Chapter **31**

Mental Disorders

Steven Hyman, Dan Chisholm, Ronald Kessler, Vikram Patel, and Harvey Whiteford

Mental disorders are diseases that affect cognition, emotion, and behavioral control and substantially interfere both with the ability of children to learn and with the ability of adults to function in their families, at work, and in the broader society. Mental disorders tend to begin early in life and often run a chronic recurrent course. They are common in all countries where their prevalence has been examined. Because of the combination of high prevalence, early onset, persistence, and impairment, mental disorders make a major contribution to total disease burden. Although most of the burden attributable to mental disorders is disability related, premature mortality, especially from suicide, is not insignificant. Table 31.1 summarizes discounted disability-adjusted life years (DALYs) for selected psychiatric conditions in 2001.

Mental disorders have complex etiologies that involve interactions among multiple genetic and nongenetic risk factors. Gender is related to risk in many cases: males have higher rates of attention deficit hyperactivity disorder, autism, and substance use disorders; females have higher rates of major depressive disorder, most anxiety disorders, and eating disorders. Biochemical and morphological abnormalities of the brain associated with schizophrenia, autism, mood, and anxiety disorders are being identified using approaches such as postmortem analysis and noninvasive neuroimaging. Major worldwide efforts under way to identify risk-conferring genes for mental disorders are proving challenging, but initial results are promising. Identifying the gene or genes causing or creating vulnerability for a disorder should help us understand what goes wrong in the brain to produce mental illness and should have a clinical effect by contributing to improved diagnostics and therapeutics (Hyman 2000).

Twin studies make it clear that environmental risk factors also play an important role in mental disorders; concordance for disease among identical twins, although substantially higher than among nonidentical twins, is still well below 100 percent (Kendler and others 2003). However, as is the case for genetic factors, investigation of environmental risk factors has proved difficult. For schizophrenia, where nongenetic components of risk may include obstetrical complications and season of birth (Mortensen and others 1999), perhaps as a proxy for infections early in life, research has been hampered by the modest proven effect of the nongenetic risk factors identified to date. For depression, anxiety, and substance use disorders, where environmental risk factors are more robust, adverse circumstances associated with risk, such as early childhood abuse, violence, poverty, and stress (Patel and Kleinman 2003) correlate with multiple disorders and could be affected by selection bias as well as by bias associated with self-reporting. Generalizable, prospective cross-cultural studies are needed to delineate nongenetic risk factors more clearly. Posttraumatic stress disorder (PTSD) is the mental disorder for which clear environmental triggers are best documented. Even here, though, enormous interindividual variability occurs in the threshold of stress severity associated with PTSD as well as in the evidence from twin studies of genetic influences on stress reactivity in triggering PTSD.

The last half of the 20th century saw enormous progress in the development of treatments for mental disorders. Beginning in the early 1950s, effective psychotropic drugs were discovered that treated the symptoms of schizophrenia, bipolar disorder, major depression, anxiety disorders, obsessive-compulsive disorder, attention deficit hyperactivity disorder, and others. The safety and efficacy of antipsychotic, mood-stabilizing,

Table 31.1 Disease Burden of Selected Major Psychiatric Disorders, by World Bank Region

	World Bank region							
	Sub-Saharan Africa	Latin America and the Caribbean	Middle East and North Africa	Europe and Central Asia	South Asia	East Asia and the Pacific	High-income countries	World
Total population (millions)	668	526	310	477	1,388	1,851	929	6,159
Total disease burden (thousands of DALYs)	344,754	104,287	65,570	116,502	408,655	346,941	149,161	1,535,870
Total neuropsychiatric disease burden (thousands of DALYs)	15,151	18,781	8,310	14,106	37,734	42,992	31,230	168,304
Total burden (thousands of discounted DALYs per year)								
Schizophrenia	1,146	1,078	696	778	2,896	3,934	1,115	11,643
Bipolar disorder	1,204	883	567	668	2,237	3,118	1,056	9,733
Depression	3,275	5,219	2,027	4,268	14,582	14,054	8,408	51,833
Panic disorder	519	409	264	340	1,081	1,401	536	4,550
Total burden (DALYs per year per 1 million population)								
Schizophrenia	1,716	2,049	2,247	1,630	2,087	2,126	1,201	1,894
Bipolar disorder	1,803	1,678	1,830	1,400	1,612	1,685	1,137	1,583
Depression	4,905	9,919	6,544	8,944	10,507	7,594	9,054	8,431
Panic disorder	777	777	852	713	779	757	577	740
Percentage of total disease burden								
Schizophrenia	0.33	1.03	1.06	0.67	0.71	1.13	0.75	0.76
Bipolar disorder	0.35	0.85	0.86	0.57	0.55	0.90	0.71	0.63
Depression	0.95	5.00	3.09	3.66	3.57	4.05	5.64	3.37
Panic disorder	0.15	0.39	0.40	0.29	0.26	0.40	0.36	0.30
Percentage of neuropsychiatric disease burden								
Schizophrenia	7.56	5.74	8.38	5.52	7.67	9.15	3.57	6.92
Bipolar disorder	7.95	4.70	6.82	4.74	5.93	7.25	3.38	5.78
Depression	21.62	27.79	24.39	30.26	38.64	32.69	26.92	30.80
Panic disorder	3.43	2.18	3.18	2.41	2.86	3.26	1.72	2.70

Source: WHO Global Burden of Disease 2001 estimates recalculated by World Bank region (http://www.fic.nih.gov/dcpp/gbd.html).

antidepressant, anxiolytic, and stimulant drugs have been established through a large number of randomized clinical trials. Psychosocial treatments have been developed and tested using modern methodologies. Brief, symptom-focused psychotherapies such as cognitive-behavioral therapies have been shown to be efficacious for panic disorder, phobias, obsessive-compulsive disorder, and major depression.

There is, however, an important caveat about the current knowledge base for treatment. As is the case for almost all of medicine, randomized clinical trials have been performed largely with highly selected populations in specialized research settings in industrial countries. A need exists to subject existing treatments to effectiveness trials in more representative populations and diverse settings, especially in developing countries. That limitation notwithstanding, a substantial body of knowl-

edge exists to guide treatment. It is particularly unfortunate, therefore, that timely diagnoses and the application of research-based treatments significantly lag behind the state of knowledge in industrial and developing countries alike. As a result, substantial opportunities exist to decrease the enormous burden attributable to mental disorders worldwide by closing the gap between *what we know* and *what we do.*

Mental disorders are stigmatized in many countries and cultures (Weiss and others 2001). Stigma has been facilitated by the slow emergence of convincing scientific explanations for the etiologies of mental disorders and by the mistaken belief that symptoms are caused by a lack of will power or reflect some moral taint. Recent scientific findings combined with educational efforts in some countries have begun to reduce the stigma (Rahman and others 1998), but shame and fear associated with

mental illness remain substantial obstacles to help seeking, to diagnosis, and to treatment worldwide. The stigmatization of mental illness has resulted in disparities, compared with other illnesses, in the availability of care, in research, and in abuses of the human rights of people with these disorders.

This chapter focuses on the attributable and avoidable burden of four leading contributors to mental ill health globally: schizophrenia and related nonaffective psychoses, bipolar affective disorder (manic-depressive illness), major depressive disorder, and panic disorder. The choice of these disorders is determined not only by their contribution to disease burden, but also by the availability of data for the cost-effectiveness analyses. Even where such data are available, they are often from industrial countries and extrapolation has been necessary. The exclusion of other mental disorders, such as childhood disorders, from analysis is not because the authors consider these disorders unimportant but because of the paucity of data. Also, this chapter does not specifically deal with the important issue of suicide. A background paper on suicide in developing countries has been developed as part of the Disease Control Priorities Project (DCPP) and is available (Vijayakumar, Nagaraj, and John 2004). The economic analysis presented in this chapter uses the cost-effectiveness analysis methodology specifically developed for the DCPP. The authors recognize that mental disorders impose costs and burdens on families as well as individuals that are not captured by the DALY. Treatment will alleviate some of this burden in addition to alleviating symptoms and disability.

A description of the major clinical features, natural course, epidemiology, burden, and treatment effectiveness for each group of disorders is given in the next section. For diagnostic criteria, readers are referred to *The ICD-10 Classification of Mental and Behavioral Disorders* (ICD-10) (WHO 1992) or *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IVTR) (American Psychiatric Association 2000). A discussion follows of population-level costs and cost-effectiveness of interventions capable of reducing the current burden associated with four disorders in different developing regions of the world (tables 31.2–31.6), before moving to a discussion of key issues and implications for mental health policy and improvement of services in developing regions of the world.

