarring" [2]. Subsequently, this view was confuted in part on the basis of the findings of a series of long-term studies carried out over the twentieth century, demonstrating a more complex picture of the course and outcome of the disorder, with a large heterogeneity in results [3] explained, at least in part, by differences in study methods and samples. Indeed, despite the overall relatively poor outcome of schizophrenia reported in follow-up studies, evidence of subgroups of patients affected by schizophrenia emerged, highlighting extended periods of recovery, at times even in the absence of intensive mental health treatments [4]. Thus, little by little a new paradigm, consisting in a less negative view of the disorder, has developed, based largely on the findings of long-term outcome studies of schizophrenia that provide evidence in favor of the potential for recovery. Indeed, in many cases symptom remission and improvement of functioning early in the course of the disease was

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deemed feasible, together with a more or less sustained improvement in later life. Based on these findings, two ways of conceptualizing schizophrenia, the so-called "broken brain" and the "recovery model," have been confronted in recent years [5]. Some authors have contested the "myth of schizophrenia as a progressive brain disease" [6], in consideration of the fact that the progressive deterioration in functioning may not be intrinsically linked to the disorder, being interpreted rather as the consequence of a series of additional factors (e.g., poor access and adherence to treatments, concurrent external conditions, social and financial impoverishment). Indeed, nowadays recovery is deemed possible and represents the therapeutic goal for people with schizophrenia; it is however acknowledged that not all those affected by this disorder will succeed in achieving recovery [7]. The concept of the "recovery model" was encouraged by a growing influence of "user/consumer" movements geared towards fostering a role of subjective experiences, empowerment, and interpersonal support, which ultimately led to the implementation worldwide of services focused on a collaborative approach to treatments [8]. Indeed, the vision of recovery as a personal experience has triggered a change in mental health policies in many countries, generating an at times profound transformation in mental health systems [9]. Accordingly, two clear-cut parallel visions of recovery have developed, one adhered to by clinicians and the other based on the personal, subjective experience of people suffering from schizophrenia. The two visions represent completely separate and distinct concepts, each with their own specific dimensions, although at the same time interconnected and reciprocally influencing [10].

1.2 Clinical Recovery

1.2.1 Conceptual Heterogeneity of Clinical Recovery

In the wake of the advancement of pharmacological and psychosocial treatment options [10, 11], clinical recovery is currently seen as the ultimate treatment goal in schizophrenia, beyond the achievement of symptom reduction, remission and prevention of recurrences, and functional improvement. However, although intuitive and appealing, the concept of clinical recovery continues to lack a univocal definition, unlike the concept of clinical remission, for which an operative definition was reached years ago [12], gaining broad consensus from both researchers and clinicians [13], although not devoid of criticism [14].

Indeed, on analyzing how clinical recovery is conceived, we are clearly faced with a series of significantly different components put forward by different authors. The heterogeneity of the concept emerges from the depiction of recovery yielded by the definitions afforded by some of the most eminent clinical researchers in the field. Based on these definitions, recovery may encompass symptom remission and functional elements such as cognition, social functioning and quality of life [15], be inclusive of freedom from distressing psychotic symptoms and relapses, satisfaction with life and daily activities and appropriate functioning in everyday life [7], or may comprise remission of symptoms together with engagement in productive activity (work, school), independent management of day-to-day needs, cordial family relations,

recreational activities, and satisfying peer relationships [16]. Given the "protean" definitions and lack of precision in the meaning of the word "recovery," which promotes "ambiguity and confusion" with a consequent "potential for miscommunication," several years ago Lieberman proposed the use of "qualifying terms" for recovery as a possible solution. For instance, he suggested referring to "recovery of cognitive functioning" or "recovery of vocational functioning," etc. to indicate significant improvements in specific areas [17]. To summarize the state of the art, recovery is at times conceived as a "*unidimensional*" construct, simply indicating a more or less sustained remission [18], or, more frequently, as a "*bidimensional*" construct, including both clinical remission and functional remission as aspects to be concurrently considered [10, 13, 19, 20]. Indeed, although a positive correlation is generally present between remission and functioning, a large proportion of poorly functioning subjects may still be detected among remitted patients [21], with a significant influence of more or less stringent remission criteria on rates of functional remission [14]. Finally, clinical recovery may be represented by a "*multidimensional*" construct, including not only "objective" dimensions such as symptom remission and functioning, but also "subjective" aspects including self-evaluated well-being and/or quality of life [22].

