



Mental and Addictive Disorders and Medical Comorbidities

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Abstract

Purpose of Review Mental and addictive disorders commonly co-occur with medical comorbidities, resulting in poor health and functioning, and premature mortality. This review provides an overview of the intertwined causal pathways and shared risk factors that lead to comorbidity. Additionally, this review examines the strategies to prevent the onset of and to effectively manage chronic medical conditions among people with mental and addictive disorders.

Recent Findings Recent research provides further evidence for the shared genetic and biological, behavioral, and environmental risk factors for comorbidity. Additionally, there is evidence of effective approaches for screening, self-management, and treatment of medical conditions among people with mental disorders. There are promising health system models of integrated care, but additional research is needed to fully establish their effectiveness.

Summary A combination of public health and clinical approaches are needed to better understand and address comorbidity between mental and addictive disorders and chronic medical conditions.

Keywords Mental disorders · Addictive disorders · Medical disorders · Chronic disease · Comorbidity

Introduction

Globally, mental disorders, substance use disorders, and chronic medical conditions are highly prevalent and each type of disorder makes considerable contributions to the global burden of disease in terms of years lived with disability and early mortality [1–3]. Likewise, comorbidity, or the co-occurrence of two or more conditions, across these three categories is very common. People with mental or addictive disorders are at an elevated risk of developing a variety of chronic medical conditions [4, 5, 6•, 7], including diabetes [8–11], hypertension and cardiovascular disease [12, 13], and asthma [14]. Having a mental disorders also increases an individual's risk of subsequent alcohol drug use and dependence [15].

Conversely, people with chronic medical conditions experience high rates of mental disorders, such as depression [16, 17]. Comorbid conditions have a cumulative adverse impact on health, functioning, and quality of life [18, 19].

People with mental disorders have a higher risk of early mortality compared to the general population, resulting in approximately 10 years of life lost [20]. Approximately two-thirds of individuals with mental disorders die from natural causes, most likely due to chronic medical conditions [20]. Patterns of comorbidity and mortality among people with mental disorders are similar to those in the general population [7, 21]. However, compared to the general population, people with mental disorders or substance use have higher risks of mortality due to a variety of medical conditions, including infections [22, 23], cancer [22–24], heart disease [22, 25], and lung disease [21, 22].

For this article, we reviewed recent literature on the comorbidity between mental and addictive disorders and chronic medical conditions. We examine the intertwined causal pathways and shared risk factors that lead to comorbidity. We also describe recent efforts to establish effective practices in preventing chronic medical conditions from developing, screening and early detection, and treating and managing medical conditions among people with mental and addictive disorders. Our review focuses on research literature, particularly systematic reviews, published between January 2013 and June 2018.

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Onset and Pathways Between Mental Disorders and Medical Conditions

Recent research has sought to explain the temporal relationship between the onset of mental disorders and chronic medical conditions. The onset of mental and addictive disorders often occurs by early adulthood [26, 27], while chronic medical conditions can take longer to develop [28, 29]. In an examination of community-dwelling adults from 17 countries, Scott and colleagues demonstrated that specific mental and addictive disorders predicted up to 13% of chronic disease onset [6••]. The duration of mental illness is associated with an increased risk of developing a chronic medical condition. For example, results from a meta-analysis of 38 studies showed that people with multiple episodes of serious mental illness (SMI) had 1.85 times the risk of diabetes compared to the general population, while the risk of diabetes among first-episode patients was not significantly different than that of the general population [11•].

Additionally, people with chronic medical conditions have an elevated risk of developing a mental disorder. In a large cohort study of primary care patients, almost all chronic medical conditions examined were associated with an increased risk of incident major depressive disorder (MDD). The greatest risks for developing MDD were among patients with diabetes, rheumatoid arthritis, hypertension, and asthma [17]. Results from a meta-analysis indicate that people with diabetes have a higher risk of incident depression compared to individuals without diabetes, even after adjusting for confounders [16]. One hypothesis is that the burden of symptoms and managing a chronic medical condition, such as diabetes, can predispose an individual to depression [30•].

The connections between mental and addictive disorders and chronic medical conditions are complex. Increasing evidence supports a bidirectional relationship between mental disorders and chronic medical conditions, whereby having a mental disorder increases the risk of a subsequent chronic medical condition and vice versa [31, 32]. They also may share common risk factors, including genetic and biological diatheses, health risk behaviors, treatment and healthcare systems factors, and social determinants of health.