SCHIZOPHRENIA AND NONAFFECTIVE PSYCHOSES

Schizophrenia is a chronic disorder punctuated by episodes of florid psychotic symptoms, such as hallucinations and delusions. Hallucinations are sensory perceptions that occur in the absence of appropriate stimuli. Hallucinations may occur in any sensory modality but in schizophrenia are most commonly auditory—for example, hearing voices or noises. Delusions are fixed false beliefs that are not explained by the person's culture and that the patient holds despite all reasonable evidence to the contrary.

Patients also exhibit *negative symptoms*—that is, deficits in normal capacities, such as marked social deficits, impoverishment of thought and speech, blunting of emotional responses, and lack of motivation. Additionally, patients typically have cognitive symptoms, such as disorganized or illogical thinking and an inability to hold goal information in mind to make decisions or plan actions.

Natural History and Course

Schizophrenia, as defined in current diagnostic manuals, is almost certainly heterogeneous, but still does not comprise all nonaffective psychoses (NAPs). In addition to schizophrenia, NAPs include schizophreniform disorder, characterized by schizophrenia-like symptoms of inadequate duration to qualify as schizophrenia. Because they cannot be readily disentangled in community epidemiological surveys, schizophrenia and other NAPs are considered together. Because of the data available, however, the cost-effectiveness analyses reported below are restricted to schizophrenia. Despite likely etiological heterogeneity, schizophrenia exhibits consistency in its symptom pattern across those countries and cultures studied (Jablensky and others 1992).

Incidence studies show that onset of schizophrenia and other NAPs is typically in middle to late adolescence for males and late adolescence to early adulthood for females, although later onsets are observed. Childhood-onset cases are quite rare but particularly severe (Nicolson and Rapoport 1999). Often, schizophrenia is first diagnosed with the occurrence of an acute episode of florid psychotic symptoms. The first psychotic episode is often preceded by prodromal symptoms such as social withdrawal, irritability or dysphoria, increasing academic or work-related difficulties, and increasing eccentricity. However, such symptoms are not specific; studies of whether early diagnosis and intervention can improve outcomes are under way (McGorry and others 2002).

The course of schizophrenia is typically one of acute exacerbations of severe psychotic symptoms, followed by full or partial remission. Psychotic episodes may be followed by a full remission after the first and occasionally other early episodes, but over time, residual symptoms and disability typically continue between relapses (Robinson and others 1999). The time between relapses is markedly extended by maintenance treatment with antipsychotic drugs, generally at lower doses than are needed to treat acute episodes. Cognitive and occupational functioning tends to decline over the first years of the illness and then to plateau at a level that is generally well below what would have been expected for the individual. Residual impairment, though, has substantial cross-cultural variation for reasons that are not well understood. Schizophrenia has consistently been found in epidemiological surveys to be highly

comorbid, usually with anxiety disorders, mood disorders, and substance use disorders (Kendler and others 1996).

Epidemiology and Burden

A great many studies of NAP incidence have been carried out in clinical samples. In a review of these studies, Jablensky (2000) found incidence estimates to be in the range of 0.002 to 0.011 percent per year for schizophrenia and 0.016 to 0.042 percent per year for overall NAP. Those annual estimates can be multiplied by the number of birth cohorts at risk to yield an estimate of lifetime risk in any one cohort. Assuming conservatively that the main age range of risk is between ages 15 and 55, researchers estimate lifetime risk is in the range of 0.08 to 0.44 percent for schizophrenia and in the range of 0.64 to 1.68 percent for NAPs. Lifetime prevalence estimates from community epidemiological surveys of NAPs are quite consistent with those from clinical studies, in the range of 0.3 to 1.6 percent (see, for example, Hwu, Yeh, and Cheng 1989; Kendler and others 1996).

Although schizophrenia is a relatively uncommon disorder, aggregate estimates of disease burden are high—around 2,000 DALYs lost per 1 million total population (table 31.1)—because the condition is associated with early onset, long duration, and severe disability.

Interventions

A substantial body of evidence exists on the efficacy of various treatments for schizophrenia and NAP and on the effectiveness of various models of health care delivery for persons with these disorders. This evidence comes primarily from industrial countries. The efficacy data show conclusively that antipsychotic drugs reduce severity of the episodes, hasten resolution of florid symptoms, and reduce duration of hospitalization. Maintenance treatment with antipsychotic drugs prolongs the period between relapses (Joy, Adams, and Lawrie 2001).

A second generation of antipsychotic medications (also called *atypical*) is replacing older *neuroleptic* antipsychotic drugs throughout the industrial world. In some clinical trials, second-generation drugs show small advantages in efficacy over first-generation drugs, but their widespread adoption results from marked improvement in tolerability. Their relative lack of side effects compared with first-generation drugs has led to improved quality of life and improved treatment adherence. Second-generation drugs are not without side effects, however; for example, some are associated with substantial weight gain and increased risk of diabetes. One drug, clozapine, has greater efficacy than other antipsychotic drugs, but because of a 1 percent risk of agranulocytosis, its use requires weekly blood counts and is cumbersome and expensive.

Psychosocial interventions also play an important role in managing schizophrenia (Bustillo and others 2001). Cognitive-behavioral approaches to managing specific symptoms and improving medication adherence, group therapy, and family interventions all have demonstrated efficacy in improving clinical outcomes. Community-based models of mental health care delivery with case management and assertive outreach programs have been shown in health systems of industrial countries to be effective ways of managing schizophrenia in the community, for example, by reducing the need for hospital admissions. However, the applicability of these models to developing countries, as is discussed later, is hard to estimate because of differences in health system characteristics. Long-term remission rates for schizophrenia in developing countries appear to be significantly higher than those reported in industrial countries (Harrison and others 2001), likely resulting from such factors as strong family social support.

Despite their clear usefulness, current treatments do not prevent schizophrenia, and no clear evidence demonstrates that they induce full recovery or prevent premature mortality. Instead, treatment reduces time in episode of florid psychosis and increases time between episodes; thus treatment effects can be understood in terms of improvements in disability. Reported treatment effect sizes from meta-analyses in the literature, converted into improvements in the average level of disability (Andrews and others 2003; Sanderson and others 2004), show improvements (compared with no treatment) of 18 to 19 percent (antipsychotic drugs alone) and 30 to 31 percent (antipsychotic drugs with adjunctive psychosocial treatment). Placed on a disability scale of 0 to 1, where 0 equals no disability, an "average" case of schizophrenia moves from a disability level of 0.63 (untreated weight from the Global Burden of Disease study, Murray and Lopez 1996) to 0.43 to 0.54 (treated).

MOOD DISORDERS

The cardinal features of mood disorders are pervasive abnormalities in the predominant emotional state of the person, such as depressed, elated, or irritable. In mood disorders, these core emotional symptoms are accompanied by abnormalities in physiology, such as changes in patterns of sleep, appetite, and energy, and by changes in cognition and behavior. In developing countries, concurrent somatic symptoms are also commonly reported and may be the chief complaint. A generally accepted subclassification of mood disorders distinguishes unipolar depressive disorders from bipolar disorder (defined by the occurrence of mania). This distinction is based on symptoms, course of illness, patterns of familial transmission, and treatment response.

Bipolar Disorder

Bipolar disorder is characterized by episodes of mania and depression, often followed by relative periods of healthy mood

(euthymia). Mixed states with symptoms of both mania and depression also occur. Mania is typically characterized by euphoria or irritability, a marked increase in energy, and a decreased need for sleep. Individuals with mania often exhibit intrusive, impulsive, and disinhibited behaviors. They may be excessively involved in goal-directed behaviors characterized by poor judgment; for example, a person might spend all funds to which he or she has access and more. Self-esteem is typically inflated, frequently reaching delusional proportions. Speech is often rapid and difficult to interrupt. Individuals with mania also 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 who have unipolar depressions alone. Unlike anxiety and unipolar mood disorders, which are more common in women, bipolar disorder has an equal gender ratio of lifetime prevalence, although the ratio of depressive-to-manic episodes is higher among bipolar women than men.

Natural History and Course. 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 is increasingly recognized, although it remains controversial. Late onset is less common. The vast majority of patients with bipolar disorder have recurrent episodes of illness, both mania and depression. Classic descriptions of bipolar disorder suggest recovery to baseline functioning between episodes, but many patients have residual symptoms that may cause significant impairment (Angst and Sellaro 2000). These states of mania, depression, and lesser (or absent) symptoms are used in the intervention analysis below.

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 four or more cycles per year, termed *rapid cyclers,* tend to be more disabled and less responsive to existing treatments. Once cycles are established, most acute episodes start without an identifiable precipitant; the best documented exception is that manic episodes may be initiated by sleep deprivation, making a regular daily sleep schedule and avoidance of shift work important in management (Frank, Swartz, and Kupfer 2000).