1.2.2 Prevalence of Clinical Recovery

1.2.2.1 Methodological Issues

One of the main issues arising with regard to recovery relates to the number of patients that actually succeed in attaining the same. Unfortunately, a series of factors make it difficult to provide a reliable answer to this question. Firstly, the conceptual heterogeneity of clinical recovery and the methodological differences present in the instruments and criteria of evaluation used to assess the different dimensions of recovery should be taken into account. Indeed, with regard to remission, a considerably relevant difference in criteria and instruments for evaluation has characterized the scientific literature [23, 24], at least prior to the introduction of the above-cited "consensus criteria" [12]. However, a different application of these criteria, with particular focus on the duration of remission, continues to represent a source of heterogeneity. Taking into consideration the evaluation of functioning, the situation does not seem to have changed compared to 2007 when Burn and Patrick affirmed that "scales varied greatly in terms of measurement approach, number and types of domains covered and scoring systems" [25]. Indeed, a "reference" scale for the evaluation of personal and social functioning, similar to the PANSS or BPRS scales with regard to symptomatology, is still lacking, with a similar or even worse situation existing for the evaluation of quality of life or subjective well-being. Indeed, a series of other sources of methodological heterogeneity should be considered together with all the previously mentioned aspects, including how clinical recovery is measured (i.e., how many "dimensions" are taken into account as previously described), the characteristics of the sample considered in the study (e.g., incident cases, prevalent cases or mixed samples; patients with schizophrenia or with schizophrenia spectrum psychoses or simply with "psychosis"), the study design (e.g., cross-sectional or longitudinal studies), to mention solely the main

sources of variance. Bearing these issues in mind, the finding of a wide variability of data emerging from some of the most representative studies on clinical recovery conducted in recent years, as described below, should not be surprising.

1.2.2.2 Data from Studies Based on Prevalent Cases

A large body of data derives from studies based on prevalent cases, i.e., including patients of different ages who were at different stages of their illness. In a 1-year follow-up study conducted in Spain on 452 remitted outpatients with schizophrenia, in which symptomatic remission (SR) was defined according to the "consensus" criteria and remission in functioning (RF) was indicated as a Global Assessment of Functioning scale score of at least 80, 22.8% patients fulfilled the recovery definition (SR + RF) at baseline, a proportion that was found to have increased to 27.1% after 1 year [26, 27]. However, taking into account the entire sample initially recruited (n = 1010), the rates of recovery were, respectively, 10.1% at baseline (102/1010) and 10.2% 1 year later (103/110). The 3-year international, prospective, observational study on antipsychotic treatment named "Schizophrenia Outpatients Health Outcomes (SOHO)" study adopted a stringent definition of recovery, including both long-lasting symptomatic and functional remission as well as an adequate quality of life for a minimum of 24 months and up until the 36-month visit; during the 3-year follow-up period the prevalence of recovered subjects among the 6642 patients analyzed was only 4% [28]. In the Italian Network for Research on Psychoses follow-up study, 616 of the original cohort of 921 patients affected by schizophrenia were available for re-assessment 4 years after first evaluation. Patients were deemed as being recovered at follow-up when two criteria were met: the presence of symptomatic remission based upon the "consensus" criteria (limited to severity without the duration criterion), and the presence of functional recovery, defined as a weighted score of at least 76.2 on SLOF "interpersonal relationships," "work skills," and "everyday life skills" scales; according to these criteria, 20.1% of the sample (124/616) were found to have attained recovery [29]. The Chicago Follow-up Study conducted on 64 schizophrenic patients who were compared with samples of patients with other psychoses (12 schizophreniform patients, 81 other psychotic patients) and 117 nonpsychotic patients, all recruited at the time of hospital admission, were re-evaluated five times over a 15-year period; recovery was defined by outcome status achieved during the follow-up period of 1 year on the basis of operational criteria requiring the absence of major symptoms throughout the follow-up year (absence of psychotic activity and absence of negative symptoms), adequate psychosocial functioning, including instrumental (or paid) work half-time or more during the follow-up year and no psychiatric rehospitalizations during the follow-up year; according to these criteria, 41% of patients were found to have recovered during the 15-year follow-up period [30]. These studies show a large variation in recovery rates, ranging from 4% to approx. 40%, with lower rates more evident in studies focused on multiple dimensions and/or linked to the requirement of longer duration of periods prior to deeming patients recovered.

