

Chapter 4

Adult Mental Disorders

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INTRODUCTION

Burden of Disease

Mental disorders are a diverse group of conditions that primarily impair cognition, emotion, and behavioral control; occur early in life; and have a high aggregate prevalence in all countries where epidemiology has been investigated (Demyttenaere and others 2004; Kessler, Berglund, and others 2005; WHO 1992). The combination of high prevalence, early onset, clinical course that is either chronic or remitting and relapsing, and impairment of critical brain functions makes mental disorders a major contributor to the global disease burden discussed in chapter 2 in this volume (Whiteford and others 2015). The greatest fraction of the burden results from years lived with disability (YLDs), particularly for ages 15–49 years—a critical life interval for completing education, starting a family, and increasing productivity at work (figure 4.1) (WHO 2014b). The global cost of mental health conditions is projected to be as high as US\$6 trillion by 2030, of which 35 percent would be contributed by low- and middle-income countries (LMICs) (Bloom and others 2011).

Although mental disorders directly account for fewer than half of one percent of all deaths, they contribute significantly to premature mortality through multiple medical causes (discussed in chapter 3 in this volume, Charlson and others 2015) and are a major risk factor for suicide (WHO 2014c; chapter 9 in this volume, Vijayakumar and others 2015). An estimated

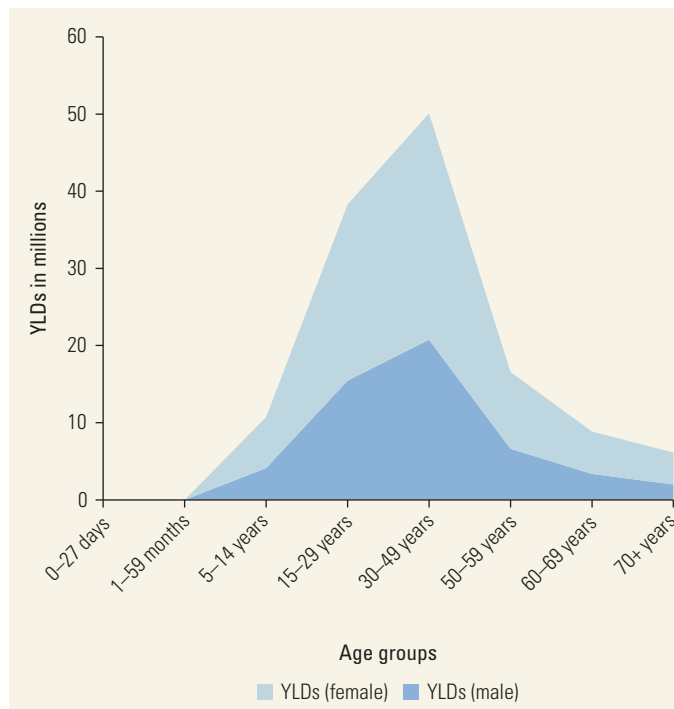
8 million deaths annually due to medical conditions are attributable to mental disorders (Walker, McGee, and Druss 2015).

Mental disorders are associated with social stigma in many countries and cultures (Weiss and others 2001). The slow emergence of scientific explanations for the etiologies of mental disorders and the mistaken belief that symptoms reflect either a lack of will power or some moral failure facilitate negative attitudes and discrimination. Patients with psychotic symptoms can seem frightening, but persons with mental illnesses are far more likely to commit suicide than homicide and to be victims of crimes than perpetrators (*The Lancet* 2013; Walsh and others 2003). Shame and fear are substantial obstacles to help-seeking, diagnosis, and treatment. Individuals with mental disorders are often imprisoned, without access to adequate care, for minor legal transgressions that result directly from their illnesses. In many mental hospitals and other settings, people with these disorders may not be accorded basic human rights. Stigmatization has contributed to disparities in availability and access to care and medications and insurance coverage, as well as research funding, compared with other chronic illnesses (Wang, Aguilar-Gaxiola, and others 2007).

This chapter updates data on the disease burden, as well as interventions to treat the four leading contributors to adult mental illness globally—schizophrenia, bipolar disorder, depressive disorders, and anxiety disorders. These were selected because of their high contribution to the global disease burden, accounting

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Figure 4.1 Years Lived with Disability Caused by Unipolar Depression, Anxiety Disorders, Bipolar Disorder, and Schizophrenia Globally



Source: WHO 2014b.

Note: YLDs = years lived with disability.

for 66 percent of disability-adjusted life years (DALYs) lost and 69 percent of YLDs due to mental and behavioral disorders, as well as based on the availability of data for cost-effectiveness analyses. We begin with a brief summary of the etiology of these disorders, followed by a more detailed description of the burden and epidemiology of each group of disorders and the evidence on treatment. Throughout this chapter, although we attempt to emphasize data from LMICs, most of the data are from high-income countries (HICs).

Risk Factors

The etiologies of mental disorders involve interactions among genetic, developmental, social, and environmental risk factors. Mental disorders are polygenic, meaning that hundreds of risk variants in DNA sequence exist across global populations, much like type 2 diabetes mellitus and hypertension. An individual's risk results from the aggregation of some disease-associated alleles (alternative forms of a gene at a given locus) in combination with environmental factors. Strong evidence suggests that multiple psychiatric disorders share a significant fraction of genetic risk factors (Lee and others 2013).

Among the disorders discussed in this chapter, schizophrenia and bipolar disorder are the most highly influenced by genes, with estimated heritabilities of 65 to 80 percent (Sullivan, Daly, and O'Donovan 2012). Genotyping of nearly 40,000 individuals with schizophrenia and a larger number of healthy comparison subjects has revealed 108 genomewide significant loci that contribute to risk, with different combinations of risk alleles acting in different individuals (Ripke and others 2014). Genes exert less influence, and environmental risk factors more, in depressive and anxiety disorders (Sullivan, Daly, and O'Donovan 2012).