Bipolar disorder has consistently been found in epidemiological surveys 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 classic symptoms of bipolar

disorder also exhibit chronic psychotic symptoms superimposed on their mood syndrome. These individuals are said to have schizoaffective disorder. Their prognosis tends to be less favorable than for the usual 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. Individuals with this combination of symptoms have outcomes similar to patients with schizophrenia (Tsuang and Coryell 1993).

Epidemiology and Burden. Lifetime and 12-month prevalence estimates of bipolar disorder have been reported from a number of community psychiatric epidemiological surveys. Lifetime prevalence estimates are in the range 0.1 to 2.0 percent (Vega and others 1998; Vicente and others 2002), with a weighted mean across surveys of 0.7 percent. Prevalence estimates for past-year episodes have a similarly wide range (0.1 to 1.3 percent) (Vega and others 1998) and a weighted mean of 0.5 percent. It is important to note that good evidence exists suggesting 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 ICD criteria for the disorder (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.

Epidemiological data show that bipolar disorder is associated with substantial impairments in both productive and social roles (Das Gupta and Guest 2002). Epidemiological evidence documents consistent delays in patients initially seeking professional treatment (Olfson and others 1998), especially among early-onset cases, as well as substantial undertreatment of current cases. Each of these characteristics—chronic, recurrent course; significant impairments to functioning; modest treatment rates—contributes to estimates of aggregate disease burden that approach those for schizophrenia (1,200 to 1,800 DALYs lost per 1 million population, making up more than 5 percent of the burden attributable to neuropsychiatric disorders as a whole—see table 31.1).

Interventions. Analyses of the primary treatment approaches for bipolar disorder are based on the three health states that characterize the disorder—mania, depression, and euthymia. Robust evidence from controlled trials shows that antipsychotic drugs and some benzodiazepines produce a relatively rapid reduction in symptoms of a manic phase. Mood-stabilizing drugs act more slowly, but they reduce the severity and duration of acute manic episodes. Maintenance treatment with two mood-stabilizing drugs—lithium and valproic acid (administered as sodium valproate)—has been shown to have

significant, albeit partial, efficacy in reducing rates of both manic and depressive relapses. The drawback of lithium is that toxic levels are not much greater than therapeutic levels; thus, serum-level monitoring is required.

For the cost-effectiveness analyses, lithium and valproic acid, which have empirical data supporting their efficacy in treating and preventing manic and depressive episodes, were considered. Because evidence suggests that psychosocial approaches enhance compliance with medication (Huxley, Parikh, and Baldessarini 2000), adjuvant strategies also were assessed. The primary treatment effect was a change in the population-level disability associated with bipolar disorder (a weighted average of time spent in a manic, depressed, or euthymic phase of illness). Both an acute treatment effect—calculated as the product of initial response and reduced episode duration—and a prophylactic treatment effect were ascribed to lithium and valproic acid, resulting in an estimated improvement of close to 50 percent over the untreated composite disability weight of 0.445 (Chisholm and others forthcoming). This estimate then was adjusted for expected nonadherence to treatment in real-world clinical settings—slightly lower for lithium than for valproic acid (Bowden and others 2000). A secondary effect of treatment—reduction of the case fatality rate by two-thirds—was also ascribed to lithium, though, because of an absence of current evidence, not to valproic acid (Goodwin and others 2003). This reduction was derived through a change in the standardized mortality ratio from 2.5 to 1.5, estimated on the basis of natural history studies reported for the prelithium era (for example, Astrup, Fossum, and Holmboe 1959; Helgason 1964) to the postlithium era (for example, Goodwin and others 2003).

Major Depressive Disorder

The core symptom of major depression is a disturbance of mood; sadness is most typical, but anger, irritability, and loss of interest in usual pursuits may predominate. Often the affected person is unable to experience pleasure (anhedonia) and may feel hopeless. In many countries of the developing world, patients will not complain of such emotional symptoms, but rather of physical symptoms, such as fatigue or multiple aches and pains.

Typical physiological symptoms that occur across cultures include 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. Behaviorally, some individuals with depression exhibit slowed motor movements (psychomotor retardation), whereas others may be agitated. Cognitive symptoms may include thoughts of worthlessness and guilt, suicidal thoughts, difficulty concentrating, slow thinking, and poor memory. Psychotic symptoms occur in a minority of cases.

Natural History and Course. Major depression is an episodic disorder that generally begins early in life (median age of onset in the mid to late 20s in community epidemiological surveys), 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 clear depressive disorder. Most individuals suffering from a depressive episode will have a recurrence (Mueller and others 1999), with recurrence risk greater among those with early-onset disease. Many individuals do not recover completely from their acute episodes and have chronic milder depression punctuated by acute exacerbations (Judd and others 1998). The current term for chronic, milder depression lasting more than two years is *dysthymia*. Although the symptoms of minor depression are, by definition, less severe than those of a major depressive episode, chronicity ultimately makes even this lesser form of the illness very disabling in many cases (Judd, Schettler, and Akiskal 2002). Depression has consistently been found in epidemiological surveys to be highly comorbid with other mental disorders, with roughly half the people who have a history of depression also having a lifetime anxiety disorder. Comorbidities of depression and anxiety disorders are generally strongest with generalized anxiety disorder and panic disorder (Kessler and others 1996).

Epidemiology and Burden. Prevalence of nonbipolar depression has been estimated in a number of large-scale community epidemiological surveys. Lifetime prevalence estimates of having either major depressive disorder or dysthymia in these surveys are in the range 4.2 to 17.0 percent (Andrade and others 2003; Bijl and others 1998), with a weighted mean of 12.1 percent. Six- to 12-month prevalence estimates have a similarly wide range (1.9 to 10.9 percent) (Andrade and others 2003; Robins and Regier 1991), with a weighted mean of 5.8 percent. These wide differences in prevalence likely represent the difficulties inherent in self-reporting of conditions that are invariably stigmatized across cultures. Prevalence estimates are consistently highest in North America and lowest in Asia (with prevalence estimates of major depressive disorders generally a good deal higher than those of dysthymia).

Epidemiological data document consistent delays in patients initially seeking professional treatment for depression, especially among early-onset cases (Olfson and others 1998), as well as substantial undertreatment. For example, World Mental Health surveys in six Western European countries found that only 36.6 percent of people with active nonbipolar depression in the 12 months before the survey received any professional treatment for this disorder during the subsequent year

(ESEMeD/MHEDEA 2000 Investigators 2004). The situation is even worse in developing countries, where the vast majority of people with depression who seek help do so in general health care settings and complain of nonspecific physical symptoms. Such individuals receive a correct diagnosis in less than one-quarter of cases and typically are treated with medicines of doubtful efficacy (Linden and others 1999).

Depression is consistently found in community surveys to be associated with substantial impairments in both productive and social roles (Wang, Simon, and Kessler 2003). As with bipolar depression, but exacerbated by its high incidence, the recurrent nature and disabling consequences of (unipolar) depression mean that overall disease burden estimates are high in all regions of the world (5,000 to 10,000 DALYs per 1 million population, as much as 5 percent of the total burden of disease from all causes; table 31.1). Depression is, in fact, ranked as the fourth leading cause of disease burden globally and represents the single largest contributor to nonfatal burden (Ustun and others 2004).

Interventions. Efficacy has been demonstrated for several classes of antidepressant drugs and for two psychosocial treatments for depression (Paykel and Priest 1992). The older tricyclic antidepressants (TCAs) and newer drugs, including the selective serotonin reuptake inhibitors (SSRIs), have similar efficacy. The newer drugs have milder side-effect profiles and are consequently more likely to be tolerated at therapeutic doses (Pereira and Patel 1999). SSRIs have not been widely used in developing countries because of their higher cost, although as the patent protection expires, this situation is likely to change (Patel 1996). Of the psychosocial treatments with demonstrated efficacy, the most widely accepted are cognitive-behavioral approaches. Alone or in combination, drug and psychosocial treatments speed recovery from acute episodes. Maintenance treatment with drugs decreases relapse risk (Geddes and others 2003). Some evidence suggests that a course of psychotherapy may also delay relapses. Although most of the clinical trials have been carried out in industrial countries, at least three high-quality trials have demonstrated the efficacy of antidepressants, group therapy, or both in developing countries (Araya and others 2003; Bolton and others 2003; Patel and others 2003).