Genetic and Biological Factors

Common genetic and biological factors can predispose individuals to both mental disorders and chronic medical conditions. A shared genetic disposition has been established between depression and cardiovascular disease [33] and depression and diabetes [34]. Additionally, epigenetic changes can affect gene expression in ways that can increase an individual's risk for multiple conditions [35].

Recent research has further supported the link between depression and inflammatory processes that can contribute to

cardiovascular disease [36•, 37]. In a narrative review of the connection between depression and cardiovascular disease, Fiedorowicz highlighted the dose-response between the severity of depressive symptoms and poorer vascular function [38]. Depression is associated with increased activation of the hypothalamic-pituitary-adrenal (HPA) axis, which results in elevated levels of pro-inflammatory markers and cortisol. In turn, high levels of cortisol have been associated with metabolic changes, such as insulin resistance, that can contribute to diabetes [8, 39].

Stress due to adverse childhood events (ACEs), trauma, or other chronic stressors has profound and detrimental impact on biological functioning and health. Stress activates the immune system, causing cascades of chemicals, such as cytokines, to be released throughout the body. Repeated triggering of body's response to stress leads to inflammation, which, in turn, increases an individual's risk for developing a mental disorder and/or medical condition [37, 40]. ACEs, stress, and trauma lay the biological and environmental groundwork that place individuals at increased risk for developing a variety of conditions [41]. ACEs are associated with later tobacco and heavy alcohol use [42, 43], poor diet [42], obesity [44], and depressive and anxiety symptoms [43]. ACEs have a cumulative effect, in which individuals who experience greater numbers of ACEs report poorer health outcomes compared to individuals with no or fewer ACEs [43, 45]. Emerging evidence suggests that combinations of adverse life events with mental disorders additively increase the risk for developing a subsequent medical condition. For example, in an exploratory longitudinal study of individuals with PTSD, severity of PTSD symptoms and experiences of early life adversity increased the risk of poor cardiometabolic outcomes [46].

Behavioral Factors

People with mental disorders commonly engage in behaviors that can put them at risk for developing chronic medical conditions. Compared to individuals without mental disorders, people with mental disorders are more likely to smoke and use other drugs [47–49], be physically inactive [50], and have a poor diet [51].

These behavioral risks may be particularly acute for patients with serious mental disorders such as schizophrenia and bipolar disorder. In a survey of about 2000 people, individuals with schizophrenia and bipolar disorder were two to three times more likely to be current smokers and smoked significantly more cigarettes per day compared to individuals without a psychiatric disorder [48]. Regarding physical activity, findings from an analysis of nationally-representative data in the USA showed that people with serious psychological distress were less likely to be highly or moderately active and more likely to be inactive compared to people without serious psychological distress [50]. Based on a systematic

review of dietary patterns, people with schizophrenia consumed diets lower in fiber and fruits, but higher in saturated fats, compared to the general population [51]. One outcome of these health risk behaviors is obesity, which can increase the risk for several chronic medical conditions. In a large longitudinal study of women with PTSD, the authors noted that increased body mass index, along with antidepressant use, were two key risk factors for type 2 diabetes [9].

Health risk factors, however, do not occur in isolation; rather they cluster in ways that can increase the risks for poor health outcomes. Vermeulen-Smit and colleagues examined the clustering of health risk behaviors in a nationally-representative sample in the Netherlands [52••]. They identified four clusters with varying levels of smoking, drinking, physical activity, and quality of diet. Compared to the most healthy group, individuals in the three groups with clustered health risk factors were more likely to also have a diagnosis of any mood disorder, major depression, or a substance use disorder [52••].

Treatment and Healthcare Systems Factors

Treatment factors may also place people with mental disorders at a higher risk for developing chronic medical conditions. Psychiatric medications contribute to the elevated risks for chronic medical conditions among people with mental disorders. Antipsychotic medications, in particular, can lead to significant weight gain and increase the risk for metabolic syndrome [53, 54]. Proposed pathways to explain this association suggest that antipsychotic medications may interfere with the signals of satiety, leading to increased caloric intake, and may increase sedation, thus lowering activity [55]. A systematic review and meta-analysis by Vancampfort and colleagues demonstrated that type 2 diabetes prevalence was significantly higher in people with SMI who took almost any antipsychotic medication compared to people with SMI who did not [11•].