The relative risk of developing psychopathology involves interactions with genetic and developmental risk factors (Digangi and others 2013). Adverse circumstances in childhood have been associated with risk; histories of early childhood abuse, violence, poverty, and experiences of significant loss correlate with risk of multiple mood and anxiety disorders (Heim and others 2010; Patel and Kleinman 2003). Through complex pathways, people with chronic physical illnesses like diabetes, chronic obstructive pulmonary disease, cardiovascular disease, arthritis, and cancer have a greater likelihood of developing mental disorders, particularly depression (Moussavi and others 2007). Similarly, individuals who have sustained traumatic brain injuries have a greater likelihood of developing mental disorders (Jorge and others 2004). Environmental triggers are best documented in post-traumatic stress disorder (PTSD), but even here individuals vary enormously in the threshold of stress severity associated with PTSD. Replicated environmental risk factors for schizophrenia include urban birth, migrant status, season of birth, and possibly viral infections during pregnancy (Sorensen and others 2014). These environmental risk factors are proxies for causal mechanisms that remain to be identified and that interact with genetic risk factors to produce illness (McGrath and Scott 2006).

Gender is associated with the risk of many mental disorders; men have higher rates of schizophrenia, and women have higher rates of depressive and anxiety disorders (Patel and others 2006). The reasons for these differences are likely related to genetic and social factors that may expose a particular gender to a higher burden of risk factors. Bipolar disorder affects men and women equally.

MOOD AND ANXIETY DISORDERS

Mood disorders differ from normal variation in emotional state by their persistence across time

and situations—each episode lasting weeks or even months—and accompanying physiological and cognitive symptoms. Mood disorders are divided into unipolar depressive disorders and bipolar disorder, in which manic episodes also occur. The unipolar-bipolar distinction is well supported by studies of families, genetics, and treatment response.

During an episode of a mood disorder, a person may be predominantly sad or emotionally withdrawn (depressive disorders), elated (mania), or irritable (mania or depression). The emotions are relatively inflexible; for example, a person with a depressive disorder cannot respond appropriately to happy or rewarding stimuli. The physiological disturbances typical of mood disorders include abnormalities in sleep, appetite, libido, and energy. Cognitive abnormalities associated with mood disorders include impairment in attention and memory, as well as mood-dependent changes in the content of thought.

Severe depression and mania may be characterized by psychotic symptoms. Due to frequent occurrence of psychotic symptoms during the manic phase of bipolar disorder, it can also be considered a type of psychotic disorder. In many LMICs, concurrent somatic symptoms are commonly reported with mood and anxiety disorders and may be the chief complaint. For example, patients suffering from depression might not complain of emotional symptoms but of fatigue or multiple aches and pains. Many reasons have been suggested for this phenomenon, including the stigma associated with mental disorders and patients' expectation that physical symptoms have more salience in medical consultations.

Depressive Disorder

Clinical Features and Course

Clinically significant depression is distinguished from normal sadness or grief by its severity, persistence across time and situations, duration, and associated physiological and behavioral symptoms. The cardinal symptoms include a period of persistent sadness or other negative affective states, such as loss of interest in previously pleasurable pursuits, or anhedonia (inability to experience pleasure). Physiological symptoms occur across cultures, including sleep disturbance, most often insomnia (with early morning awakening), but occasionally excessive sleeping; appetite disturbance (usually loss of appetite and weight loss), but occasionally excessive eating; and decreased energy, fatigue, multiple aches, and pains.

The cognitive symptoms may include thoughts of worthlessness and guilt, suicidal thoughts, difficulty

concentrating, slow thinking, ruminations, and poor memory. Some individuals with depression exhibit slowed motor movements (psychomotor retardation), while others may be agitated. Psychotic symptoms occur in a minority of cases, most often congruent with the depressed mood. Thus, a person might hear relentlessly critical voices.

Epidemiology and Burden of Disease

Depression is an episodic disorder that generally begins early in life (median age of onset is in the mid- to late 20s), although new onsets can be observed across the lifespan. Childhood onset is being increasingly recognized, although not all childhood precursors of adult depression take the form of a clearly diagnosable depressive disorder. A pattern of remissions and relapses is typical, with recurrence risk greater among those with early-onset disease (Lewinsohn and others 2000). Many individuals do not recover fully from acute episodes and suffer a persistent depressive disorder that exerts negative effects on public health worldwide (Gureje 2011) and is a risk factor for suicide.

Depression is often comorbid with other mental disorders (Kessler, Chiu, and others 2005); roughly half of the people who have a history of depression also have an anxiety disorder in their lifetime. Depression is frequently comorbid with obesity and general medical disorders, such as type 2 diabetes mellitus, coronary artery disease, and chronic pain disorders.

The 12-month prevalence of depressive disorder, dysthymia, or bipolar disorder among the 17 countries that participated in the World Health Organization's (WHO) World Mental Health (WMH) surveys ranged between 1.1 percent in Nigeria and 9.7 percent in the United States, with an interquartile range (IQR)—which covers the 25th to 75th percentiles—of 3.4 to 6.8 percent and substantial cross-country variations (Kessler and others 2008).¹ These wide differences in prevalence may represent both methodological differences (notably difficulties in self-reporting conditions that are stigmatized across cultures) and true differences due to the interplay among the genetic, developmental, and environmental factors that might differ across countries.

Depression also leads to substantial impairments in productive and social roles (Wang, Simon, and Kessler 2003) and is the single largest contributor to the non-fatal burden globally (WHO 2014b). Depression is a leading risk factor for suicide—a risk that is exacerbated if concurrent with substance use disorders or psychotic symptoms (Isometsa 2014).

People with depression frequently delay seeking professional treatment—particularly those with early-onset cases (Olfson and others 1998)—and frequently receive

undertreatment. The WMH surveys found that the proportion of persons with mood disorders receiving any treatment in the first year of onset of the disorder ranged from 6 percent in China and Nigeria to 52.1 percent in the Netherlands, with an IQR of 16.0–42.7 percent. Overall, the use of mental health services is lower in LMICs and largely corresponds to countries' overall spending on health. A higher proportion of people receives care from general medical services (except in some countries, including Colombia, Israel, and Mexico), indicating the need to focus on interventions through general health care platforms (Wang, Aguilar-Gaxiola, and others 2007).

Anxiety Disorders

Clinical Features and Course

Anxiety disorders represent symptomatically diverse, albeit related, forms of dysregulation of fear responses in the brain, likely excessive activation of subcortical fear circuitry with inadequate regulation by the prefrontal cortex. In anxiety disorders, even innocuous stimuli induce a significant and often prolonged response including tension, vigilance, activation of the sympathetic nervous system, subjective fear, and, in some circumstances, panic.