For the cost-effectiveness analyses, depression was modeled as an episodic disorder with a high rate of remission and subsequent recurrence, and with excess mortality from suicide (Chisholm and others 2004). None of the selected depression interventions was accorded a reduction in case fatality, however, owing to the lack of robust clinical evidence that antidepressants or psychotherapy in themselves alter the relative risk of death by suicide (Storosum and others 2001). The main modeled impact of intervention targeted toward episodic treatment of a new depressive episode was a reduction in the duration of time depressed, equivalent to an increase in the remission rate (25 to 40 percent improvement over no treatment; Malt and others 1999; Solomon and others 1997). In addition, all interventions were attributed a modest improvement in the level of disability for an unremitted depressive episode (10 to 15 percent), resulting from increased proportions of cases moving from more to less severe health states. For the estimated 56 percent of prevalent cases eligible for maintenance treatment (at least two lifetime episodes), an additional effect of efficacious maintenance treatment was incorporated into the analysis by reducing the incidence of recurrent episodes by 50 percent (Geddes and others 2003). Estimates of intervention effectiveness include the positive change that would occur naturally and also incorporate any placebo effect, which, in the treatment of depression, is not inconsiderable (Andrews 2001).

ANXIETY DISORDERS

Anxiety disorders are a group of disorders that have as their central feature the inability to regulate fear or worry. Although anxiety in itself is likely to feature in the clinical presentation of most patients, somatic complaints such as chest pain, palpitations, respiratory difficulty, headaches, and the like are also common, and these symptoms may be more common in developing countries. A number of different types of anxiety disorder exist, some of which are now briefly described.

The central feature of *panic disorder* is an unexpected panic attack, which is a discrete period of intense fear accompanied by physiologic symptoms such as a racing heart, shortness of breath, sweating, or dizziness. The person may have an intense fear of losing control or of dying. Panic disorder is diagnosed when panic attacks are recurrent and give rise to anticipatory anxiety about additional attacks. People with panic disorder may progressively restrict their lives to avoid situations in which panic attacks occur or situations from which it might be difficult to escape should a panic attack occur. They commonly avoid crowds, traveling, bridges, and elevators, and ultimately some individuals may stop leaving home altogether. Pervasive phobic avoidance is described as agoraphobia.

Generalized anxiety disorder is characterized by chronic unrealistic and excessive worry. These symptoms are accompanied by specific anxiety-related symptoms such as sympathetic nervous system arousal, excessive vigilance, and motor tension. *Posttraumatic stress disorder* follows serious trauma. It is characterized by emotional numbness, punctuated by intrusive reliving of the traumatic episode, generally initiated by environmental cues that act as reminders of the trauma; by disturbed sleep; and by hyperarousal, such as exaggerated startle responses.

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. The affected person has intense fear that he or she will act in a way that will be humiliating. Separating social anxiety disorder from extremes of normal temperament, such as shyness, is difficult. Nonetheless, social anxiety disorder can be quite disabling. *Simple phobias* are extreme fear in the presence of discrete stimuli or cues, such as fear of heights.

The core features of *obsessive-compulsive disorder* are obsessions (intrusive, unwanted thoughts) and compulsions (performance of highly ritualized behaviors intended to neutralize the negative thoughts and emotions resulting from the obsessions). One symptom pattern might be repetitive hand washing beyond the point of skin damage to neutralize fears of contamination.

Natural History and Course

The anxiety disorders differ in their age of onset, course of illness, and symptom triggers. One of these disorders, PTSD, is dependent for its etiology on one or more powerfully negative life events. Although the anxiety disorders are discussed as a group, panic disorder is chosen because of the available data for the purposes of the cost-effectiveness analysis.

Prevalence estimates of anxiety disorders based on community epidemiological surveys vary widely, from a low of 2.2 percent (Andrade and others 2003) to a high of 28.5 percent (Kessler and others 1994), with a weighted mean across surveys of 15.6 percent. Prevalence estimates for anxiety disorders in the past 6 to 12 months have a similarly wide range (1.2 to 19.3 percent) (Andrade and others 2003; Kessler and others 1994), with a weighted mean of 9.4 percent. Despite wide variation in overall prevalence, several clear relative prevalence patterns can be seen across surveys. Specific phobia is generally the most prevalent lifetime anxiety disorder, with social phobia generally the second most prevalent lifetime anxiety disorder. Panic disorder and obsessive-compulsive disorder are generally the least prevalent.

These surveys also provide evidence about the persistence of anxiety disorders, indirectly defined as the ratio of 6-month or 12-month to lifetime prevalence. This ratio averages approximately 60 percent for overall anxiety disorders, indicating a high rate of persistence across the life course. The highest persistence is generally found for social phobia, and the lowest for agoraphobia. These estimates of high persistence are consistent with results obtained from longitudinal studies of patients (Yonkers and others 2003).

Anxiety disorders have consistently been found in epidemiological surveys to be highly comorbid both among themselves and with mood disorders (for example, de Graaf and others 2003). The vast majority of people with a history of one anxiety disorder typically also have a second anxiety disorder, while more than half the people with a history of either anxiety or mood disorder typically have both types of disorder. Retrospective reports from community surveys consistently show that anxiety disorders have early average ages of onset. An impressive cross-national consistency can be seen in these patterns, with an estimated median age of onset of anxiety at approximately 15.

Epidemiological surveys have also looked at the treatment of anxiety disorders. As with depression, consistent evidence in these surveys suggests that delays in initially seeking professional treatment for an anxiety disorder are widespread after first onset (Olfson and others 1998). This finding is especially true among early-onset cases. Epidemiological data also show that only a minority of current cases receive any formal treatment in Western countries, whereas treatment of anxiety disorders is virtually nonexistent in many developing countries. The most recently published surveys, the World Mental Health surveys in six Western European countries, found that only 26.3 percent of people with an active anxiety disorder in the 12 months before the survey received any professional treatment (ESEMeD/MHEDEA 2000 Investigators 2004).

Anxiety disorders have consistently been found to be associated with substantial impairments in both productive roles (for example, work absenteeism, work performance, unemployment, and underemployment) and social roles (social isolation, interpersonal tensions, and marital disruption, among others) (see, for example, Kessler and Frank 1997). As noted earlier, for the purposes of this chapter, one of the anxiety disorders—panic disorder—has been chosen to describe interventions and undertake cost-effectiveness analysis. Panic disorder is as disabling as obsessive-compulsive disorder and PTSD, accounts for about one-third of all seriously impairing anxiety disorders, is one of the most common anxiety disorders presenting for treatment, and imposes an estimated burden of 600 to 800 DALYs per 1 million population.

Good evidence exists that both drug and psychosocial treatments are effective for managing anxiety disorders. Antidepressant drugs (both older TCAs and SSRIs) have been shown to be effective for the treatment of several anxiety disorders, including panic disorder, reducing the duration and intensity of the disorder. Although high-potency benzodiazepines are efficacious for panic disorder, these drugs carry a risk of dependence and are not considered the first line of treatment. Psychosocial treatments, especially cognitive-behavioral therapy, are also effective in diminishing both panic attacks and phobic avoidance.

Interventions for Panic Disorder

Although evidence-based interventions for panic disorder have yet to be evaluated or made widely available in developing

countries, the potential population-level impact of a number of interventions—including older and newer antidepressants, anxiolytic drugs (benzodiazepines), and psychosocial treatments—was examined. Interventions reduce the severity of panic attacks and improve the probability of making a full recovery. Effect sizes for symptom improvement were drawn from a meta-analysis of the long-term effects of intervention of panic disorder (Bakker and others 1998) and converted into an equivalent change in disability weight (Sanderson and others 2004). Concerning remission, a number of controlled and naturalistic studies (for example, Faravelli, Paterniti, and Scarpato 1995; Yonkers and others 2003) reveal a consistent remission rate of 12 to 13 percent for pharmacological and combination strategies—except for benzodiazepine use, for which the evidence is that longer-term recovery is actually worse than placebo (Katschnig and others 1995)—which represents a 62 percent improvement in efficacy over the untreated remission rate (7.4 percent).

COST-EFFECTIVENESS METHODS AND RESULTS

This section estimates the burden attributed to schizophrenia, bipolar disorder, depression, and panic disorder that could be averted (through scaling up) by proven, efficacious treatments. It is followed by calculations of the expected cost and cost-effectiveness of such treatments. Analysis is conducted at the level of six low- and middle-income geographical World Bank regions.

Estimation of Population-Level Effectiveness of Treatments

In modeling the impact of mental health interventions, we used a state-transition model (Lauer and others 2003) that traces the development of a population, taking into account births, deaths, and the disease in question. In addition to population size and structure, the model makes use of a number of epidemiological parameters (incidence and prevalence, remission, and cause-specific and residual rates of mortality) and assigns age- and gender-specific disability weights to both the disease in question and the general population. The output of the model is an estimate of the total healthy life years experienced by the population over a lifetime period (100 years). The model was run for a number of possible scenarios, including no treatment at all (natural history), current treatment coverage, and scaled-up coverage of current as well as potential new interventions. For the treatment scenarios, an implementation period of 10 years was used (thereafter, epidemiological rates and health state valuations return to natural history levels). The model derived the number of additional healthy years gained (equivalent to DALYs averted) each year in the population compared with the outcome for no treatment at all. DALYs averted in future years were discounted at a rate of 3 percent

(reflecting a societal preference for health benefits to be realized sooner), but no age-weighting was used.