1.2.2.3 Data from Studies Based on Incident Cases

It may be of interest to review studies based on the investigation of incident cases, generally defined as "first-episode studies," to verify whether outcome in terms of recovery is better in younger cohorts of patients who are at the initial stage of the disorder. A follow-up study of 70 out of 143 antipsychotic-naïve patients with first-episode schizophrenia or schizoaffective disorder, selected on the basis of nationwide Danish registers, and re-evaluated after 4–18 years, found 23% fully recovered (i.e., showing symptomatic plus functional remission) subjects, a proportion which fell to 17% when vocational status was added to the recovery criteria [31]. A post hoc analysis of a German cohort of 392 young previously untreated patients with schizophrenia followed over 36 months in the context of the European SOHO study found a 23.6% rate of recovery in terms of symptomatic plus functional remission, but when a third criterion was also considered (subjective well-being), recovery rate fell to 17.1% [32]. A Dutch follow-up study examined prospectively a sample of first-episode patients ($N = 125$), evaluating recovery during the last 9 months of a 2-year follow-up period, revealing how the rate of recovery, considered as a combination of symptomatic and functional remission, related to approx. one-fifth (19.2%) of patients [33]. The 2-year follow-up of the Danish prospective Opus Study assessed the "full recovery" of a cohort of first-episode patients ($n = 547$), linked to patients meeting criteria for both symptom remission and social and (or)vocational recovery, together with the absence of hospitalization during the preceding year; this study reported that 17% of patients had "fully recovered" [34]. The fifth year follow-up of the OPUS study showed a rate of recovery of 18% ($N = 265$ subjects), defined as absence of psychotic or negative symptoms in subjects living independently, GAF (f) > 59, and who either worked or studied [35]. At the 10-year follow-up of the same study, conducted on a total of 304 patients, 14% met the criteria for symptomatic and psychosocial recovery [36]. In the Early Psychosis Prevention and Intervention Centre (EPPIC) study, a naturalistic, prospective follow-up study of an epidemiologic sample of 723 consecutive first-episode patients, 651 of the baseline cohort of 723 participants were re-evaluated at a median of 7.4 years after initial presentation, with 66.9% ($n = 484$) re-interviewed; approximately a quarter of these patients achieved both symptomatic remission and social/vocational recovery [37]. A study conducted in Hong Kong on a sample of 107 patients (70% of the original sample) with a diagnosis of schizophrenia-spectrum disorder who received an early intervention service in 2001–2002 were re-interviewed at a 10-year follow-up; the study found that 25% of patients were recovered in terms of both symptomatic and functional recovery [38]. A prospective follow-up study of 118 first-episode patients affected by schizophrenia or schizoaffective disorder conducted in the USA adopting composite criteria for full recovery (concurrent remission of positive and negative symptoms and adequate social/vocational functioning in terms of fulfillment of age-appropriate role expectations, performance of daily living tasks without supervision, and engagement in social interactions) found that after 5 years only 13.7% of subjects met full recovery criteria for 2 years or longer; the following rates were

achieved for each single follow-up: 9% at the third year, 11% at the fourth year, and 12% at the fifth year [39]. In a 7-year follow-up of a 2-year open randomized clinical trial comparing a dose reduction/discontinuation (DR) vs maintenance treatment (MT) in a cohort of 128 first-episode, remitted patients, Wunderink et al. [40] found that the recovery rates of the 108 patients re-evaluated at the final follow-up were, respectively, 40.4% and 17.6% in the DR and MT groups. The overall picture emerging from these studies on incident cases tends to indicate a certain variability of recovery rates, with somewhat higher rates in studies using less stringent criteria and/or lower duration required for recovery, and lower rates in studies where recovery included more stringent criteria in terms of recovery dimensions and duration.

1.2.2.4 Data from Meta-analytical Studies

The only meta-analytic study on clinical recovery was published years ago by Jääskeläinen et al. [41]. Given the methodological heterogeneity of recovery studies, the authors decided to include in their meta-analysis only observational, non-interventistic studies focusing on schizophrenia and related psychoses based upon a bidimensional concept of recovery, in terms of both symptom and social domains for defining recovery. In particular, the authors chose to include in their meta-analysis only studies providing evidence that improvements in at least one of the two domains included in the concept of recovery had persisted for at least 2 years based on a retrospective or prospective design. In other words, cases were viewed as recovered when the improvement threshold had been reached in both the symptom and functioning domain during follow-up, but not necessarily for a 2-year duration for both domains. It should also be taken into account that this meta-analytic study includes mainly studies published before 2010, and a considerably limited number of studies investigating first-episode patients. The authors selected 50 studies and found a median proportion of cases meeting recovery criteria of 13.5% (range 8.1–20.0%). This finding is largely below the recovery rates reported by Warner [42] who considered 114 follow-up studies relating to "complete recovery" (loss of psychotic symptoms and return to pre-illness level of functioning) and/or "social recovery" (economic and residential independence and low social disruption). Based on these criteria, Warner found a rate ranging from 11 to 33% of fully recovered patients and from 22 to 53% of socially recovered subjects. The evident differences between the data published by Jääskeläinen et al. and the findings of Warner may be largely due to the differences in defining recovery, including the fact that Warner did not include in his definition any criterion relating to the persistence of recovery, and the time periods considered, as Jääskeläinen et al. considered studies published mostly from 1940 onwards, while Warner also included studies published between 1904 and 2000. Another important finding emerging from the meta-analysis was the lack of any evidence of a greater proportion of women with schizophrenia meeting recovery criteria compared to men. This evidence is in contrast with the better outcome of schizophrenia traditionally attributed in general to women [43] and with findings from several follow-up studies, showing clearly higher recovery rates among females [44–46]. In interpreting this discrepancy, it should be taken into account that the prevalence of recovery rates (and of both

