

## Chapter 12

# Cost-Effectiveness and Affordability of Interventions, Policies, and Platforms for the Prevention and Treatment of Mental, Neurological, and Substance Use Disorders

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## INTRODUCTION

Since the turn of the millennium, considerable progress has been made in developing an evidence base on which interventions are effective and feasible for improving mental health in low- and middle-income countries (LMICs). Such evidence provides a critical input to the formulation of plans and priorities to address the large and growing burden of mental, neurological, and substance use (MNS) disorders. However, for successful and sustainable scale-up of effective interventions and innovative service delivery strategies, decision makers require not only evidence of an intervention's impact on health and other outcomes, such as equity or poverty, but also evidence of its cost and cost-effectiveness. Cost data provide information relevant to the financial planning and implementation of prioritized, evidence-based strategies; cost-effectiveness analysis indicates the relative efficiency or value for money associated with interventions or innovations.

The application of economic evaluation to MNS disorders has largely focused on the assessment of a specific intervention's costs and health outcomes, relative to some comparator, which may be treatment as usual, another innovation, or no intervention.

Such assessments have often been conducted alongside clinical trials, enabling health economic researchers to add resource use questions to study protocols, generate estimates of each trial participant's health care costs, and relate these costs to primary outcome measures in the form of cost-effectiveness ratios. We review this type of economic evidence over the course of this chapter, with a particular focus on studies that have been successfully carried out in LMICs. However, the number of completed studies remains small and insufficient to inform resource allocation decisions in all the national settings where cost-effectiveness information would be valuable, including the many countries where informal or traditional health care represents the predominant model of service availability. This paucity of economic evidence reflects the overall lack of resources and infrastructure for mental health services in LMICs, including research capacity.

Partly to address the paucity of cost-effectiveness trials, as well as their intrinsic specificity to the setting in which they are conducted, a broader, modeling-based approach has also been used to build up economic evidence for international mental health policy and planning. This approach includes the earlier editions of the Disease Control Priorities (DCP) project and

the World Health Organization's (WHO) CHOosing Interventions that are Cost-Effective (CHOICE) project. Such model-based studies rely on existing data, as well as several analytical assumptions; these studies have adopted an epidemiological, population-based approach that identifies the expected costs and health impacts of delivering evidence-based interventions at scale in the population as a whole, whether a specific country or an entire region. We also review this form of economic evidence and comment on important gaps in the current evidence base, as well as the relative strengths and limitations of this approach.

One important limitation of conventional cost-effectiveness analysis—whether garnered through trial-based or model-based approaches—is that it is restricted to consideration of the specific implementation costs and health-related outcomes of an intervention; it does not typically extend to the nonhealth or wider economic or social value of investing in mental health innovation and service scale-up. In particular, cost-effectiveness analysis in its conventional form has little to say about the equitable distribution of costs and health gains across different groups of the target population. Incorporation of such concerns into economic evaluation represents a major objective of extended cost-effectiveness analysis, which is explored and addressed specifically in chapter 13 in this volume (Chisholm, Johansson, and others 2015).

In this chapter, we review the available cost-effectiveness evidence for the different levels and underpinning strategies of the mental health care system, with a focus on information generated in or for LMICs. Based on the overall analytical framework and priority intervention matrices developed for this volume, the remainder of the chapter is presented as follows. First, we consider the economic evidence for mental health prevention and protection at the population and community levels of the health and welfare system, including legislative, regulatory, and informational measures at the public policy level (population platform), as well as school-, workplace-, and community-based programs (community platform). We then examine the economic evidence relating to the identification and treatment of MNS disorders (health care platform), focusing on the relative cost-effectiveness or efficiency of treatment programs implemented in nonspecialized versus more specialized health care settings. Finally, we assess the financial costs and budgetary implications of implementing or scaling up a set of prioritized, cost-effective interventions.

Our review is based on available, published literature. A systematic search of the literature for LMICs was undertaken in PubMed to find articles published

since 2000 in English. The search combined terms for specific mental health interventions with economic terms such as “cost,” “cost-effectiveness,” or “quality-adjusted life year (QALY),” as well as the names of all LMICs and their respective regions (see annex 12A for a list of search terms used to identify relevant literature). Where little or no literature was found for LMICs on interventions of potential importance, this systematic search was augmented by selective searches of the literature available since 1995 for high-income countries (HICs); however, these results are not included in the figures or tables. Annex 12B provides the search statistics.