Estimation of the baseline epidemiological situation that would prevail without treatment used incidence and prevalence estimates from the Global Burden of Disease 2000 study of the World Health Organization (WHO) (see online Global Burden of Disease documentation for the four disorders at http://www.who.int/evidence/bod). Current pharmacological or psychosocial treatments do not exert a primary preventive effect on the onset of the four conditions (although some evidence exists that treating depression in parents may reduce risk for offspring), indicating that currently observed incidence rates coincide with those that would pertain under no treatment. Prevention of recurrences of acute episodes (secondary prevention) has been demonstrated for maintenance treatments for major depression and bipolar disorder. Maintenance treatment with antipsychotic drugs decreases the risk of recurrent acute episodes of schizophrenia. For each condition, a range of treatment strategies was considered and assessed, including older (and widely available) psychotherapeutic drugs, newer pharmacotherapies, psychosocial treatments, and combination treatments (see table 31.2 for a list of interventions included).

Estimation of Population-Level Treatment Costs

Cost estimation followed the principles and procedures described in chapter 7 for carrying out economic analyses of disease control priorities in developing countries. For depression and panic disorder, treatment was assumed to occur in a primary care setting, whereas for schizophrenia and bipolar disorder, which often produce highly disruptive behaviors, both hospital- and community-based outpatient service models were derived and compared. Both program- and patient-level costs were identified and estimated. Program-level costs included the infrastructure and administrative support for implementing mental health treatments, as well as training inputs (for example, two to three days per trainee were estimated for training primary care doctors and case managers in psychotropic medication management). Patient-level resource inputs included medication regimens (for example, fluoxetine, 20 milligrams daily), laboratory tests (for example, lithium blood levels), primary care visits (including any contacts with a case manager), and hospital outpatient and inpatient care. Estimated patient-level resource inputs for each of the four disorders were informed by empirical economic evaluative studies (for example, Patel and others 2003; Srinivasa Murthy and others 2005) as well as a multinational Delphi consensus study of resource use for psychiatric disorders in seven developing countries (Ferri and others 2004). Region-specific unit costs or prices were applied to all resource inputs (see Mulligan and others 2003) to give an annual cost for each case as well as for all cases at the specified level of treatment

Table 31.2 Interventions for Reducing the Burden of Major Psychiatric Disorders in Developing Countries

Disorder	Intervention	Example
Schizophrenia	Older (neuroleptic) antipsychotic drug	Haloperidol
Treatment setting: hospital outpatient	Newer (atypical) antipsychotic drug	Risperidone
Treatment coverage (target): 80 percent	**Older antipsychotic drug and psychosocial treatment**	Haloperidol plus family psychoeducation
	Newer antipsychotic drug and psychosocial treatment	Risperidone plus family psychoeducation
Bipolar affective disorder	Older mood-stabilizing drug	Lithium carbonate
Treatment setting: hospital outpatient	Newer mood-stabilizing drug	Sodium valproate
Treatment coverage (target): 50 percent	**Older mood-stabilizing drug and psychosocial treatment**	Lithium plus family psychoeducation
	Newer mood-stabilizing drug and psychosocial treatment	Valproate plus family psychoeducation
Depression	Episodic treatment	
Treatment setting: primary health care	**Older TCA**	Imipramine or amitriptyline
Treatment coverage (target): 50 percent	**Newer antidepressant drug (SSRI; generic)**	Fluoxetine
	Psychosocial treatment	Group psychotherapy
	Older antidepressant drug and psychosocial treatment	Amitriptyline plus group psychotherapy
	Newer antidepressant drug and psychosocial treatment	Fluoxetine plus group psychotherapy
	Maintenance treatment	
	Older antidepressant drug and psychosocial treatment	Imipramine plus group psychotherapy
	Newer antidepressant drug and psychosocial treatment	Fluoxetine plus group psychotherapy
Panic disorder	Benzodiazepines	Alprazolam
Treatment setting: primary health care	**Older TCA**	Amitriptyline
Treatment coverage (target): 50 percent	**Newer antidepressant drug (SSRI; generic)**	Fluoxetine
	Psychosocial treatment	Cognitive therapy
	Older antidepressant drug and psychosocial treatment	Amitriptyline plus cognitive therapy
	Newer antidepressant drug and psychosocial treatment	Fluoxetine plus cognitive therapy

Source: Authors' own estimates and recommendations.
Note: Interventions in **bold** are the most cost-effective treatments of choice.

coverage. Costs incurred over the 10-year implementation period were discounted at 3 percent and expressed in U.S. dollars (rather than international dollars, which attempt to adjust for differences in purchasing power between countries).

Coverage

In each World Bank region, treatment costs and effects were ascribed to the population in need, both at current levels of intervention coverage and at a scaled-up, target level of coverage (80 percent for schizophrenia, 50 percent for the other conditions). Target coverage levels were predicated on the basis of what could feasibly be achieved given existing rates of treatment (Ferri and others 2004; Kohn and others 2004), as well as on prerequisites for increased coverage, such as recognition of common mental disorders in primary care. Estimation of current regional levels of effective coverage is hampered by lack of data; nevertheless, an attempt was made to approximate the expected proportion of the diseased population receiving

evidence-based pharmacological and psychosocial treatments (Ferri and others 2004; Kohn and others 2004), plus those in contact with traditional healers (the effectiveness of which was conservatively approximated by ascribing a placebo effect size for each disorder).

Results

Tables 31.3 through 31.6 provide estimates of the population-level effects (measured in DALYs averted), costs, and cost-effectiveness of each intervention by world region for the four types of psychiatric disorder considered in this chapter. A number of key findings emerge from this analysis.

Treatment Effectiveness. Results for schizophrenia and bipolar disorder are similar (albeit at differing coverage levels), ranging from less than 100 DALYs averted per 1 million population under the current situation in Sub-Saharan Africa and South Asia to 350 to 400 DALYs averted per 1 million population for

Table 31.3 Cost-Effectiveness Results: Schizophrenia

Model definition: Treatment setting: (a) hospital-based; (b) community-based Treatment coverage: 80 percent	World Bank region					
	Sub-Saharan Africa	Latin America and the Caribbean	Middle East and North Africa	Europe and Central Asia	South Asia	East Asia and the Pacific
Total effect (DALYs averted per year per 1 million population)						
Current situation	74	136	115	258	87	148
Older (neuroleptic) antipsychotic drug	149	219	214	254	177	231
Newer (atypical) antipsychotic drug	160	235	230	273	190	248
Older antipsychotic drug plus psychosocial treatment	254	373	364	353	300	392
Newer antipsychotic drug plus psychosocial treatment	261	383	373	364	308	403
Total cost (US$ million per year per 1 million population)						
Current situation	0.42	2.07	1.31	3.13	0.51	1.11
Hospital-based service model						
Older (neuroleptic) antipsychotic drug	0.60	3.09	2.40	2.24	0.74	1.18
Newer (atypical) antipsychotic drug	2.80	6.33	5.41	6.16	3.36	4.63
Older antipsychotic drug plus psychosocial treatment	0.67	3.27	2.56	2.36	0.81	1.26
Newer antipsychotic drug plus psychosocial treatment	2.87	6.56	5.61	6.31	3.44	4.73
Community-based service model						
Older (neuroleptic) antipsychotic drug	0.40	1.58	1.42	1.17	0.44	0.66
Newer (atypical) antipsychotic drug	2.59	4.85	4.45	5.11	3.07	4.12
Older antipsychotic drug plus psychosocial treatment	0.47	1.81	1.61	1.32	0.52	0.75
Newer antipsychotic drug plus psychosocial treatment	2.67	5.09	4.66	5.28	3.16	4.22
Cost-effectiveness (US$ per DALY averted)						
Current situation	5,695	15,192	11,400	12,134	5,900	7,533
Hospital-based service model						
Older (neuroleptic) antipsychotic drug	4,047	14,123	11,205	8,793	4,164	5,120
Newer (atypical) antipsychotic drug	17,433	26,893	23,543	22,530	17,702	18,700
Older antipsychotic drug plus psychosocial treatment	2,623	8,781	7,040	6,685	2,693	3,212
Newer antipsychotic drug plus psychosocial treatment	10,996	17,146	15,027	17,329	11,164	11,746
Community-based service model						
Older (neuroleptic) antipsychotic drug	2,668	7,230	6,618	4,595	2,499	2,855
Newer (atypical) antipsychotic drug	16,174	20,583	19,352	18,685	16,178	16,622
Older antipsychotic drug plus psychosocial treatment	**1,839**	**4,847**	**4,431**	**3,745**	**1,743**	**1,917**
Newer antipsychotic drug plus psychosocial treatment	10,232	13,313	12,485	14,481	10,239	10,484

Source: Authors' own estimates.
Note: Intervention data in **bold** are the most cost-effective treatments of choice.