symptom and functional remission considered singly) among females is largely focused on European countries, particularly Southern and Northern Europe, with opposite data reported for Latin America, and lacking any clear differences for other areas of the world [47]. Jääskeläinen et al. also reported a lack of evidence to confirm that the proportion of cases that recover changes significantly over time, a finding which is consistent with the findings of Warner [42]. Moreover, the authors indicate that recovery rates do not change as a function of the diagnostic criteria adopted in the study, given that no difference in prevalence rates was detected between studies using non-Kraepelinian vs Kraepelinian diagnostic systems, a finding in contrast with the largely cited metanalysis on outcome studies in schizophrenia by Hegarty et al. [48] which showed that the more stringent or Kraepelinian criteria were correlated with worse outcomes. The meta-analysis of Jääskeläinen et al. moreover failed to detect evidence that recovery is less prevalent in the presence of increasingly stringent criteria, specifically in terms of both symptom and functioning remission lasting 2 years, and that recovery is more prevalent in first-episode samples compared with general samples. The only significant difference found in the meta-analysis related to the finding of significantly higher median recovery rates among patients living in lower-middle income (36.4%) than among patients of upper-middle (12.1%) and high-income countries (13.0%), a finding which is in line with literature data showing better outcomes in developing countries [49, 50], but in contrast with other studies which refute this common assumption [51, 52].

1.2.3   Time Course of Recovery

One of the most intriguing questions relates to the potential degree of stability of recovery. Medium-long term studies conducted at different times using different methodologies have reported how recovery seems to assume a relatively stable course over time. Harrow et al. [30] in their 15-year multi-follow-up study reported a proportion of recovered patients corresponding to 19% after 4.5 years of follow-up, 22% after 7.5 years, and 19% both at the 10th and 15th year. Grossman et al. [46] in their 20-year follow-up study reported separate data for males and females (Table 1.1), with more prevalent cases for women and a fluctuation of recovery rates in general. However, more recent data have been published from first-episode follow-up studies. For example, the Opus study [35] has reported a recovery rate of, respectively, 22%, 29%, and 25% at 2.5, 5, and 10 years. According to the metanalysis by Jääskeläinen et al. [41], the chances of recovery in studies with a duration of recovery lower than or exceeding 5 years were similar (respectively 13.2% and 14.5%). The finding of

Table 1.1 Recovery rates by time and gender according to Grossman et al. [47]

	2 years	4.5 years	7.5 years	10 years	15 years	20 years
Males	7%	16%	19%	10%	23%	25%
Females	31%	21%	21%	39%	25%	32%

recovery rates that remained more or less stable over the years emerging in several studies may be misleading, as almost all follow-up studies tend to indicate solely the proportion of subjects who were recovered at the time of each follow-up, failing to indicate how many patients had continued to be deemed recovered and for how long throughout follow-up. However, a limited number of studies may shed further light on this issue. In the context of the Opus Study, an interesting paper by Albert et al. [53] investigating predictors and trajectories of recovery of a cohort (n = 225) of patients affected by a first episode of non-affective psychosis found rates of recovery (remission of positive and negative symptoms, working or studying and having a GAF score of 60 or above, not living in supported housing or being hospitalized during the last 2 years of the follow-up) of 9% at the first year, 16% at the second year, and 15.7% at the fifth year; in particular the study identified three groups featuring different trajectories among the 40 recovered patients: (1) the "early stable" recovery group (4% of the total sample), comprising subjects who met recovery criteria at the first, second, and fifth year; (2) the "early unstable" group, including subjects who met recovery criteria at the last follow-up as well as at either the first or the second follow-up (5.8% of the total sample); (3) the "late recovery" group, comprising those who met recovery criteria only at the 5-year follow-up (8% of the total sample). In other terms, the findings underline how recovery is largely a fluctuating, unstable condition, given that: (a) only a minority of patients maintain recovery for 3 consecutive years; (b) a substantial part of the cohort fluctuated from illness to recovery over time; and (c) subjects who were identified as recovered after 5 years are a mixed group, made up in a limited proportion by early recovered patients who remained stable throughout the entire follow-up (22.5% in the cited study) and in a more consistent proportion by patients who achieved recovery status over one of the subsequent years (32.5% in the cited study), with the most consistent proportion represented by those who achieved recovery later (45% in the cited study). The naturalistic, prospective 3-year follow-up study of first-episode patients affected by non-affective psychoses carried out by Ayesa-Arriola et al. [54] was specifically devoted to describing patterns of recovery in a sample of 373 consecutive FEP patients. This study used recovery criteria based on both symptomatic remission according to the Remission Working Group and functional remission, in terms of a score 1 or less at the Disability Assessment Scale. Four patterns of recovery emerged from the study: (a) a "Good stable" course which characterized patients who maintained recovery status throughout the 3-year follow-up period (26% of the sample); (b) a "Good unstable" course, in which patients failed to recover by the first year but achieved recovery by the second or third year (21% of the sample); (c) a "Poor unstable" course, characterizing patients who recovered in the first year, but lost this status in subsequent years (10% of the sample); and (d) a "Poor stable" course, comprising patients who failed to recover throughout the 3-year period (43%). A total of 47% of patients had recovered by the third year of follow-up, while 53% failed to achieve recovery or achieved it only temporarily. Although the different methodologies used hinder any direct comparison of the results obtained, both studies converge to indicate that a discrete proportion of first-episode patients achieved persistent recovery lasting 3–5 years. The percentage of patients who maintained recovery over a longer time span (5 years)