Articles included in the review were graded using the checklist of Drummond and others (2005) to generate a quality score for each article, with most studies graded between 7 and 10. Annex 12C provides a list of studies that were used to generate the tables and figures presented in this chapter. It presents detailed information on the intervention characteristics and comparators, target population group, geographic location, methodology, results, and quality scores. All cost-effectiveness results are presented in 2012 US\$ except where noted otherwise. Consistent with earlier iterations of DCP, reported regional estimates refer to the World Bank's categorization of countries by income.

## COST-EFFECTIVENESS OF MENTAL HEALTH PROMOTION AND PROTECTION MEASURES AT THE POPULATION AND COMMUNITY LEVELS

Economic evaluation has yet to be extensively applied to mental health promotion, largely because of the challenges associated with using conventional methods and principles of cost-effectiveness analysis in the context of such programs, in particular, the limitations of experimental study design; the multifaceted, complex, and long-term nature of anticipated program benefits; and the shortage of sensitive or suitable outcome measures (Petticrew and others 2005). Moreover, many of the determinants of poor mental health and mental health inequalities lie outside the health sector, thereby requiring an evaluation of intersectoral action. Certain mental health promotion strategies are not amenable to controlled studies, because it is not feasible or ethical to exclude a segment of the target population from exposure to the intervention in question. Since cost-effectiveness is by definition a relative concept, this limitation makes estimation of the relative or comparative efficiency of one strategy over another problematic. Where such comparisons are not possible, prospective observational studies,

time-series analyses, or ecological studies within a single population can still be conducted and may provide a sufficient basis for decision making. An alternative approach is via modeling studies, which attempt to simulate empirical studies on the basis of publicly available data sources.

Chapter 10 of this volume (Petersen and others 2015) identifies a number of good and best practices for protecting mental health at the population and community levels, including the following:

- Laws and regulations to reduce harmful alcohol use
- Laws and regulations to reduce access to lethal means of suicide
- School-based social emotional learning programs to prevent the onset of mental disorders and promote mental health in children and adolescents
- Community-based parenting programs, particularly during infancy and early childhood
- Training programs to help gatekeepers to identify people with mental illness.

We consider the economic evidence for each of these policy options. Clearly, there are other potential approaches that can be tested and adopted that can help to promote and protect mental health. For example, cash transfers and microfinance have been used to support the health of women and children in several settings and have the potential to improve mental health outcomes such as cognitive development in young children. Better understanding of the impact and costs of cash transfers and other social programs, such as microfinance, is essential for addressing the cycle of poverty and mental disorders (Lund and others 2011).

### **Laws and Regulations to Reduce Harmful Alcohol Use**

Population-based measures for reducing the demand for or access to alcohol include fiscal instruments (excise taxes), legal limits (minimum drinking age, maximum blood alcohol content levels when driving), and regulation (advertising bans and restricted access to retail outlets). Within the category of pricing policies, consistent evidence shows that the consumption of alcohol is responsive to an increase in final prices, and this can be effectuated via higher excise taxes on alcoholic beverages. Tax increases of 20 percent or even 50 percent represent a highly cost-effective response in countries with a high prevalence of heavy drinking, defined as greater than 5 percent of adults. For example, Rehm and others (2006) estimated that in LMICs in Europe and Central Asia, Latin America and the Caribbean, and Sub-Saharan Africa, a disability-adjusted life year (DALY) can be averted for US\$200–US\$400, equivalent to 2,500–5,000

DALYs averted per US\$1 million expenditure (reported values have been updated to 2012 price levels).