Table 31.4 Cost-Effectiveness Results: Bipolar Disorder

Model definition: Treatment setting: (a) hospital-based; (b) community-based Treatment coverage: 50 percent	World Bank region					
	Sub-Saharan Africa	Latin America and the Caribbean	Middle East and North Africa	Europe and Central Asia	South Asia	East Asia and the Pacific
Total effect (DALYs averted per year per 1 million population)						
Current situation	79	128	97	199	93	153
Older mood-stabilizing drug (lithium)	292	336	296	381	319	389
Newer mood-stabilizing drug (valproate)	211	300	273	331	278	351
Older mood-stabilizing drug plus psychosocial treatment	312	365	322	413	346	422
Newer mood-stabilizing drug plus psychosocial treatment	232	330	300	365	306	386
Total cost (US$ million per year per 1 million population)						
Current situation	0.31	1.22	0.74	1.27	0.42	0.67
Hospital-based service model						
Older mood-stabilizing drug (lithium)	0.61	2.77	1.92	2.03	0.82	1.30
Newer mood-stabilizing drug (valproate)	0.79	2.87	2.04	2.20	1.03	1.53
Older mood-stabilizing drug plus psychosocial treatment	0.63	2.79	1.95	2.05	0.84	1.32
Newer mood-stabilizing drug plus psychosocial treatment	0.81	2.90	2.08	2.22	1.06	1.55
Community-based service model						
Older mood-stabilizing drug (lithium)	0.46	1.78	1.20	1.37	0.59	0.93
Newer mood-stabilizing drug (valproate)	0.64	1.91	1.36	1.57	0.82	1.17
Older mood-stabilizing drug plus psychosocial treatment	0.48	1.80	1.23	1.39	0.62	0.95
Newer mood-stabilizing drug plus psychosocial treatment	0.67	1.95	1.39	1.59	0.85	1.19
Cost-effectiveness (US$ per DALY averted)						
Current situation	3,967	9,518	7,668	6,398	4,463	4,373
Hospital-based service model						
Older mood-stabilizing drug (lithium)	2,091	8,246	6,478	5,341	2,553	3,348
Newer mood-stabilizing drug (valproate)	3,727	9,579	7,501	6,648	3,709	4,358
Older mood-stabilizing drug plus psychosocial treatment	2,016	7,644	6,036	4,957	2,424	3,119
Newer mood-stabilizing drug plus psychosocial treatment	3,480	8,800	6,937	6,100	3,459	4,016
Community-based service model						
Older mood-stabilizing drug (lithium)	1,587	5,295	4,068	3,608	1,862	2,394
Newer mood-stabilizing drug (valproate)	3,057	6,386	4,971	4,727	2,943	3,338
Older mood-stabilizing drug plus psychosocial treatment	**1,545**	**4,928**	**3,823**	**3,359**	**1,787**	**2,241**
Newer mood-stabilizing drug plus psychosocial treatment	2,874	5,908	4,645	4,359	2,765	3,092

Source: Authors' own estimates.

Note: Intervention data in **bold** are the most cost-effective treatments of choice.

Table 31.5 Cost-Effectiveness Results: Depression

Model definition: Treatment setting: primary health care Treatment coverage: 50 percent	World Bank region					
	Sub-Saharan Africa	Latin America and the Caribbean	Middle East and North Africa	Europe and Central Asia	South Asia	East Asia and the Pacific
Total effect (DALYs averted per year per 1 million population)						
Current situation	133	264	218	308	218	243
Episodic treatment: older antidepressant drug (TCA)	599	995	920	874	987	891
Episodic treatment: newer antidepressant drug (SSRI)	632	1,049	971	925	1,042	941
Episodic psychosocial treatment	624	1,036	958	936	1,028	927
Episodic psychosocial treatment plus older antidepressant	745	1,237	1,144	1,100	1,228	1,107
Episodic psychosocial treatment plus newer antidepressant	745	1,237	1,144	1,100	1,228	1,107
Maintenance psychosocial treatment plus older antidepressant	1,174	1,953	1,806	1,789	1,937	1,747
Maintenance psychosocial treatment plus newer antidepressant	1,174	1,953	1,806	1,789	1,937	1,747
Total cost (US$ million per year per 1 million population)						
Current situation	0.36	0.90	0.63	0.74	0.56	0.67
Episodic treatment: older antidepressant drug (TCA)	0.30	1.28	0.96	0.81	0.47	0.47
Episodic treatment: newer antidepressant drug (SSRI)	0.66	1.86	1.47	1.39	1.04	0.99
Episodic psychosocial treatment	0.37	1.67	1.27	0.97	0.55	0.53
Episodic psychosocial treatment plus older antidepressant	0.50	1.96	1.53	1.21	0.77	0.72
Episodic psychosocial treatment plus newer antidepressant	0.90	2.60	2.10	1.85	1.40	1.29
Maintenance psychosocial treatment plus older antidepressant	0.96	3.44	2.77	2.19	1.45	1.38
Maintenance psychosocial treatment plus newer antidepressant	1.80	4.80	3.99	3.56	2.81	2.59
Cost-effectiveness (US$ per DALY averted)						
Current situation	2,692	3,414	2,905	2,391	2,546	2,777
Episodic treatment: older antidepressant drug (TCA)	**505**	**1,288**	**1,039**	**929**	**478**	**533**
Episodic treatment: newer antidepressant drug (SSRI)	1,042	1,771	1,516	1,501	1,003	1,048
Episodic psychosocial treatment	592	1,611	1,330	1,035	537	570
Episodic psychosocial treatment plus older antidepressant	674	1,586	1,335	1,104	627	653
Episodic psychosocial treatment plus newer antidepressant	1,203	2,101	1,834	1,682	1,140	1,161
Maintenance psychosocial treatment plus older antidepressant	**817**	**1,760**	**1,533**	**1,226**	**749**	**788**
Maintenance psychosocial treatment plus newer antidepressant	1,535	2,459	2,211	1,990	1,449	1,481

Source: Authors' own estimates.
Note: Intervention data in **bold** are the most cost-effective treatments of choice.

Table 31.6 Cost-Effectiveness Results: Panic Disorder

Model definition: Treatment setting: primary health care Treatment coverage: 50 percent	World Bank region					
	Sub-Saharan Africa	Latin America and the Caribbean	Middle East and North Africa	Europe and Central Asia	South Asia	East Asia and the Pacific
Total effect (DALYs averted per year per 1 million population)						
Current situation	49	94	64	88	57	90
Anxiolytic drug (benzodiazepine)	144	182	170	183	168	195
Older antidepressant drug (TCA)	232	290	272	290	269	312
Newer antidepressant drug (SSRI; generic)	245	307	287	307	284	330
Psychosocial treatment (cognitive-behavioral therapy)	233	292	273	292	270	313
Older antidepressant plus psychosocial treatment	262	329	308	329	304	353
Newer antidepressant plus psychosocial treatment	276	346	324	346	320	372
Total cost (US$ million per year per 1 million population)						
Current situation	0.06	0.13	0.08	0.07	0.05	0.10
Anxiolytic drug (benzodiazepine)	0.10	0.20	0.15	0.15	0.10	0.12
Older antidepressant drug (TCA)	0.09	0.18	0.14	0.14	0.08	0.11
Newer antidepressant drug (SSRI; generic)	0.15	0.27	0.21	0.23	0.16	0.20
Psychosocial treatment (cognitive-behavioral therapy)	0.11	0.27	0.21	0.17	0.09	0.11
Older antidepressant plus psychosocial treatment	0.15	0.32	0.26	0.23	0.13	0.17
Newer antidepressant plus psychosocial treatment	0.22	0.41	0.34	0.32	0.22	0.26
Cost-effectiveness (US$ per DALY averted)						
Current situation	1,192	1,378	1,208	824	948	1,109
Anxiolytic drug (benzodiazepine)	681	1,075	892	842	572	629
Older antidepressant drug (TCA)	**369**	**619**	**508**	**474**	**305**	**339**
Newer antidepressant drug (SSRI; generic)	**630**	**865**	**747**	**741**	**567**	**606**
Psychosocial treatment (cognitive-behavioral therapy)	468	927	786	594	338	365
Older antidepressant plus psychosocial treatment	556	977	844	685	443	474
Newer antidepressant plus psychosocial treatment	788	1,188	1,050	918	671	709

Source: Authors' own estimates.
CBT = cognitive behavioral therapy
Note: Intervention data in **bold** are the most cost-effective treatments of choice.

combination drug and psychosocial interventions in Europe and Central Asia and East Asia and the Pacific. Second-generation (atypical) antipsychotic drugs were considered slightly more effective than first-generation drugs (on the basis of a modest intrinsic efficacy difference and differences in tolerability and adherence); lithium was considered modestly more effective as a mood-stabilizing drug than valproate (on the basis of its additional positive effect on suicide rates). Adjuvant psychosocial treatment in combination with pharmacotherapy significantly added to expected population-level health gain.