Although anxiety per se is likely to feature in the clinical presentation of most patients, somatic complaints such as chest pain, palpitations, respiratory difficulty, or headaches are common. These symptoms may be more commonly reported in LMICs.

Panic Disorder. The central feature of panic disorder is an unexpected panic attack: a discrete period of intense fear accompanied by physiological symptoms, such as a racing heart, shortness of breath, sweating, or dizziness, with an intense fear of losing control or dying. Panic disorder is diagnosed when the attacks are recurrent and give rise to anticipatory anxiety about additional attacks. People with panic disorder may progressively restrict their lives and ultimately stop leaving their homes altogether to avoid situations like crowds, traveling, bridges, or elevators, in which panic attacks occur.

Generalized Anxiety Disorder. Generalized anxiety disorder is characterized by chronic, unrealistic and excessive worry, accompanied by anxiety-related symptoms such as sympathetic nervous system arousal, excessive vigilance, and motor tension.

Post-Traumatic Stress Disorder. PTSD follows significant trauma and is characterized by emotional numbness, punctuated by intrusive reliving of the traumatic

episode triggered by cues that act as reminders of the trauma; disturbed sleep (including nightmares); and hyperarousal, such as exaggerated startle responses.

Social Anxiety Disorder. *Social anxiety disorder (social phobia)* is characterized by a persistent fear of social situations or performance situations that expose a person to potential scrutiny by others. It may be difficult to separate social anxiety disorder from extremes of normal temperament, such as shyness. Nonetheless, social anxiety disorder can be quite disabling.

Simple Phobias. *Simple phobias* are extreme fear in the presence of discrete stimuli or cues such as heights or spiders.

Obsessive-Compulsive Disorder. Obsessive-compulsive disorder (OCD) was historically considered an anxiety disorder, but is now recognized to reflect dysfunction of a different brain circuit, striatal-thalamic-cortical loops (Pauls and others 2014). While OCD symptoms engender severe anxiety, the core symptoms are intrusive, unwanted thoughts followed by actions and rituals meant to neutralize them. For example, the thought that a doorknob is contaminated may lead to excessive hand-washing. When severe, OCD rituals can consume much time in the day and can be distressing and disabling. Childhood onsets are common and are more likely to be familial than later onsets.

Epidemiology and Burden of Disease

Anxiety disorders are the most common mental disorders in most of the countries that participated in the WMH surveys. The 12-month prevalence of anxiety disorders ranges between 3.0 percent (China) and 19.0 percent (the United States), with an IQR of 6.5–12.2 percent (Kessler and others 2008). Despite wide variation in overall prevalence, specific phobia and social phobia are generally the most prevalent lifetime anxiety disorders, with a weighted mean prevalence of 6.4 percent and 4.6 percent, respectively. Panic disorder and OCD are generally the least prevalent, with weighted means of 1.7 percent and 1.3 percent, respectively.

Anxiety disorders have consistently been found in epidemiological surveys to be highly comorbid, both among themselves (multiple anxiety disorders) and in combination with mood disorders. Most people with a history of one anxiety disorder typically have a second anxiety disorder. More than half of the people with a history of either an anxiety or mood disorder typically have both types of disorders. Retrospective reports from community surveys consistently show that anxiety disorders have early average ages of onset, a median of

approximately age 15 years, based on cross-national patterns (de Graaf and others 2003; Kessler, Chiu, and others 2005).

There is considerable delay in seeking care for anxiety disorders. Data from the WMH surveys report that, among the countries studied, the proportion of persons with anxiety disorders receiving treatment within the first year of the onset of the disorder ranged from 0.8 percent in Nigeria to 36.4 percent in Israel among the countries studied, with an IQR of 3.6–19.8 percent. The median delay in seeking care varied significantly between countries, ranging from three years in Israel to as many as 30 years in Mexico (Wang, Angermeyer, and others 2007).

Anxiety disorders have consistently been found in epidemiological surveys to be associated with substantial impairments in productive roles (such as work absenteeism, work performance, unemployment, and underemployment) and social roles (such as social isolation, interpersonal tensions, and marital disruption).

Bipolar Disorder

Clinical Features and Course

Bipolar disorder is defined by the presence of mania as well as depression, but the relative frequency and duration of the two poles vary widely. Moreover, mixtures of symptoms are quite common. Patients with bipolar disorder have recurrent episodes of illness—manias and depression—and may recover to baseline functioning between episodes. However, many patients have residual symptoms, most often depressive symptoms, which may cause significant impairment (Angst and Sellaro 2000). Individuals who have had at least one manic episode are considered to have bipolar disorder, even if they have not yet experienced a depressive episode. Some classification systems distinguish bipolar I disorder, in which patients meet the full criteria for manic episodes, from bipolar II disorder, in which patients experience only mild manic episodes.

Mania is typically characterized by euphoria or irritability, a marked increase in energy, and a decreased need for sleep. Individuals with mania often exhibit impulsive and disinhibited behaviors. There may be excessive involvement in goal-directed behaviors characterized by poor judgment. Self-esteem is typically inflated, frequently reaching delusional proportions. Speech is typically rapid and difficult to interrupt. Individuals with mania may exhibit cognitive symptoms; patients cannot stick to a topic and may jump rapidly from idea to idea, making comprehension of their train of thought difficult. Psychotic symptoms are common during manic episodes. The depressive episodes of people with bipolar disorder are symptomatically indistinguishable

from those of people who have unipolar depression, but those with bipolar disorder tend to be less responsive to treatment. Mixed states may occur, with symptoms of both mania and depression.

The rate of cycling between mania and depression varies widely among individuals. One common pattern of illness is for episodes initially to be separated by a relatively long period, perhaps a year, and then to become more frequent with age. A minority of patients with bipolar disorder has four or more cycles per year (Coryell and others 2003). These individuals tend to be more disabled and less responsive to treatment. Once cycles are established, acute relapses may occur without an identifiable precipitant, with the exception of sleep deprivation (Leibenluft and others 1996), making a regular daily sleep schedule and avoidance of shift work important in disease management.