is significantly lower (4%) than the sample (26%) who achieved recovery of shorter-lasting duration (3 years). Unfortunately, no extended follow-up studies reporting patterns of recovery were identified in the literature, although the expectation of finding a relatively low proportion of subjects achieving persistent recovery lasting for more than 5 years is somewhat realistic. This is likely not surprising, considering that recovery implies the achievement of both a sustained clinical remission and functioning—a somewhat difficult goal to reach as demonstrated by data from research. Indeed, remission in schizophrenia can occur at any time, although the probability tends to decrease over the longitudinal course of the disease, with a persisting risk of relapse over time, even in presence of long-term maintenance treatment with antipsychotics [55]. Moreover, although symptomatic remission is by definition a prerequisite to recovery, taken alone it is not sufficient [56], particularly as not all patients displaying symptomatic remission are also functionally remitted. Indeed, research studies have demonstrated how functioning is a multi-determined dimension, in which symptomatology represents only one of a series of other determinants. To this regard, data from the study conducted by the Italian Network on Psychosis, one of the largest longitudinal studies conducted to date on schizophrenia, clearly indicates that real-life functioning of people with schizophrenia is correlated with a complex interplay of a multiplicity of clinical, contextual, and personal factors [29, 57–59].

1.2.4   Recovery Beyond Schizophrenia

Generally speaking, clinical recovery is viewed as the most comprehensive outcome target for psychotic disorders, thus raising the question as to whether more effective recovery is achieved in non-schizophrenic disorders than in schizophrenia. Findings obtained in a series of studies favor the latter hypothesis. The study conducted by Grossman et al. [45] found a cumulative rate of patients experiencing recovery throughout the 20-year follow-up of 61% in women and 41% in males, with regard to schizophrenia, and 85% in women and 64% in males for psychoses "other than schizophrenia." The study by Harrow et al. [30] revealed the distribution of patients who had attained recovery at any time during the 15-years follow-up, corresponding to 41% of patients with schizophrenia, 55% of those with schizophreniform psychoses, 67% of patients with "other psychoses" and 78% of nonpsychotic patients; rates of recovery in patients affected by schizophrenia were consistently lowest at each follow-up appointment (Table 1.2). Albert et al. [53] reported how after 5 years the rate of recovery in patients with a diagnosis of schizophrenia was 13.5% versus

Table 1.2 Recovery rates by time and diagnosis according to Harrow et al. [30]

	2 years	4.5 years	7.5 years	10 years	15 years
Schizophrenia	13%	19%	22%	19%	19%
Schizophreniform	18%	27%	33%	27%	25%
Other psychoses	20%	37%	40%	39%	43%
Non-psychotic	39%	46%	51%	51%	50%

23.6% of those with a non-schizophrenic psychotic disorder (F2 ICD 10 Category). In a study investigating the long-term outcome of non-affective psychoses, Pinna et al. [60] assessed a sample of DSM IV schizophrenia ($n = 46$) and schizoaffective ($n = 66$) patients with a comparable long-term illness (208.0 ± 119 and 187 ± 104 months, respectively); remission was cross-sectionally evaluated (no criteria of duration adopted) using criteria of the Remission Working Group, while functional remission was considered as having a PSP scale score of at least 70; patients were deemed recovered when in remission in terms of both symptomatology and functioning. According to these criteria, 43.5% of schizophrenics and 54.5% of schizoaffective patients were deemed symptomatically remitted, with, respectively, 3% and 25.8% being considered functionally remitted; in both cases differences were not statistically significant. On the contrary, 6.5% of schizophrenic and 22.7% of schizoaffective patients were judged as having achieved recovery, a highly significant difference. In a prospective longitudinal study of 56 patients recruited during the first adequate treatment for schizophrenia ($n = 35$) or other psychotic disorders ($n = 21$) (psychotic bipolar disorder, delusional disorder, psychotic disorder NOS) Svendsen et al. [61] used the Remission Working Group criteria to evaluate symptom remission, with functional remission defined as having an employment level equal to full-time work or studies, and social activities equivalent to at least weekly patient-initiated contact with family and/or friends. At 7-year follow-up, 14% of subjects with schizophrenia and 67% of those with other psychoses were found to have achieved recovery, in terms of both symptom and functional remission. In this study, irrespective of the evident variance in prevalence rates, once again attributable to methodological differences among studies, as expected, a significantly higher proportion of recovered subjects was detected among non-schizophrenic psychotic patients.