With the exception of Europe and Central Asia, less than 10 percent of the disease burden currently is being averted, whereas the implementation of combined interventions at a scaled-up level of coverage is expected to avert 14 to 22 percent of the burden of schizophrenia (coverage level, 80 percent) and 17 to 29 percent of the burden of bipolar disorder (coverage level, 50 percent).

For primary care treatment of common mental disorders, including depression and panic disorder, current levels of effective coverage avert only 3 to 8 percent of the existing disease burden, whereas scaling up of the most effective interventions to a coverage level of 50 percent could be expected to avert more than 20 percent of the burden of depression and up to one-third of the burden of panic disorder. Considered at a population level, episodic treatments for depressive episodes did not differ substantially within regions (averting 10 to15 percent of current burden); more substantial health gain is expected by providing maintenance treatment to individuals with recurrent depression (approximately 1,200 to 1,900 DALYs averted per 1 million population; 18 to 23 percent of burden). Such an approach has been found to reduce the risk of relapse by half. Although the evidence to date from developing regions is meager, our results suggest that SSRIs such as fluoxetine, alone or in combination with psychosocial treatment, are the most effective treatments for panic disorder, with health gains considerably better than those estimated for benzodiazepine anxiolytic drugs such as alprazolam.

Treatment Costs. Community-based service models for schizophrenia and bipolar disorder were found to be appreciably less costly than hospital-based service models (for example, interventions for bipolar disorder were 25 to 40 percent less costly). The total cost per capita of community-based outpatient treatment with first-generation antipsychotic or mood-stabilizing drugs, including all patient-level resource needs as well as infrastructural support, ranged from US$0.40 to US$0.50 in Sub-Saharan Africa and South Asia to US$1.20 to US$1.90 in Latin America and the Caribbean and in Europe and Central Asia (equivalent patient costs per year, US$170 to US$300 and US$300 to US$800, respectively). The cost per capita for interventions using second-generation (atypical) antipsychotic drugs still under patent is much higher (US$2.50 to US$5.00). By contrast, some of the newer antidepressant drugs (SSRIs) are now off patent, and their use in treating depression and panic disorder was accordingly costed at their generic, nonbranded price. The patient-level cost of treating a 6-month episode of depression ranged from as little as US$30 (older antidepressants in Sub-Saharan Africa or South Asia) to US$150 (newer antidepressants in combination with brief psychotherapy in Latin America and the Caribbean). Total annual costs for all incidents of depressive episodes receiving treatment, including training and other program-level costs, were as much as US$2 to US$5 per capita for a maintenance treatment program using newer antidepressants, three times more costly than episodic treatment with newer antidepressant drugs only. Patient-level resource inputs for panic disorder interventions cost US$50 to US$200 per case per year, and overall costs including program costs of training and administration amounted to US$0.10 to US$0.30 per capita.

Cost-Effectiveness. Compared with both the current situation and the epidemiological situation of no treatment (natural history), the most cost-effective strategy for averting the burden of psychosis and severe affective disorders in developing countries is expected to be a combined intervention of first-generation antipsychotic or mood-stabilizing drugs with adjuvant psychosocial treatment delivered through a community-based outpatient service model, with a cost-effectiveness ratio of below US$2,000 in Sub-Saharan Africa and South Asia, rising to US$5,000 in Latin America and the Caribbean (equivalent to more than 500 DALYs averted per US$1 million expenditure in Sub-Saharan Africa and South Asia and 200 DALYs averted in Latin America and the Caribbean). Currently, the high acquisition price of second-generation antipsychotic drugs makes their use in developing regions questionable on efficiency grounds, although this situation can be expected to change as these drugs come off patent. By contrast, evidence indicates that the relatively modest additional cost of adjuvant psychosocial treatment reaps significant health gains, thereby making such a combined strategy for schizophrenia and bipolar disorder treatment more cost-effective than pharmacotherapy alone.

For more common mental disorders treated in primary care settings (depressive and anxiety disorders), the single most cost-effective strategy is the scaled-up use of older antidepressants (because of their lower cost but similar efficacy compared with newer antidepressants). However, as the price margin between older and generic newer antidepressants continues to diminish, generic SSRIs—which have milder side effects and are more likely to be taken at a therapeutic dose (Pereira and Patel 1999)—can be expected to be at least as cost-effective and, therefore, the pharmacological treatment of choice in the future. Because depression is often a recurring condition, proactive care management, including long-term maintenance treatment with antidepressant drugs, represents a cost-effective way of significantly reducing the enormous burden of depression that exists in developing regions now (400 to 1,300 DALYs averted per US$1 million expenditure).

POLICY AND SERVICE IMPLICATIONS

Many attempts have been made during the past 50 years to have mental health care placed higher on national and international agendas. In 1974, a WHO Expert Committee on the

Organization of Mental Health Services in Developing Countries (WHO 1975) made the following recommendations:

- Develop a national mental health policy and create a unit within the Health Ministry to implement it.
- Budget for workforce development, essential drug procurement, infrastructure development, data collection, and research.
- Decentralize service provision and integrate mental health into primary health care.
- Train and supervise primary health care providers in mental health using specialist mental health staff.

Thirty years later, international agencies, nongovernmental organizations, and professional bodies continue to make those exact recommendations. One reason for the lack of action in mental health has been the paucity of information on the cost-effectiveness of mental health interventions. Advocacy without the necessary science can readily be ignored in countries with massive health problems and meager resources. This chapter aims to address this deficiency.

Symptoms of mental disorders are often attributed to other illnesses, and mental disorders are often not considered health problems (Jacob 2001). Many nonscientific explanations for mental illness exist, and stigma exists to varying degrees everywhere (Weiss and others 2001) with widespread delays or failure to seek appropriate care (James and others 2002).

When care is sought, a hierarchy of interventions comes into play, ranging from self-help, informal community support, traditional healers, primary health care, specialist community mental health care, and psychiatric units in general hospitals to specialist long-stay mental hospitals. The mix of interventions depends on the availability of resources within a country or region (Saxena and Maulik 2003). The more resource-constrained the country or region is, the greater is the reliance on self-help, informal community support (especially family-based), and primary health care.

Traditional healers are often the first source individuals with mental illness and their families turn to for professional assistance (see, for example, Abiodun 1995). A recent review of common mental disorders among primary health clinics and traditional healers in urban Tanzania showed that the prevalence of common mental disorders among those attending traditional healers was double that of patients at primary health care centers (Ngoma, Prince, and Mann 2003). Traditional healers are a heterogeneous group and include faith healers, spiritual healers, religious healers, and practitioners of indigenous or alternative systems of medicine. In some countries, they are part of the informal health sector, but in other countries, traditional healers charge for their services and should be considered part of the private health care sector. Often, traditional healers have high acceptability and are accessible; at times, traditional healers work closely (and apparently effectively) with conventional mental health services (Thara, Padmavati, and Srinivasan 2004). Alternatively, animosity and competition can exist, and recent examples of human rights violations by traditional healers demonstrate the heterogeneity of this group of providers.

The formal diagnosis and treatment of mental disorders occur in both primary and specialist health services. Examples in nearly a dozen countries now show it is feasible and practicable to treat common mental disorders in primary health care settings (for example, Chisholm and others 2000; De Jong 1996; Mohit and others 1999). The challenge is to enhance systems of care by taking effective local models and disseminating them throughout a country.

Concern has been expressed that the more sophisticated psychotherapies used in mental health care are beyond the human resources of developing countries. However, basic psychological therapies can be effective, though there is some evidence, at least for depression, that the newer drug therapies are more cost-effective than psychological therapies (Patel and others 2003). Psychoeducational family intervention has been shown to be suitable for rehabilitation in schizophrenia in rural China (Ran and others 2003) and to be cost-effective compared with other standard treatment (Xiong and others 1994). Evidence also shows that nurses can replace physicians as primary health care providers in certain circumstances without loss of effectiveness (Climent and others 1978). Primary care practitioners need support to develop skills and experience in diagnosing and treating mental disorders: they need a sustainable supply of medicines, access to supervision, and incentives to see patients with mental illness (Abas and others 2003). Community approaches using low-cost, locally available resources may improve treatment adherence and clinical outcomes even in rural and underresourced settings (Chatterjee and others 2003; Srinivasa Murthy and others 2005).