Epidemiology and Burden of Disease

Bipolar disorder has an equal gender ratio. Retrospective reports from community epidemiological surveys consistently show that bipolar disorder has an early age of onset in the late teens through mid-20s. Onset in childhood has been recognized (Geller and Luby 1997), but childhood diagnoses remain controversial; the revision in the recent *Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5)* offers disruptive mood dysregulation disorder as an alternative explanation of severe childhood mood disturbance with temper tantrums (APA 2013).

Epidemiological surveys have consistently found bipolar disorder to be highly comorbid with other psychiatric disorders, especially anxiety and substance use disorders (ten Have and others 2002). The extent of comorbidity is much greater than for unipolar depressive disorders or anxiety disorders. Some individuals with classical symptoms of bipolar disorder also exhibit chronic psychotic symptoms superimposed on their mood syndrome—and are then diagnosed with schizoaffective disorder. Their prognosis tends to be less favorable than for the classical bipolar patient, although somewhat better than for individuals with schizophrenia. Schizoaffective disorder may also be diagnosed when chronic psychotic symptoms are superimposed on unipolar depression. The latter have outcomes similar to patients with schizophrenia (Tsuang and Coryell 1993).

A recent systematic review of 29 epidemiological studies covering 20 countries reported 6- and 12-month point prevalence estimates of bipolar disorder of 0.74 and 0.84 percent, respectively, with no significant differences correlated with gender or economic status (Ferrari, Baxter, and Whiteford 2011). Notably, good evidence exists that bipolar disorder has a wide subthreshold

spectrum that includes people who are often seriously impaired even though they do not meet full *DSM* or International Classification of Diseases criteria for bipolar I or II disorders (Perugi and Akiskal 2002). This spectrum might include as much as 5 percent of the general population. The ratio of recent-to-lifetime prevalence of bipolar disorder in community surveys is quite high (0.71), indicating that bipolar disorder is persistent.

Bipolar disorder is associated with substantial impairments in productive and social roles (Das Gupta and Guest 2002), and there are consistent delays in initially seeking professional treatment (Olfson and others 1998), particularly among early-onset cases, and substantial undertreatment of current cases. Each of these characteristics—chronic, recurrent course; significant impairments to functioning; and modest treatment rates—contributes to the significant disease burden approaching that for schizophrenia.

PSYCHOTIC DISORDERS: SCHIZOPHRENIA

Clinical Features and Course

Schizophrenia is a severe neuropsychiatric syndrome associated with significant lifelong disability as well as premature mortality from suicide and other causes. Schizophrenia exhibits three main symptom domains:

- *Psychotic, or positive, symptoms* include hallucinations and delusions that are generally experienced as having a basis in reality outside the person's psyche.
- *Negative, or deficit, symptoms* include loss of motivation, blunted affect, and impoverishment of thought and language.
- *Cognitive symptoms* include significant impairments in attention, working memory, declarative memory, verbal fluency, and multiple aspects of social cognition. In addition, many individuals with schizophrenia suffer from mood disturbances, usually depression.

Negative and cognitive symptoms, currently untreatable, are highly disabling, in great measure because of a loss of ability to control thought, emotion, and behavior (Lesh and others 2011). Indeed, individuals with schizophrenia remain disabled even when their positive symptoms are well controlled.

Schizophrenia typically begins in the mid-teen years with a prodrome (also described as a psychosis risk state) characterized by significant declines across multiple cognitive domains, social isolation, odd and eccentric thinking, and later by attenuated psychotic symptoms (Fusar-Poli and others 2013). Longitudinal structural magnetic resonance imaging studies suggest

that the prodrome is associated with excessive cortical thinning, especially in prefrontal and temporal cortices (Vidal and others 2006). Abnormal synaptic loss (pruning) beginning in the prodrome is thought to cause significant loss of neural processes and synapses, consistent with the significant observed cognitive impairment (Lesh and others 2011).

The diagnosis of schizophrenia is generally made with a first onset of florid psychotic symptoms. First episodes of schizophrenia generally respond well to antipsychotic drugs, but the response attenuates over time. Ultimately, most patients have residual psychotic symptoms and acute psychotic relapses despite treatment.

The course of schizophrenia, beyond the first psychotic episode, is typically one of relapses of severe psychotic symptoms, followed by partial remission. The time between relapses is extended by maintenance treatment with antipsychotic drugs at lower doses than are needed to treat acute episodes. Cognitive and occupational functioning tend to decline over the first years of the illness and then to plateau at a level well below what would have been expected for the individual (Lesh and others 2011). Nonetheless, residual impairment has substantial cross-cultural variation that is hypothesized to reflect greater maintenance of social integration in societies where outcomes are better.

Based on emerging genetic findings as well as observation of symptom diversity, severity, and treatment response, it is clear that schizophrenia is highly heterogeneous (Ripke and others 2014; Sullivan, Daly, and O'Donovan 2012). Schizophrenia is now seen as a spectrum of disorders that includes both related nonaffective psychoses and likely some affective psychoses, such as schizoaffective disorder, although the *DSM-5* does not yet recognize this breadth (APA 2013).

Epidemiology and Burden of Disease

Schizophrenia affects between 0.5 and 1.0 percent of the population worldwide, with a male-female ratio of 1.4 to 1.0 (McGrath and others 2004). Seven or eight persons per 1,000 are likely to be affected by schizophrenia in their lifetime. Point prevalence is estimated to be 4.6 per 1,000 persons (Saha and others 2005). The incidence rates vary greatly by gender, urban status, and migrant status. A systematic review of 158 studies found a median incidence rate of 15.2 per 100,000 persons, with a 10 and 90 percent quantiles range of 7.7–43.0. The incidence rate was found to be influenced by gender, with a higher incidence in men (median male-female ratio of 1.4 to 1.0, with a 10 and 90 percent quantiles range of 0.9–2.4). And there was a higher incidence in migrants than native-born

individuals (median migrant–native-born incidence rate ratio of 4.6, with a 10 and 90 percent quantiles range of 1.0–12.8) (McGrath and others 2004).

Although schizophrenia is a relatively uncommon disorder, aggregate estimates of disease burden are high because the condition is associated with early onset, long duration, and severe disability. Schizophrenia leads to loss of approximately 1,994 DALYs per one million population (WHO 2014a).