1.2.5   Recovery in the Elderly

The vast majority of studies focused on recovery in schizophrenia and other psychoses have been conducted on young adult or adult patients, thus raising the question as to whether recovery is achievable in elderly psychotic patients. The few studies that have addressed this issue may be of use in helping to provide an answer. Auslander and Jeste [62] compared a sample of 155 elderly patients affected by schizophrenia with a matched sample of community-dwelling elderly people; the criteria applied required patients to have been in full symptomatic remission for the past 2 years (Sustained remission), over the same period of time been living independently without caretaker supervision, they should not have undergone psychiatric hospitalization over the last 5 years, with a current caregiver-reported status of psychosocial functioning within "normal range," and should either not have been taking antipsychotic medications or taking no more than one-half of the highest daily dose since enrollment. The authors reported that twelve (8%) of the 155 elderly patients met the criteria for sustained remission, and were living independently, and could therefore be considered "recovered." The same authors explained

that the relatively low rate of recovery detected might be explained, at least in part, by the strict criteria adopted in defining sustained remission and in the selection of subjects. Cohen et al. recruited a sample of 198 community-dwelling persons aged 55 and over who had developed schizophrenia before the age of 45, together with a community comparison group (N = 113) [63]; symptom remission was evaluated based on the criteria of the Remission Working Group, while functional remission was evaluated based on the ability to independently manage medications and money and having at least one confidant; recovery was deemed achieved once criteria for both symptom and functional remission had been met. Based on these criteria, remission and recovery criteria were met by 49% and 17%, respectively, of the Schizophrenia group, remarkably similar figures therefore to those observed in younger age groups. The same group [64], on analyzing data derived from their previous follow-up studies performed in New York City, reported how 26% of elderly patients attained concurrent clinical remission and high community integration at baseline, i.e., "objective recovery"; only 12% of the sample simultaneously attained clinical remission and high community integration at both time points; moreover, only 18% experienced no clinical remission and had low community integration at both assessments. To summarize, 7 out of 10 people featured some combination of the remission and community integration. More recently, Cohen et al. [65] published a study on early-onset schizophrenia spectrum disorder in which a subsample of 102 of 248 community-dwelling subjects over the age of 55 was reassessed at a mean of 52 months from first evaluation; clinical recovery was assumed when criteria for both symptom remission (evaluated by a modified version of the Schizophrenia Working group) and functioning, in terms of community integration (score of 9 or more on the Community Integration Scale), were met. The study reported that 12% of subjects remained persistently in clinical recovery at both baseline and follow-up (defined as Tier 1), while 18% failed to meet the criteria for clinical recovery (defined as Tier 5) at any time. The remaining subjects (approx. 70% of the sample) displayed a variable mix of components of clinical recovery during follow-up, namely: (a) a stable state group (named tiers 3), comprising 11% of the sample, characterized by persistent clinical remission but no community integration (6%) or persistent community integration without any clinical remission (5%); (b) a fluctuating group (defined as tiers 4), constituted by 37% of the sample, including subjects who had achieved clinical remission or community integration at only one point in time; and (c) a stable group (defined as tiers 5) including those who had never achieved recovery, as failing to attain either clinical remission or community integration at any point in time. Overall, the figures emerging from this study demonstrate the possibility of achieving recovery in the elderly at rates similar to or better than those detected in younger age groups, highlighting how different patterns of recovery may be observed for the elderly in the same way as for all other age groups. In an editorial on "Late life schizophrenia," commenting data on recovery in the elderly, Meersters [66] reminded us that "…it is clear that at present enduring recovery is too high a goal for the large majority of younger schizophrenia patients… most likely, the same holds true for old," and that "..if recovery is considered as an all-or-nothing goal, these findings are clearly discouraging. Such a

dichotomous approach, however, does not do justice to the versatile reality of coping with everyday life that most clinicians who work with older schizophrenia patients will recognize. Although most patients do not attain complete recovery, many show significant improvements in psychosocial functioning and well-being as they age. Interestingly, this parallels the finding in successful aging research, that positive self-appraisal increases with age, even in the midst of physical and cognitive declinage…".