In most countries, acute inpatient beds are being moved from mental hospitals into general or district hospitals. Although this policy potentially improves accessibility and increases the links with, and support provided to, primary mental health care, concerns can be raised as to whether general hospitals can adapt to provide adequate services to people with severe mental disorders. However, such services have been effectively established in a number of countries (see, for example, Alem and others 1999; Kilonzo and Simmons 1998), showing this form of service delivery to be feasible when it is clinically indicated.

Nongovernmental organizations are important providers of mental health care. An estimated 93 percent of African and 80 percent of Southeast Asian countries have nongovernmental organizations in the mental health sector. They provide diverse services—including advocacy, informal support, housing, suicide prevention, substance misuse counseling, dementia support, rehabilitation, research, and other programs—that

complement, or in some cases substitute for, public and private clinical services (Levkoff, Macarthur, and Bucknall 1995; Patel and Thara 2003).

Services for children and adolescents, the majority of the population in many developing countries, are even more deficient than those for adults. Priority needs to be given to these services (Rahman and others 2000). At the other end of the life spectrum, many developing countries are facing aging populations with grossly underdeveloped aged care services (Levkoff, Macarthur, and Bucknall 1995). The high level of civil conflict and natural disasters requires attention to postconflict and posttrauma mental health conditions. The prevalence of these disorders is demonstrated by a recent study (Livanou, Basoglu, and Kalendar 2002) showing that, of 1,000 survivors of the August 1999 earthquake in Turkey, the incidence of PTSD was 63 percent and of depression was 42 percent.

Specialist mental health providers, especially mental hospitals, tend to focus the services they provide on the lower-prevalence, higher-disability disorders, such as schizophrenia and bipolar disorder. Modern treatments, if available and used, allow most patients to be treated effectively out of hospital. Specifically, the use of antipsychotic and mood-stabilizing drugs and the development of strategies for community-based treatment have led to the closing of large numbers of psychiatric inpatient beds in many countries and their replacement with community services and general hospital psychiatric units (for example, Larrobla and Botega 2001).

However, in some countries, the majority of psychotic patients remain in long-term inpatient facilities that engage in custodial care, which is often of poor quality; moreover, basic rights are often violated at such facilities (van Voren and Whiteford 2000). Even if the quality of care is reasonable, accessibility is a problem: these hospitals are often situated in urban areas, but populations are largely rural and have limited transportation (Saraceno and others 1995). Furthermore, the concentration of resources in these facilities can leave little for other service components (Gallegos and Montero 1999). For example, in Indonesia, 97 percent of the mental health budget is spent on public mental hospitals (Trisnantoro 2002). For many developing countries, the debate about the role of, or problems with, mental hospitals is subsumed within a gross deficiency of psychiatric beds of any kind.

The priority for virtually all countries is generating sufficient resources for primary mental health care and deciding how to expand and best use scarce specialist resources. The quality of care is often very poor, and huge variations exist in resource availability between countries (Saxena and Maulik 2003; WHO 2001). Very few countries have what could be considered an optimal mix of these services, and there are no universally accepted planning parameters. However, conceptual models for developing national mental health policy and guidelines for service planning exist that can be useful in developing countries (Tansella and Thornicroft 1998; Townsend and others 2004; WHO 2003).

CONCLUSION: PUBLIC SUPPORT FOR A COST-EFFECTIVE INTERVENTION PACKAGE

In developing countries, much of the mental health care spending is reported to be out of pocket. Individuals purchase modern and traditional treatments if they can afford to do so. Although a large private health sector exists in low-income countries (Mills and others 2002), the quality and cost vary. Although unregulated markets fail in health, they fail even more in mental health. It is unlikely that a country will be able to rely on an unregulated private sector to deliver services that will reduce the burden of mental disorders.

In addition to being a large and growing component of disease burden, mental disorders meet virtually all the criteria by which we determine the need for government involvement in health care (Beeharry and others 2002). They affect the poor, cause externalities, and inflict catastrophic costs; moreover, private demand is inadequate. Indeed, the authors recognize that the main measure of outcome used in this and other chapters—the disability-adjusted life year—is limited to capturing change in service user–level symptoms, disability, recovery, and case-fatality. The DALY does *not* capture the positive change that treatment may have on a number of other significant consequences of mental disorders, including family burden (in particular, productive time and household resources given up in the care of the sick family member) and lost productivity, at the level of both the individual and the household (treatment accelerates return to paid work or usual household activities) and, by implication, at the level of society in general. The evidence base for these productivity increases, although modest in volume, constitutes an important additional argument alongside "cost per DALY" considerations for investing in mental health.

The total budgetary requirements and health consequences of a cost-effective package of mental health care can begin to be mapped out by selecting one intervention for each of the four disorders considered in this chapter. Although the data available for this exercise have limitations and will need to be refined with further research, table 31.7 summarizes the estimated costs and effects of a package consisting of (a) outpatient-based treatment of schizophrenia and bipolar disorder with first-generation antipsychotic or mood-stabilizing drugs and adjuvant psychosocial treatment, (b) proactive care of depression in primary care with generic SSRIs (including maintenance treatment of recurrent episodes), and (c) treatment of panic disorder in primary care with generic SSRIs. The estimated benefit of such a package would be an annual reduction of 2,000 to 3,000 DALYs per 1 million population, at a cost of US$3 million to US$9 million (that is, US$3 to US$4 per capita in Sub-Saharan

Table 31.7 Costs and Effects of a Specified Mental Health Care Package

	World Bank region					
	Sub-Saharan Africa	Latin America and the Caribbean	Middle East and North Africa	Europe and Central Asia	South Asia	East Asia and the Pacific
Total effect (DALYs averted per year per 1 million population)						
Schizophrenia: older antipsychotic drug plus psychosocial treatment	254	373	364	353	300	392
Bipolar disorder: older mood-stabilizing drug plus psychosocial treatment	312	365	322	413	346	422
Depression: proactive care with newer antidepressant drug (SSRI; generic)	1,174	1,953	1,806	1,789	1,937	1,747
Panic disorder: newer antidepressant drug (SSRI; generic)	245	307	287	307	284	330
Total effect of interventions	1,985	2,998	2,779	2,862	2,867	2,891
Total cost (US$ million per year per 1 million population)						
Schizophrenia: older antipsychotic drug plus psychosocial treatment	0.47	1.81	1.61	1.32	0.52	0.75
Bipolar disorder: older mood-stabilizing drug plus psychosocial treatment	0.48	1.80	1.23	1.39	0.62	0.95
Depression: proactive care with newer antidepressant drug (SSRI; generic)	1.80	4.80	3.99	3.56	2.81	2.59
Panic disorder: newer antidepressant drug (SSRI; generic)	0.15	0.27	0.21	0.23	0.16	0.20
Total cost of interventions	2.9	8.7	7.0	6.5	4.1	4.5
Cost-effectiveness (DALYs averted per US$1 million expenditure)						
Schizophrenia: older antipsychotic drug plus psychosocial treatment	544	206	226	267	574	522
Bipolar disorder: older mood-stabilizing drug plus psychosocial treatment	647	203	262	298	560	446
Depression: proactive care with newer antidepressant drug (SSRI; generic)	652	407	452	502	690	675
Panic disorder: newer antidepressant drug (SSRI; generic)	1,588	1,155	1,339	1,350	1,765	1,649

Source: Authors' own estimates.

Africa and South Asia, and US$7 to US$9 per capita in Latin America and the Caribbean). Accordingly, for every US$1 million invested in such a mental health care package, 350 to 700 healthy years of life would be gained over what would occur without intervention.

At a country level, data such as those presented in this chapter can be used to estimate the proportion of burden currently averted, the proportion that can be averted with current knowledge and optimal coverage, and the burden not able to be averted with current knowledge. Such modeling has been done for some countries (for example, Andrews and others 2004).

Although much remains to be learned about the etiology and treatment of mental disorders, the potential clearly exists for a considerable reduction in the burden caused by them. For these gains to be made, the challenge is to overcome the cultural, financial, and structural barriers that prevent people from seeking and receiving treatment. We need to close the gap between what we know and what we do in treating mental disorders. We can alleviate the substantial burden of these disorders and reverse or limit many of the devastating social and economic impacts.

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