INTERVENTIONS FOR MOOD, ANXIETY, AND PSYCHOTIC DISORDERS

This section updates the evidence contained in *Disease Control Priorities in Developing Countries*, 2nd ed., based on a systematic search of systematic reviews. Where no reviews were found, randomized controlled trials testing the effectiveness of interventions for mood, anxiety, and psychotic disorders were included.

Population Platform Interventions

Mental Health Awareness Campaigns

Awareness campaigns through mass media can be instrumental in reducing prejudice (Clement and others 2013) and improving the use of services (Grilli, Ramsay, and Minozzi 2002). A community-based awareness program in Nigeria was helpful in making mental disorders a priority on the local political agenda (Eaton and Agomoh 2008).

Awareness campaigns must attempt to dispel myths and fight discrimination against people affected by mental disorders while educating and increasing awareness of mental disorders. Interventions based on education and improvement of social contact with persons with mental disorders appear to be the most effective to increase knowledge, reduce stigma, change behavior, and decrease the “desire for social distance” (Evans-Lacko and others 2012; Yamaguchi and others 2013). However, campaigns focused on increasing public understanding of the biological correlates alone may not lead to better social acceptance of people with mental disorders (Schomerus and others 2012). Experience from the mass media interventions in the United Kingdom suggests that it may be helpful to include messages on how to help (Evans-Lacko and others 2010).

Mental Health Legislation

Fewer than half of LMICs have enacted legislation focused on mental health (WHO 2011). Where they exist, mental health laws focus on human rights protection, involuntary admission and treatment, guardianship, freedom

from discrimination, and inspection of institutions. The WHO’s Assessment Instrument for Mental Health Systems (WHO-AIMS) survey in 2009 observed that about 42 percent of all participating low-income countries and 30 percent of the lower-middle-income countries had legislation to protect people with mental disorders against discrimination in employment, compared with 80 percent of upper-middle-income countries (WHO 2009).

By means of action or inaction, legislation can itself contribute to human rights abuses. In the WHO-AIMS survey, LMICs reported higher frequency of involuntary admissions to mental hospitals and other inpatient units, as well as higher incidences of human rights abuses in hospitals and many fewer provisions for inspections of health facilities (WHO 2009).

Community Platform Interventions

Community-based interventions primarily seek to promote health and prevent illness in settings such as workplaces and schools, as well as within families and other community networks.

Workplaces

Workplace attributes related to organizational culture, employment status, exposure to workplace trauma, and job dissatisfaction can contribute to psychosocial risk factors for mood disorders. Although largely drawn from studies in HICs, work-related stress management through physical exercise and cognitive and behavioral approaches such as problem-solving techniques, meditation, and relaxation training can help prevent and improve symptoms of anxiety and depression among employees (Martin, Sanderson, and Cocker 2009; Penalba, McGuire, and Leite 2008). For employees with diagnosed depression, collaboration among all parties dealing with the management of affected employees is important. Provision of integrated care and access to worksite stress reduction programs, with assured confidentiality for the employee, can reduce symptoms of depression (Furlan and others 2012).

Schools

Schools are a good platform for increasing community awareness about mental health. Evidence from a randomized controlled trial in rural Pakistan demonstrated that increasing mental health awareness among school children also increased awareness among parents and neighbors (Rahman and others 1998).

Preventive interventions, such as structured physical activity, delivered in schools can reduce students’ anxiety and improve self-esteem (Bonhauser and others 2005).

Similarly, programs that advance positive thinking have been effective in preventing depression in school children (Yu and Seligman 2002). As in workplace stress reduction programs, psychological and educational counseling can decrease anxiety among students (Sharif and Armitage 2004).

Family

Family interventions through support groups or formal family therapies promote understanding of mental disorders among family members and support positive family environments by reducing overinvolvement and excessive criticism of affected members within families. The ultimate goal is to reduce relapse and hospitalization events in patients and reduce the stress felt by family members living with the patient.

Family interventions—including brief interventions over a limited number of sessions—are effective for schizophrenia (Okpokoro, Adams, and Sampson 2014; Pharaoh and others 2010) and bipolar disorder (Justo, Soares, and Calil 2007). Although there is a relative paucity of high-quality studies on family interventions, it is reasonable to utilize family interventions in the management of psychotic disorders, particularly in LMICs where most people with psychosis stay with families who are also the primary caregivers. Existing interventions can be used with relevant adaptation of the therapies according to the local social and cultural context.

Health Care Platform Interventions

Treatments for Mood and Psychotic Disorders

Self-Care and Management. Self-care enables people living with mental disorders to take the first step in effective prevention and management of their conditions. Systematic reviews suggest that regular exercise promotes physical and mental well-being in individuals with depression (Cooney and others 2013) and psychoses (Gorczynski and Faulkner 2010). Similarly, relaxation techniques (Jorm, Morgan, and Hetrick 2008) and music therapy (Maratos and others 2008) effectively reduce depressive symptoms. The use of media-delivered psychotherapy interventions is effective for self-care in persons with anxiety disorders (Mayo-Wilson and Montgomery 2013). For people with psychotic disorders, education forms a component of self-care: knowing early warning symptoms and signs of bipolar disorder and schizophrenia and their management has been found to improve functioning and delay recurrence, reducing the need for hospitalization (Morriss and others 2007).

Pharmacotherapy and Psychotherapy. Many psychotherapies based on cognitive mechanisms underlying

the symptoms of mood and anxiety disorders have been developed and subjected to well-designed clinical trials that have demonstrated their efficacy for depressive and anxiety disorders (Beck and Haigh 2014). Cognitive remediation therapies for schizophrenia are in the early stages of development, but appear promising.

Table 4.1 reviews the evidence for pharmacotherapy and psychotherapy for mood, anxiety, and psychotic disorders. Although the evidence that strongly supports the efficacy of a range of pharmacological and psychotherapeutic interventions is from HICs, the interventions have been validated in a wide range of cultures, ethnicities, and levels of economic development. However, contextual adaptation of psychosocial interventions should occur routinely. Integration with social welfare departments in LMICs could also be helpful in addressing the burden of life stressors in these settings.