In lower-prevalence contexts, such as East Asia and Pacific and South Asia, population-level effects drop off and cost-effectiveness ratios rise accordingly. The impact of alcohol tax increases stands to be mitigated by illegal production, tax evasion, and illegal trading, which account for approximately 30 percent of all consumption in European and Latin American subregions and up to 80 percent in certain parts of Sub-Saharan Africa. Reducing this unrecorded consumption by 20–50 percent via concerted tax enforcement efforts by law enforcement and excise officers is estimated to cost 50–100 percent more than a tax increase, but it produces similar levels of health gain in the population (Anderson, Chisholm, and Fuhr 2009). In settings with higher levels of unrecorded production and consumption, such as India, increasing the proportion of consumption that is taxed may be a more effective pricing policy than simply increasing the excise tax; excise tax increases may only encourage further illegal production, smuggling, and cross-border purchases (Patel and others 2011).

The impact of reducing access to retail outlets for specified periods of the week to limit the availability and implementing a comprehensive advertising ban to limit the marketing of alcoholic beverages have the potential to be very cost-effective countermeasures, but only if they are fully enforced; compared with doing nothing, each DALY averted costs between US\$200 and US\$1,200 (Rehm and others 2006). For impaired-driving policies and countermeasures, there is good evidence from HICs on the effectiveness of impaired-driving laws and their enforcement via roadside breath testing and checkpoints. The estimated cost-effectiveness of such countermeasures in LMICs ranges from US\$800 to US\$3,000 per DALY averted. However, the applicability—and by extension, the cost-effectiveness—of such measures may be limited in settings where large segments of the population do not drive or where noncommercial alcoholic home brews represent the predominant form of consumption.

Country-level information on the cost-effectiveness of legislation to control alcohol use is limited, with only one study conducted in a low-income setting. A country contextualization study of the WHO-CHOICE model in Nigeria, a lower-middle-income country, showed that alcohol taxation does generate appreciable health gains. However, these gains did not result in a significant improvement in cost-effectiveness, because it was expected that an increase in taxes would lead to a rise in the amount of illicit and untaxed consumption of alcohol. The study did find that implementation of random roadside breath

testing for alcohol could potentially generate considerably more healthy life years than could other interventions and would do so at a lower cost (Gureje and others 2007).

### **Laws to Restrict Access to Means of Self-Harm and Suicide**

There is a paucity of robust economic studies to inform policy makers about the budgetary requirements and return on investment associated with scaled-up efforts to prevent self-harm or suicide (Zechmeister and others 2008). A recent WHO review of suicide prevention strategies that included cost as a parameter of interest, however, showed that two-thirds of the strategies assessed as being effective or promising were categorized as low cost; low cost was also closely associated with universal or selective, as opposed to more indicated or targeted, prevention approaches (WHO 2010). Australia's ACE-Prevention (Assessing Cost-Effectiveness in Prevention) project assessed the cost-effectiveness of reducing access to means via revised legislation for gun ownership and estimated that the cost per healthy life year gained would exceed US\$57,000; guidelines for more responsible media reporting would cost US\$30,800 per healthy life year gained if at least one suicide is averted (Vos and others 2010).

Partly to address this paucity of available evidence, an extended cost-effectiveness analysis was undertaken for this volume relating to a pesticide ban in India to prevent self-harm and suicide, based on the experience of Sri Lanka's ban on pesticides in the 1990s (Nigam and others 2015). The authors estimated that 3,750 deaths could be averted per year if 80 percent of the population no longer had access to endosulfan, a commonly used Class II pesticide. Implementation of the ban plus hospital treatment for self-harm cases was estimated to cost US\$0.10 per capita, yielding a cost-effectiveness ratio of close to US\$1,000 per life-year gained (Nigam and others 2015). However, the analysis did not take into account costs potentially falling to other sectors or agents as a result of the ban, or potential substitution effects.

### **School-Based Social Emotional Learning Programs**

Integrated mental health promotion programs in schools targeting children and adolescents have long-term benefits, including improved emotional and social functioning and academic achievement (Tennant and others 2007; Weare and Nind 2011). Furthermore, economic analyses from HICs indicate that social emotional learning (SEL) interventions in schools are cost-effective, resulting in savings from better health outcomes, as well as reduced expenditure in the criminal justice system

(Knapp and others 2011; McCabe 2007). Although such life skills programs seem to represent good value for money, there is a need to ascertain this via formal cost-effectiveness studies on specific early childhood development and classroom-based educational strategies, even in HICs (Barry and others 2009; Mihalopoulos and others 2011).