1.3 Clinical and Personal Recovery

As mentioned previously, although clinical and personal recovery are separate and distinct concepts, they are interconnected and reciprocally influencing, thus highlighting the appropriateness of fostering a deeper understanding of their relationships.

1.3.1 Personal Recovery; Definitions, Characteristics, Processes, Stages

The concept of personal recovery was developed from the point of view of users of mental health services with the aim of prioritizing more meaningful, personalized treatment goals. Personal recovery has often been compared with the traditional treatment targets of symptomatic remission or improvement in social and occupational functioning (functional remission) [67–69]. A widely used definition of personal recovery is "a deeply personal, unique process of changing one's attitudes, values, feelings, goals, skills and/or roles. It is a way of living a satisfying, hopeful, and contributing life even with limitations caused by the illness" [70]. Accordingly, it resembles a process or a "journey," as often described: "a journey of healing and transformation that enables a person to live a meaningful life in a community of his or her choice while striving to achieve maximum human potential" [71]. According to the latter definition developed by the USA Substance Abuse and Mental Health Services Administration (SAMHSA), recovery does not necessarily signify symptom remission or attainment of normal functioning [72], but rather refers to subjective experiences of optimism, empowerment, interpersonal support, peer support, and stigma reduction [8]. One of the major difficulties in studies investigating personal recovery has been represented by an uncertainty as to how to operationalize this process, given the relevant number of aspects that could potentially be included and evaluated within this concept (Table 1.3). Chiu et al. [73] attempted to empirically test the SAMHSA recovery model assuming subjective Quality of life as a proxy indicator of consumer-defined recovery. In their study, 204 patients aged 18–60 affected by schizophrenia spectrum disorder attending two participating outpatient clinics were interviewed using a number of inventories to assess the component dimensions included in the model and a measure of self-evaluated, health-related

Table 1.3 Dimensions of personal recovery according to the SAMHSA model [73]

Perceived respect
Competence
Empowerment
Personal responsibility
Sense of self-determination
Hope
Person-centered treatment
Understanding of the recovery process
Peer support
Holistic (comprehensive) recovery: psychosocial symptoms, social support, spirituality)

quality of life; canonical correlation analysis was performed on two sets of variables, the SAMHSA recovery components and the QoL domain scores of the WHOQOL-BREF scale, revealing significant correlations between most of the recovery components proposed in the SAMHSA recovery model and the health-related quality of life measure.

In view of the acknowledged need for a greater conceptual clarity on the issue of personal recovery, Leamy et al. [74] developed a conceptual framework for personal recovery through a systematic review and a narrative synthesis. The resulting conceptual framework consists in a series of characteristics of the recovery journey (e.g., recovery as an active process, a unique process, a nonlinear process, a journey), five recovery processes comprising connectedness, hope and optimism about the future, identity, meaning in life and empowerment, and, finally, a recovery staging within a transtheoretical model of change which includes precontemplation, contemplation, preparation, action, maintenance, and growth.

1.3.2 Clinical vs. Personal Recovery

Van Eck et al. performed a meta-analysis to investigate the relationship between clinical and personal recovery in patients with schizophrenia spectrum disorders [75]. The majority of studies were conducted on chronic patients, with only one study specifically investigating early psychosis patients. The meta-analysis initially revealed a substantial heterogeneity across studies. Random effect meta-analysis of the relationship between overall symptom severity and personal recovery revealed a significant mean weighted correlation coefficient of $r = -0.21$ (95% CI $= -0.27$ to -0.14, $p < 0.001$), indicating that patients displaying a higher level of overall psychopathology reported a slightly lower personal recovery. The study also evaluated the association between personal recovery and different symptom domains (Table 1.4), again showing a high heterogeneity between studies and an inverse correlation between symptom dimensions and personal recovery measures. A small significant positive effect size was also found for the association with general

Table 1.4 Correlations between symptom dimensions and personal recovery according to van Eck et al. [75]

Symptom dimension	r	IC and significance
Positive symptoms	−0.20	95% CI = −0.27 to −0.12, $p < 0.001$
Negative symptoms	−0.24	95% CI = −0.33 to −0.15, $p < 0.001$
Affective symptoms	−0.34	95% CI = −0.44 to −0.24, $p < 0.001$)

Table 1.5 Correlations between symptom dimensions and hope according to van Eck et al. [75]

Symptom dimension	r	IC and significance
Positive symptoms	−0.14	95% CI = −0.23 to −0.05, $p = 0.004$
Negative symptoms	−0.26	95% CI = −0.32 to −0.19, $p < 0.001$
Affective symptoms	−0.43	95% CI = −0.51 to −0.35, $p < 0.001$

functioning ($r = 0.21$ (95% CI = −0.09 to 0.32, $P < 0.001$), indicating that the higher the degree of functioning, the higher the personal recovery reported by patients.