This substantial body of knowledge is relevant for guiding treatment in nonspecialist health care platforms in LMICs and has formed the basis of the recent WHO Mental Health Gap Action Programme (mhGAP) guidelines (WHO 2010). Unfortunately, this information is far too rarely applied in practice (Hyman 2014; Simon and others 2004) despite implementation research in LMICs that has sought to bridge the gap between what we know and what we do. These packages of care are described in the next section.

Specialist Care. Electroconvulsive therapy (ECT) is a well-established, effective, and relatively low-cost therapy for adults with severe or treatment-resistant depression, older people with depression (Martinez-Amoros and others 2012), and acute mania when a patient cannot tolerate medications. ECT must be administered in a clinical setting with the help of qualified personnel to deliver the treatment as well as anesthesia and muscle relaxants. Once symptoms have improved (generally six to eight treatments delivered no more frequently than every other day), the person may receive antidepressant medications. In treatment refractory cases, ECT is also used as a maintenance therapy for depression.

Combined with antipsychotic medications, ECT may also be an option for people with schizophrenia, particularly when rapid global improvement and reduction of symptoms is desired as well as in cases with no response to medications, although it has only short-term benefits (Tharyan and Adams 2005).

Among the newer treatment modalities, transcranial magnetic stimulation, which involves the use of a magnet to stimulate selected areas of the brain, may be effective for refractory depression, but the evidence remains inconclusive. Moreover, it is expensive and limited in scalability because of the need for the appropriate technology.

Table 4.1 Review of Evidence for Pharmacologic and Psychological Treatment of Mood, Anxiety, and Psychotic Disorders

Disorder	First-line treatment	Second-line treatments or adjunct treatment
<i>Mood disorders</i>		
Depressive disorder	<ul style="list-style-type: none"> • Antidepressants: <ul style="list-style-type: none"> • Tricyclic antidepressants and selective serotonin reuptake inhibitors (Silva de Lima and Hotopf 2003; von Wolff and others 2013)^a • Psychotherapy: <ul style="list-style-type: none"> • Brief psychological interventions (Cuijpers and others 2009)^b • Problem-solving therapy (Cuijpers, van Straten, and Warmerdam 2007; Huibers and others 2007)^b • Cognitive behavioral therapy (Orgeta and others 2014; Wilson, Mottram, and Vassilas 2008)^a • Behavioral therapies (Shinohara and others 2013)^a • Psychodynamic therapies (Abbass and others 2014)^a • Interpersonal psychotherapy (de Mello and others 2005)^a 	<ul style="list-style-type: none"> • For postpartum depression: <ul style="list-style-type: none"> • Psychological and social interventions (Dennis and Hodnett 2007)^a • SSRIs, but safety concerns for breastfeeding neonates are not known (Molyneaux and others 2014)^a • For psychotic depression: Combination of an antipsychotic and an antidepressant (Wijkstra and others 2013)^a • For refractory depression: <ul style="list-style-type: none"> • Combined CBT and antidepressant (Wiles and others 2013)^c • Electroconvulsive therapy (Martinez-Amoros and others 2012; UK ECT Review Group 2003)^a • Transcranial magnetic stimulation (Gaynes and others 2014)^a
Notes	<ul style="list-style-type: none"> • Antidepressants are also effective for depression in people with physical illnesses (Rayner and others 2010).^a • Antidepressants can be effectively prescribed in primary care settings (Arroll and others 2009).^a • Problem-solving therapy can be delivered by general practitioners (Huibers and others 2007).^a • Group interpersonal therapy is effective in community-based, low-resource settings (Bass and others 2006).^c • Older tricyclic antidepressants are similar in efficacy to newer drugs, but have greater side effects (Mottram, Wilson, and Strobl 2006).^a • Continuation of treatment with drugs for 9–12 months following response to medication reduces the risk of relapse (Kaymaz and others 2008;^b Wilkinson and Izmeth 2012^a). • Evidence to suggest the superiority of one type of psychological intervention over another is limited (Cuijpers and others 2008;^b Moradveisi and others 2013^c). 	
Bipolar disorder	<ul style="list-style-type: none"> • Combination of second-generation antipsychotics and mood stabilizers for acute mania (Scherk, Pajonk, and Leucht 2007)^a • Lithium, valproate, lamotrigine, and olanzapine for maintenance therapy to prevent relapse (Soares-Weiser and others 2007)^a 	<ul style="list-style-type: none"> • Psychotherapies like CBT, group psychoeducational therapy, and family therapy (Soares-Weiser and others 2007)^a
<i>Anxiety disorders</i>		
Anxiety disorders	<ul style="list-style-type: none"> • Antidepressants (Kapczinski and others 2003)^a 	
Generalized anxiety disorder	<ul style="list-style-type: none"> • CBT-based psychotherapies (Hunot and others 2007)^a 	
Panic disorder	<ul style="list-style-type: none"> • Combined therapy (CBT and antidepressants) or CBT alone (Furukawa, Watanabe, and Churchill 2007)^a 	
Post-traumatic stress disorder	<ul style="list-style-type: none"> • No psychological intervention can be recommended routinely following traumatic events, and this may also have adverse effects on some individuals (Roberts and others 2009). • SSRI antidepressants (Stein, Ipser, and Seedat 2006)^a • CBT (particularly trauma-focused CBT) (Roberts and others 2010) 	<ul style="list-style-type: none"> • Non-trauma focused CBT and eye movement desensitization and reprocessing (Bisson and others 2013)^a

table continues next page

Table 4.1 Review of Evidence for Pharmacologic and Psychological Treatment of Mood, Anxiety, and Psychotic Disorders (continued)