People with mental disorders may be less likely to be screened or to receive the recommended care and monitoring for medical conditions [55]. Recognition of the importance of screening for medical conditions among people with mental disorders may have increased over the past several years. In a systematic review of screening rates for cardiovascular risk factors among adults with SMI, Baller and colleagues found that screening rates were high for hypertension, but variable for glucose and lipid levels [56]. However, other recent research indicates that health screening rates are similar for people with mental illness and the general population [57, 58]. In a retrospective cohort study, Yarbrough and colleagues found that this pattern held for patients in a managed health care group and federally qualified health centers and was stable over a 12-year period [58]. Based on national visit-level primary care data from the USA, Iyer and Young showed that the

probability of blood pressure measurement and health screening increased over time for people with mental illness [57].

People with mental disorders continue to experience gaps in treatment. For example, Kisely and colleagues compared cancer treatment and outcomes of people with and without mental disorders in a population-based record linkage study. They found that people with mental disorders were less likely to receive surgery, radiotherapy, and chemotherapy and were more likely to experience cancer metastases, compared to the general population [59]. In a systematic review, McGinty and colleagues found that, in some studies, people with SMI were less likely to receive high-quality medical care compared to people without SMI. Medicaid beneficiaries with SMI were the most likely to receive lower quality of care, while veterans with SMI received care that was on par with the general population [60••]. Variations in screening and treatment rates could reflect differences in patient populations, health systems, insurance coverage, or if a standard screening protocol is in place.

Social Determinants of Health

In the past 5 years, more attention has been given to the influence of the social determinants of health on the development of mental disorders. Social determinants of health are defined by the World Health Organization as the “conditions in which people are born, grow, live, work, and age” [61]. These conditions include socioeconomic status; access to and quality of housing, employment, education; food security; social inclusion and discrimination; and the built environment. Social determinants of health drive health disparities and affect health by shaping health behaviors, coping mechanisms, and access to resources [62]. Reiss reported findings from a systematic review showing that children and adolescents who grew up in low socioeconomic conditions had up to three times the risk of developing a mental disorder compared to socioeconomically advantaged children and adolescents. Notably, persistent low socioeconomic status increased the risk for developing a mental disorder, while that risk lessened if children and adolescents experienced an increase in status [63]. Barnett and colleagues demonstrated that the risk of mental and medical comorbidities increased with greater socioeconomic deprivation among a large sample of individuals registered in primary care clinics in Scotland [4]. Neighborhood affluence can interact with childhood adversity such that the association between childhood adversity and the risk for chronic disease is greater among people who live in poorer neighborhoods compared to more affluent neighborhoods [64]. Additionally, social isolation and a lack of social support are associated with a variety of poor health outcomes, including coronary heart disease [65] and depression [66].

Prevention of Medical Comorbidities Among People with Mental and Addictive Disorders

Given the high prevalence of medical conditions among people with mental and addictive disorders and the resulting burden in terms of years lived with disability and premature mortality, approaches to prevent comorbidities should combine both clinical and public health models. Population-based approaches for addressing comorbidity include minimizing the onset of medical conditions among people with mental disorders; screening, early detection, and connection to treatment; and effective management and treatment of established medical conditions.

Primary Prevention of Medical Comorbidities

While there have been extensive efforts to prevent the emergence of chronic medical conditions in the general population [67], less attention has traditionally been given to reducing these risk factors among people with mental disorders. Preventing the new onset of medical conditions among people with mental disorders requires attention to reducing health risk behaviors and increasing individuals' management of their health.

Interventions aimed at reducing risk factors for chronic medical conditions among people with mental disorders have targeted weight management, diet, physical activity, and smoking. Gierisch and colleagues conducted a systematic review to evaluate programs seeking to improve cardiovascular risk factors among people with SMI. Their meta-analysis of 10 studies showed that patients in behavioral weight management interventions lost, on average, more weight than individuals in the control group. Low numbers of studies, however, prevented conclusions from being drawn about the impact of behavioral interventions on glucose and lipid control [68]. Based on findings of meta-analyses, interventions promoting physical activity are effective in reducing symptom severity among people with depressive disorders [69, 70] and people with PTSD [71]. While these studies found limited evidence about the effect of physical activity interventions on improving risk factors for chronic medical conditions, it is plausible that these interventions could have positive effects beyond mental health.

Smoking cessation programs, including behavioral strategies and medicine, are effective for people with mental and addictive disorders [72–74]. However, Sheals and colleagues performed a systematic review and meta-analysis showing that a substantial proportion of mental health professionals reported barriers to implementing smoking cessation interventions. Additionally, about 40% of mental health professions held negative beliefs about smoking cessation, often expressing the belief that their patients were not interested in quitting

smoking or that smoking cessation interventions would not be effective for their patients [75].