The study reports separately meta-analytic data relating to the relationship between symptomatology and hope (Table 1.5). All symptom dimensions show an inverse, significant correlation with hope measures, indicating that the lower the levels of positive, negative, and, above all, affective symptoms, the higher the level of hope among patients. As regard to empowerment, only the correlation with overall symptoms could be calculated, obtaining a mean weighted correlation coefficient of $r = -0.23$ (95% CI = −0.36 to −0.09, $P < 0.001$).

The relative importance of affective symptoms in boosting personal recovery and hope has been highlighted in particular by this meta-analytic study, raising the question of whether depression might contrast the achievement of personal recovery and hope or whether personal recovery and hope may be capable of preventing depression.

A study by Chang et al. [76] aimed at examining simultaneously how different recovery processes contribute to personal well-being, focused in particular on the additional contribution of personal recovery to well-being through a regression analysis after controlling for clinical and functional recovery. The results of this study demonstrated how personal recovery was not only positively associated with well-being, contributing to a 26.0% incremental variance in predicting the latter, but also that its effect on well-being was independent of clinical recovery. A recent contribution by Rossi et al. [77] in the context of the cited study of the Italian Network for Research on Psychoses was aimed at exploring the relationship between self-reported "personal recovery" (SRPR) and clinical recovery for the purpose of identifying variables capable of influencing outcome. Personal recovery measures were based on resilience, self-esteem, recovery style, coping strategies, and internalized stigma. By means of a cluster analysis of SRPR-related variables, three clusters were identified. The first cluster, characterized by highest scores on the recovery style scales, Self-Esteem Rating Scale and Problem Focused Coping Scale, and the lowest scores on the scale of Internalized Stigma, included subjects attaining the best clinical recovery measures. The third cluster was represented by those

achieving the lowest scores at the majority of self-reported personal recovery scales and included subjects with the poorest clinical outcome. The second cluster was characterized by better insight, higher levels of self-stigma, lowest self-esteem and personal strength, and highest emotional coping, and included subjects with intermediate levels of clinical recovery, thus revealing a somewhat complex pattern, with a "paradoxical" mixture of positive and negative personal and clinical features of recovery.

1.4   Concluding Remarks

Despite the heterogeneity of data relating to the proportion of patients affected by schizophrenia and related disorders, it is feasible to maintain that by far the most extensively shared definition of recovery is the attainment of both sustained symptom and functional remission. At this point, an impellent need is perceived for a shared definition of the tools to be used in evaluating functioning and in setting threshold scores to be adopted for functional remission, particularly given the availability of a shared definition and criteria for clinical remission. Data from literature demonstrate how recovery, as above defined, is attainable in approximately 15% of patients, although this proportion may likely increase in first-episode patients subjected to an early intervention program, who seem to achieve an overall better outcome, at least in the short-medium term [78], including higher recovery rates [79], a result that might possibly be ascribed to better results in terms of functioning [80, 81]. However, it should be underlined how other authors have expressed their doubt with regard to the positive impact of early interventions, at least in terms of higher recovery rates [82, 83]. It has been reported that the median estimate of the annual recovery rate for schizophrenia is 1.4%., meaning that for every 100 individuals with schizophrenia, 1 or 2 per year would meet the recovery-related criteria; therefore, approximately 14% of subjects would be expected to recover over any 10-year period [41]. The main issue however is that we are not yet sure whether this progressive increase of recovery may extend beyond the 10-year period, nor how to ensure this annual rate increases further. The authors of the above-cited study have affirmed that some evidence has been obtained to suggest that recovery outcomes failed to improve over time. This was defined by the authors as a "sobering finding, in light of the advancements in the delivery of care for those who are affected from schizophrenia." The reasons underlying the persistent negative outcomes in schizophrenia are linked to a multiplicity of factors including lack of involvement and engagement in treatment, poor treatment response and adherence, presence of cognitive deficits and comorbidity with substance use disorders and concurrent medical illness, pre-existing developmental problems and poor functioning prior to diagnosis, effects of medication, social determinants of health, and finally an adaptation to disability and shifting of expectations [84]. Moreover, the significant treatment gap for schizophrenia is highly relevant and should be duly investigated [85] with particular focus on the delay of treatments and difficulty in improving functioning of patients affected by schizophrenia, probably due to the ongoing failure to adequately apply

psychosocial treatments in clinical settings [85–87] despite proof of their effectiveness [10]. The latter finding however may be partly justified by the observation that clinical trials on psychosocial interventions, upon which recommendations included in the main treatment guidelines are based, are frequently lacking a pragmatic design, ultimately leading to uncertainty over the applicability of recommendations in everyday clinical practice [88].

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