A recent randomized control trial (RCT) on classroom-based cognitive behavioral therapy (CBT) for reducing symptoms of depression in adolescents found that despite high levels of fidelity and adherence, a universally provided CBT depression prevention program was not cost-effective, in part because of the relatively high cost per student and the marginal gain in health outcomes (Anderson and others 2014). In Chile, an HIC, a similar school-based RCT was implemented that compared a CBT depression prevention program with usual care with enhanced counseling; the results indicated that the program was not effective compared with usual care (Araya and others 2011). In India, peer education and teacher training in educational institutions that was provided as part of a multicomponent, population-based youth health promotion intervention had limited feasibility and effect because of several logistical and financial barriers (Balaji and others 2011). In Mauritius, evaluation of a school-based prevention program for adolescent depression showed short-term benefits to depression, hopelessness, coping skills, and self-esteem, but its sustainability has yet to be ascertained (Rivet-Duval, Heriot, and Hunt 2011).

These study findings can offer insights about which interventions are most likely to be acceptable and feasible as well as effective in the long term. In particular, it seems that the cost-effectiveness of more intensive, individual-based approaches such as CBT can be adversely affected by the cost of their implementation.

### **Community-Based Parenting Programs**

Systematic reviews show that early child development and parenting skills training are effective in enhancing the cognitive and social skills of children under age five years, and the training promotes mental and social development (Mejia, Calam, and Sanders 2012; Merry and others 2012). Such programs are provided on a group, individual, or self-administered basis in a variety of settings, including health clinics, community centers, and schools, by different types of providers, such as health visitors, social workers, and psychologists. These differences influence the cost and cost-effectiveness of parenting programs. Studies in the United Kingdom indicate little difference between community-based and

hospital-based implementations of this kind of program (Cunningham, Bremner, and Boyle 1995; Harrington and others 2000).

Cost-effectiveness studies in LMICs have yet to be conducted, but analyses in HICs indicate that such programs are cost-effective and pay for themselves if the averted costs of future ill-health are taken into account. In Australia, for example, Mihalopoulos and others (2007) assessed the costs and benefits of a stepped, multidisciplinary preventative family intervention called Positive Parenting Program (Triple P). The intervention is designed to prevent behavioral disorders in children by increasing parenting knowledge and skills and fostering emotional competence in children; the researchers found that the intervention costs less than the amount it saves, until the reduction in prevalence of conduct disorder falls below 7 percent, at which point net costs become positive. Similarly, in the United Kingdom, parenting programs are expected to be cost saving, with gross savings exceeding the average cost of the intervention by a factor of 8 to 1 (Knapp, McDaid, and Parsonage 2011). Since studies from HICs show such promise, it will be important to determine the feasibility, impact, and costs of these programs in lower-resourced settings.

### **Programs to Train Gatekeepers to Identify People with Mental Illness**

As discussed in chapter 10 in this volume (Petersen and others 2015), mental health first aid training is commonly used at the community level to promote identification and case detection. For example, training of police officers can reduce stigma and improve care for people with MNS disorders (Krameddine and others 2013). There are no studies of the cost-effectiveness of such programs in LMICs; however, a study from Canada showed that a one-day training course significantly increased the recognition of mental health issues, improved efficiency in dealing with mental health issues, and decreased the use of weapons or physical interactions with individuals who were mentally ill. The training cost was US\$120 per officer but led to significant cost savings of more than US\$80,000 in the following six months (Krameddine and others 2013).

## **COST-EFFECTIVENESS OF CARE AND TREATMENT FOR MENTAL, NEUROLOGICAL, AND SUBSTANCE USE DISORDERS**

Chapter 11 in this volume (Shidhaye, Lund, and Chisholm 2015) discusses health care services as a delivery platform for improving population mental health

via three key delivery channels: self-care and informal health care; primary health care; and specialist health care. Chapter 11 also identifies several core strategies for strengthening the capacity of mental health systems through collaborative care, task sharing, and integration with existing health programs. The cost-effectiveness literature relating to care and treatment for MNS disorders is reviewed here in terms of these delivery channels and health system–strengthening strategies.