The context in which interventions to improve health risk behaviors occur is important to consider. While recent large randomized control trials have reported favorable results for behavioral weight loss interventions in the USA [76, 77], other trials of health promotion programs in Denmark [78] and the United Kingdom [79] did not find significant differences between treatment and control groups. In the discussion of their results, Speyer and colleagues noted that an important difference may have been better access to primary care in Denmark compared to the USA. For example, mandatory checks of blood lipids of all patients in the Danish Schizophrenia database prompt primary care clinicians to treat cardiovascular risk factors. Speyer and colleagues stated that these guidelines likely contributed to few study participants needing a change in medication for lipids or blood pressure at baseline [78].

Early Detection of Medical Comorbidities

Screening for medical conditions among people with mental disorders increases the likelihood of early detection and connection with needed care. The fragmentation of mental health and medical care for presents a challenge for people with mental disorders in receiving screening. Lamontagne-Godwin and colleagues systematically examined 22 interventions to increase access to or uptake of screenings for medical conditions among people with SMI [80]. These interventions took place in a variety of settings, including primary care, outpatient mental health clinics, and inpatient mental health services. While there was evidence to support screening in all of these settings, the authors noted that linkages between primary care and mental health care were essential to ensuring screening completion [80].

Several barriers and facilitators to access to and uptake of screening for people with mental disorders have been identified in quantitative and qualitative studies. Patients may have limited knowledge of the purpose and availability of screening tests; experience logistical barriers, such as lack of transportation or difficulty scheduling screening; and express reluctance to attending screening appointments [80, 81]. Clinicians experience challenges in providing screening and preventive services for people with mental illnesses. Caring for patients' acute health concerns, both mental and physical health conditions, can prevent clinicians from offering preventive health services. Additionally, over half of 249 surveyed clinicians believed that people with SMI are less interested in preventive services compared to other patients [82]. At the clinic level, barriers to screening include a lack of resources and screening equipment, unclear delineation of professional roles, and a lack of integration and coordination of care between healthcare systems [80, 81].

Facilitators to screening and early detection included providers and screening professionals viewing as health promotion as important for people with mental disorders and good communication skills between patients and providers [81]. Additionally, there is evidence to support the importance of mental health providers having a sense of ownership in and flexibility when conducting screening. Integrated services, such as an onsite pharmacist, and close connection with primary care services support screening among people with mental disorders [80].

Treatment of Medical Comorbidities

Once a person with a mental disorder has developed a chronic medical condition, it is crucial for them to receive effective treatment of that condition. Patients with mental and addictive disorders face several challenges to receiving quality treatment for comorbidities. Patients report difficulty finding and accessing providers for physical health care and navigating between mental health care and primary care [83, 84]. Communication and coordination between types of services can be particularly challenging [84, 85].

Integrated and collaborative care models are prominent methods of addressing mental health and medical comorbidities. Key components of integrated care for addressing comorbidities include shared electronic medical records to identify and track patients with particular conditions, collaboration of multi-disciplinary teams of healthcare providers, and care navigators to help coordinate services and connect patients to needed and resources. Co-location of services promotes access to care with either a mental health professional in a primary care setting or a primary care provider in a behavioral health care setting. Additional considerations for healthcare providers include a delineation of roles and responsibilities, the importance training to hone skills outside one's specialty, and allocation of time for training and collaboration with the team of providers [86, 87].

While integrated and collaborative care models have been promoted as best practices for behavioral care, more evidence has come out recently about the impact of these models on a broader scale. The Primary and Behavioral Health Care Integration (PBHCI) grant program funded by the Substance Abuse and Mental Health Services provided funding for community mental health centers to provide on-site primary care services or collaborate with a primary care provider, such as a federally qualified health center. An evaluation of the early stages of this program found that patients at PBHCI clinics showed improvements in some, but not all, physical health outcomes and had higher rates of outpatient services usage compared to comparison groups [88–90].

Since the passage of the Affordable Care Act in the United States, models of healthcare delivery, such as patient-centered medical homes (PCMHs) and Accountable Care Organizations

(ACOs), are increasingly being used to address the health needs of individuals with mental disorders. Given the recent application of these models to behavioral health, little evidence is currently available about the effectiveness of PCMHs and ACOs in improving the quality of services and health for people with mental and addictive disorders.

PCMHs combine primary care with elements from collaborative care models, such as electronic information systems, care management, and quality improvement [91]. Retrospective secondary data analyses of adult Medicaid enrollees with SMI indicated that PCMH patients had greater use of primary care, better medication adherence, reduced use of the emergency room, and better linkage to primary care after an inpatient psychiatric discharge [92–94]. Adults with major depressive disorder, but not schizophrenia or bipolar disorder, were more likely to receive preventative lipid and cancer screenings [92]. However, an examination of nationally representative data indicated that patients who received care consistent with a PCMH received preventive screening and had similar healthcare usage compared to patients with a usual source of care [95, 96].