Disorder	First-line treatment	Second-line treatments or adjunct treatment
Notes	<ul style="list-style-type: none"> There is no conclusive evidence of greater effectiveness of combined pharmacotherapy and psychotherapy over either of them alone for PTSD (Hetrick and others 2010).^a 	
<i>Schizophrenia</i>	<ul style="list-style-type: none"> First-generation antipsychotics, such as haloperidol and fluphenazine, for positive symptoms (Tardy, Huhn, Engel, and Leucht 2014; Tardy, Huhn, Kissling, and Leucht 2014)^a Combination of antipsychotics and antidepressants is effective for negative symptoms (Rummel, Kissling, and Leucht 2006).^a Second-generation antipsychotics (amisulpride, clozapine, olanzapine, and risperidone). These are superior to first-generation antipsychotics in efficacy and have different side-effect profiles (Leucht and others 2009).^a 	<ul style="list-style-type: none"> CBT as adjunctive treatment for positive symptoms (Zimmermann and others 2005)^b Cognitive remediation therapies, in early stages of the disorder (Fisher and others 2013)^d Psychoeducation reduces relapse, readmission, and length of hospital stay while encouraging medication compliance (Xia, Merinder, and Belgamwar 2011).^a Psychosocial interventions for reducing the need for antipsychotic medications (Richter and others 2012)^a Clozapine for refractory schizophrenia but needs monitoring for side effects (Essali and others 2009)^a
Notes	<ul style="list-style-type: none"> Continued antipsychotic medication following a clinical response helps prevent relapse (Leucht and others 2012; Sampson and others 2013).^a Acetylcholinesterase inhibitors are effective to overcome anticholinergic side effects of antipsychotic drugs (Leucht and others 2012).^a Evidence for clear and convincing advantage for CBT over other therapies is limited (Jones and others 2012).^a 	

Note: CBT = cognitive behavioral therapy; PTSD = post-traumatic stress disorder; SSRI = selective serotonin reuptake inhibitor.

a. Systematic review.

b. Meta-analysis.

c. Randomized controlled trials in low- and middle-income countries.

d. Review.

Persons with severe mental illnesses occasionally require short periods of hospitalization and/or longer-term supported housing because of the severity of their disorders and associated behaviors or abandonment by family. Systematic reviews have suggested that acute day hospitals can be as effective as inpatient care (Marshall and others 2011) and that day hospitals may prevent the need for inpatient care (Shek and others 2009).

Occupational Therapy. Occupational therapy interventions aim to support and improve skills for daily living through life skills training, cognitive rehabilitation, supportive employment and education, and social and interpersonal skills training. Occupational therapy is effective in rehabilitating persons with depression by increasing productivity, reducing work-related stress, and helping in recovery (Hees and others 2013; Schene and others 2007). Supported employment is effective in improving a number of vocational outcomes in persons

with severe mental illnesses (Kinoshita and others 2013). Systematic reviews have shown that life skills and social skills training have moderate to strong effectiveness to promote integration of persons with severe mental illnesses in communities where they live; and interventions with a greater client-centered approach have a larger impact (Gibson and others 2011).

Packages of Care

Promotion and Prevention. Indicated or targeted prevention of mental disorders is effective in the early and subclinical stages. A meta-analysis of 32 studies (largely from Europe and the United States) concluded that preventive interventions could lower the incidence of depression by 21 percent through psychological interventions such as cognitive behavioral therapy (CBT), interpersonal therapy, individual counseling, and group sessions (van Zoonen and others 2014). Psychological treatment of subclinical

depression was shown to have some effect in preventing the onset of major depression after six months (Cuijpers and others 2014).

For people with early psychosis, early intervention services (including CBT and family interventions) appear to have clinically important benefits over standard care, but the longer-term benefits of this approach remain unclear (Bird and others 2010; Marshall and Rathbone 2011). Specifically designated early intervention teams are in place in many HICs, but LMICs have few programs and no formal evaluations.

Case Detection and Diagnosis. The WHO advocates symptom-based algorithms for the detection of mental disorders by nonspecialized health care providers in general medical service settings (WHO 2008, 2010). Cultural influence on the clinical presentation of mental disorders should be accounted for in case detection and screening programs. For example, the inclusion of unexplained somatic symptoms in screening for anxiety and depression might improve case detection in LMICs. Training and screening for detection of mood and anxiety disorders in primary care settings are being implemented globally; however, screening must be accompanied by health system changes to ensure clinical benefits for patients by allowing sustained access to evidence-based treatments (Gilbody, House, and Sheldon 2005; Kauye, Jenkins, and Rahman 2014; Patel and others 2009).

When appropriately trained, health workers can identify probable cases of rare disorders such as schizophrenia, although community case-finding should be confirmed with diagnostic interviews (de Jesus and others 2009).

Collaborative and Stepped Care. Collaborative care is an approach to the care of chronic illnesses that has been successfully implemented for management of mental disorders in primary care. These models emphasize self-care and care management, blended with other pharmacotherapeutic, psychotherapeutic and specialist care interventions, and community supports. Specifically, the model adopts a patient-centric approach and includes active collaboration with mental health professionals, so that patients with severe disorders receive specialist intervention.

Collaborative care for depression and anxiety disorders is associated with significant improvement in clinical outcomes and leads to improvement in adherence, patient satisfaction, and mental health quality of life (Archer and others 2012; Patel and others 2009). Collaborative care can also be effective for severe mental illnesses (Reilly and others 2013), as demonstrated in

a randomized controlled trial in India (Chatterjee and others 2014).

Key principles of the collaborative model include proactive case detection; a structured management plan; patient education; systematic monitoring and follow-up; and close collaboration among the patient, a case manager, primary care providers, and specialists. Successful implementation of such a model, however, depends on trained primary care staff, clear protocols and guidelines, and specialist supervision and support in the implementation of the guidelines (Patel and others 2013). Notably, the case manager's role is critical: this person acts as the link between the patient or the patient's family, the primary care physician, and the specialist, and undertakes proactive case detection, monitors progress, and provides psychosocial interventions and adherence support (if medication is prescribed). The case manager could also be an appropriately trained and supervised lay counselor or community health worker. Compelling evidence from LMICs suggests that community health workers, nonspecialized health workers, and paraprofessionals, based in primary care or community settings, can detect cases (Patel and others 2008) and effectively deliver psychosocial interventions for depressive disorder, postpartum depression, and PTSD (den Boer and others 2005; van Ginneken and others 2013).

Community Outreach for Severe Mental Disorders. The WHO's mhGAP intervention guidelines for providing mental health care in nonspecialized settings in LMICs explicitly include revival of social networks and participation in community activities as a part of treatment and care for patients with depression, anxiety, and psychosis (WHO 2010).