### **Self-Care and Informal Health Care**

The evidence base on innovative methods that provide an alternative to facility-based services and have the potential to increase access to cost-effective treatment and care in LMICs remains relatively sparse. Yet such innovation will be essential to overcome the inadequate supply of and access to mental health specialists (Patel and others 2010). With the greater support for and diffusion of global mental health research and innovation in alternative models, such as case detection by community members and self-care via e-health or other technologies, greater awareness of the potential impact of such innovations is emerging (<http://mhinnovation.net>).

Evidence on the known effectiveness, feasibility, or cost-effectiveness remains limited for the purposes of informing program design. Even in HICs where systematic reviews of the efficacy, acceptability, and affordability of these approaches have been conducted, cost-effectiveness has not received significant attention. For example, despite a growing number of e-health and self-help randomized clinical trials conducted in HICs in the past decade, most studies fail to provide information on long-term clinical benefits, acceptability, or cost-effectiveness. This lack limits the usefulness of the studies for LMICs, which have more fragmented access to web-based information (Lewis, Pearce, and Bisson 2012; Martinez and others 2014; van Boeijen and others 2005). An example of the kind of information that can be garnered from economic evaluation of these technologies is a Swedish cost-effectiveness trial of Internet-versus group-based CBT for persons with social anxiety disorders (Hedman and others 2011). The study found that both interventions reduced overall societal costs appreciably and delivered similar health benefits to the target population; however, because the Internet-based CBT is less costly, it is the more cost-effective option.

The relative cost-effectiveness of traditional and complementary systems of medicine in the treatment of MNS disorders, vis-a-vis established biopsychosocial models of care, has not been evaluated, despite the fact that such systems of care are widely available and used in LMICs (Gureje and others 2015). This lack of evaluation

reflects the highly heterogeneous nature of the practices undertaken, as well as a lack of established efficacy for them. Estimation of the costs and outcomes associated with a collaborative model of care involving the liaison between traditional and allopathic systems of medicine represents an important if challenging research question, especially in countries or regions where the practice of traditional medicine prevails.

### Primary Health Care

With the increasing attention to mental health care in LMICs and growing evidence that improvements can be achieved with limited resources and impoverished populations, there has been a rise in country-level economic evaluations. Most of the economic analyses to date have been directed to the treatment of mental disorders in health care settings, particularly for mood (affective) disorders, such as depression, and nonaffective psychotic disorders, such as schizophrenia; trial-based and model-based evaluations have been undertaken.