ACOs are provider-led organizations that offer a spectrum of services, from primary and preventive care to chronic care management, in order to meet cost and quality benchmarks [91]. In a nationally representative survey of ACOs, fewer than half of responding ACOs included behavioral health provider groups. Of the ACOs that included behavioral health, 57% reported any integration of behavioral health and primary care [97]. Notably, a focus on substance use appears to be lacking among ACOs [97–99]. Challenges to integrating behavioral health into ACOs include a scarcity of mental health providers, difficulties in establishing sustainable financing models, and complications with sharing behavioral health data [99]. Moving forward, continued evaluation of the integration of behavioral health into ACOs and PCMHs and monitoring of services use and health outcomes will be important for promoting effective healthcare practices for comorbidities.

Addressing chronic medical conditions among people with mental disorders also involves promoting self-management behaviors. The physical and emotional symptoms and strain from having multiple chronic conditions can prevent individuals from performing the range of behaviors needed to manage their conditions. In a qualitative review of studies examining self-management of multimorbidity, patients expressed more difficulties in dealing with the emotional and physical conditions of their symptoms, rather than the specific skills of managing their conditions. Patients expressed a desire for providers to listen to their needs and involve them in the decision-making process about their treatment [100].

Evidence is building about effective methods for improving self-management of comorbidities. A systematic review of 10 interventions for individuals with SMI and chronic medical conditions that followed the Chronic Disease Self-

Management model found these programs had favorable outcomes in functional status and self-management attitudes and behaviors [101]. Based on a systematic review of 18 peer support interventions, Cabassa and colleagues noted that self-management and peer navigator interventions showed promise in improving illness management behaviors [102]. In both reviews, the interventions varied widely in setting, patient population, scope, and duration. As intervention research and reviews of this literature move forward, it will be important to assess the key elements leading to changes in behavior and health outcomes, as well as identifying in which populations these interventions work best.

Living Well with Comorbidities

While effective treatment of comorbidities is important, attention must also be paid to minimizing disability and promoting patients' quality of life. The social conditions that contribute to comorbidity and quality of living with comorbidity are important factors that have received less attention. The environment in which people with mental illness live can affect the degree to which they can participate in health-promoting behaviors. In qualitative research, patients and providers have commented on the likelihood of people with SMI living in neighborhoods that lack safe, walkable areas and have little access to healthy food options [85, 103]. Establishing community conditions to support healthy behaviors is promoted as a key strategy for minimizing the detrimental effects of chronic medical conditions [104]; likewise, these conditions could have positive implications for people with mental disorders and comorbidities.

Quality of life is impacted by the degree to which people with mental disorders can participate in society. A systematic review demonstrated the beneficial impact of supported employment programs on increasing rates of employment, length of time in a job, and wages for people with SMI [105, 106]. Similarly, transitioning people with SMI into stable housing can improve quality of life and community functioning [107, 108]. There has yet to be strong research to link employment and housing support with health outcomes, but meeting the basic needs of people with SMI could have downstream effects on their behaviors and overall health.

Conclusion

Comorbidity of mental and addictive disorders with chronic medical conditions arises through shared and bidirectional risk factors. Researchers continue to seek to elucidate the genetic and biological pathways that lead to comorbidities, though the underlying causal mechanisms have yet to be fully explained. Similarly, there are gaps in the current knowledge on the influence of the social determinants of health on comorbidity, as well as the interactions between biology and environment.

Further research on risk factors for comorbidity should take multiple risk factors into account, including biological, behavioral, and socioeconomic and environmental factors.

Prevention of chronic medical conditions among people with mental disorders depends on reducing health risk behaviors, improving access and quality of care and healthcare delivery systems, and addressing social determinants of health. While there is research demonstrating the effectiveness of screening, self-management, and treatment programs for people with mental disorders, more systematic examination is needed to determine the key components of the programs that foster behavioral change and positive health outcomes, as well as effective strategies for adapting programs to different settings and populations. At a health systems level, further research is needed to identify best practices in integrating the complex care for people with comorbidities, particularly for those with addictive disorders. Preventing comorbidities and improving well-being for people with multiple conditions will involve both public health and clinical approaches.

Compliance with Ethical Standards

Conflict of Interest Elizabeth Reisinger Walker and Benjamin G. Druss each declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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