Community mental health teams that include outreach workers can effectively manage severe mental illnesses with greater acceptance and fewer hospital admissions and suicides (Malone and others 2007). A systematic review of trials from HICs suggests that intensive case management, based on an assertive community care model that involves providing community-based care for people with severe mental illnesses, focusing on the health and social care needs of the patients by a team of trained health workers, leads to a reduced need for hospitalization, increased retention in care, and improved social functioning (Dieterich and others 2010). Randomized controlled trials in the United Kingdom also show that crisis interventions delivered by a trained team can provide acceptable care to people with severe mental illnesses during the crisis phase, improve short-term mental health outcomes, reduce repeat admissions, and provide greater satisfaction for patients and families (Murphy and others 2012).

Longitudinal studies from India have observed that community-based rehabilitation for people with psychotic disorders have a beneficial impact on disability (Chatterjee and others 2009). Recently published results from a clinical trial in India also suggest that community-based care along with facility-based care is more effective than facility-based care alone for reducing disability and symptoms due to psychoses (Chatterjee and others 2014). Close participation of families, community members, and local health providers, in concert with continuous treatment, form the foundation of community-based care and rehabilitation. Activities to facilitate economic and social rehabilitation (Chatterjee and others 2003)—such as supported housing for people with severe mental illnesses (Chilvers, Macdonald, and Hayes 2006) and vocational rehabilitation (Crowther and others 2001)—are effective in promoting rehabilitation of people with severe mental disorders.

Information and Communication Packages. Information and communications technology (ICT) is emerging as a promising tool for providing care for people with mental disorders. The diverse technologies under this umbrella, along with the considerable presence of mobile phones and Internet access in most LMICs, make outreach and delivery of personalized interventions feasible. These technologies can also be effectively used to deliver interventions for self-care. Telemedicine is effective in reaching out to rural and remote areas (Pyne and others 2010), and can be provided effectively for the management of anxiety, depression, and psychotic disorders (Thara, John, and Rao 2008). Telephones and other Internet-based applications can be used to deliver health messages and prompts and peer support interventions, as well as evidence-based psychotherapies such as cognitive behavior therapy (Andersson and Cuijpers 2009).

COST-EFFECTIVENESS OF INTERVENTIONS

The preceding review reveals a diverse array of intervention approaches and models that can be utilized at different levels of the health (and welfare) system for the prevention and management of adult mental disorders, and includes an increasing body of evidence from and for settings in LMICs. However, the availability of cost-effectiveness information to complement this large and growing evidence base on effectiveness remains comparatively sparse. There is currently no cost-effectiveness evidence from LMICs relating to mental health awareness campaigns, family interventions, or use of ICT for early detection or treatment.

However, a few clinical trials have been conducted in LMICs that included an economic evaluation. These demonstrated not only the feasibility, but also the informational value of such analyses (Araya and others 2006; Buttorff and others 2012; Patel and Kleinman 2003). Explaining that a depression-free day could be gained for the price of a bus ticket, for example, was a helpful argument in the roll-out of depression care in Chile (Araya and others 2006). In India, the MANAS (MANashanti Sudhar Shodh, or project to promote mental health) trial showed that a task-shifting intervention for common mental disorders was not only cost-effective, but also cost-saving when time costs were taken into consideration (Buttorff and others 2012).

Partly because of the lack of available primary data, several cost-effectiveness modeling studies have been conducted, at the national and international levels. These studies, which rely on secondary data to generate estimates of expected cost and health gain, are reviewed in chapter 12 in this volume (Levin and Chisholm 2015). Overall, the studies indicate that, depending on the particular context and content of the interventions, cost-effectiveness ranges between US\$100 and US\$2,000 per healthy life year gained. Chapter 13 in this volume (Chisholm and others 2015) applies an extended cost-effectiveness analysis approach to several adult mental disorders (psychosis, bipolar disorder, and depression) to assess the distribution of costs and health gains across different income groups in the population, as well as the financial protection effects of scaled-up care and treatment. The analysis indicates that universal public finance can lead to a far more equitable allocation of public health resources, with lower-income groups benefitting most from enhanced financial protection (Chisholm and others 2015).

CONCLUSIONS AND RECOMMENDATIONS

Mood disorders, anxiety disorders, and psychotic disorders are a diverse group of adult mental disorders that are highly disabling and are caused by a complex interaction of genetic, developmental, and environmental risk factors. These disorders are highly stigmatized in most countries and cultures and often lead to shame and fear of rejection and discrimination.

The good news is that awareness campaigns, particularly those involving engagement with people with mental disorders, can improve general knowledge about these disorders. Appropriate legislation also can address the discrimination and human rights abuses that result from social stigma. On the whole, however, these interventions remain inadequately disseminated and implemented.

Since the mid-20th century, many medications have been discovered and psychotherapies have been validated for the treatment of mental disorders. In the context of the disorders addressed in this chapter, notable examples of pharmacotherapies are antidepressants, antipsychotics, and mood stabilizers. Notable examples of psychotherapies are brief treatments based on cognitive, behavioral, and interpersonal approaches. Collaborative care models with appropriately trained and supervised nonspecialist frontline workers can effectively deliver evidence-based packages, often constituting a combination of drug or psychological treatments as needed, with the active participation of the patient and family. These pharmacotherapies and psychotherapies have been validated across a wide range of cultures, ethnicities, and stages of economic development. There is clear evidence that these can be delivered successfully in resource-poor settings.

Families are traditionally closely involved in the care of persons with mental disorders in LMICs and should be considered important partners in treatment and rehabilitation. Occupational therapy and community-based rehabilitation are extremely important for providing those suffering from mental disorders with opportunities to live engaged, productive lives.

Even so, the treatment gap for mental disorders remains significant around the world. It is particularly large in LMICs, whose weaker health systems and fewer resources—financial and human—for mental health services limit the options for care. Although there are several potential innovations to reduce the costs and improve access to care, for example through task-sharing and use of ICT (Patel and Saxena 2014), the most urgent need of all is increased financial investment and political will to integrate mental health at all levels of the health care system in LMICs.

NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - a) lower-middle-income = US\$1,046 to US\$4,125
 - b) upper-middle-income (UMICs) = US\$4,126 to US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

1. The 17 countries participating in the WMH surveys are Belgium, China, Colombia, France, Germany, Israel, Italy, Japan, Lebanon, Mexico, the Netherlands, New Zealand, Nigeria, South Africa, Spain, Ukraine, and the United States.

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