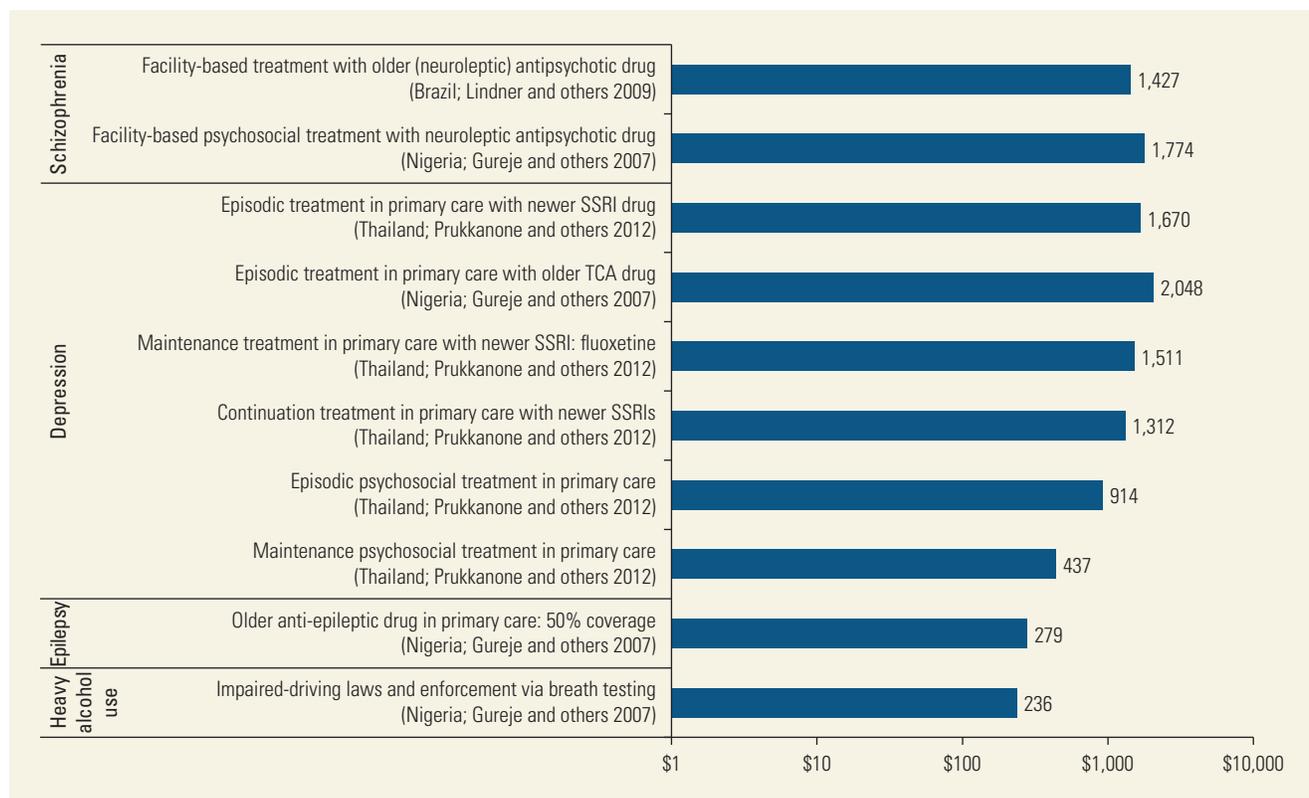
A summary of country-level cost-effectiveness studies that report on the cost per healthy life year gained is shown in figure 12.1 and annex 12D.

### National Studies

One of the first depression trials to include an economic dimension in LMICs was a stepped care, multicomponent program in Chile. The program comprised group intervention, monitoring of clinical progress and medication compliance, and coordinating of further management with primary care physicians (Araya and others 2006). The program was implemented by trained non-physician health care workers and assessed the cost-effectiveness of a task-shifting, stepped care approach to treatment. The results indicated that the innovative program was significantly more effective than the usual care of physician consultations combined with the prescription of antidepressants only and the program was achieved at a modest cost increase; it is now a nationally supported program.

In India, a study of a task-shifting approach to the treatment of depression and/or anxiety (MANAS trial)

**Figure 12.1** Country-Specific Cost-Effectiveness of MNS Interventions  
(cost per disability-adjusted life year averted or healthy life year gained, 2012 US\$)



Note: \*\* = effects measured in quality-adjusted life years gained; all other effect estimates are measured as disability-adjusted life years averted; MNS = mental, neurological, and substance use; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant. All reported cost-effectiveness estimates have been converted to 2012 US\$.

involved trained lay health workers to provide psychosocial interventions as part of primary care. The intervention was found to be cost-effective and cost saving, and it overcame barriers posed by a shortage of mental health professionals (Buttorff and others 2012).

In other country studies, a modeling approach has been used to inform decisions on priority setting and resource allocation. In Thailand, lower cost yet equally effective generic antidepressants and CBT were found to be cost-effective interventions in the acute, continuation, and maintenance treatment phases of depression up to five years after its onset (Prukkanone and others 2012). Maintenance treatment using CBT was the single-most cost-effective strategy, but this finding has to be balanced against the shortage of trained mental health personnel available to deliver psychotherapy services. Applying the same methodological approach to schizophrenia, Phanthunane and others (2011) showed that despite the higher costs of including family psychoeducation, the inclusion of this psychosocial support element increases adherence to and outcomes from medication and is the most cost-effective option. Analysis of these factors helped Thailand to prioritize a strategy to use generic newer drugs as the first-line treatment, ideally in combination with family interventions, to increase health gains and lower hospitalization costs (Phanthunane and others 2011).

In Brazil, where differences in unit prices between older and newer drugs are more marked than in HICs and hospitalization costs are relatively low, cost-effectiveness and budget impact analyses have been conducted to select the most feasible and affordable drug therapy for the treatment of schizophrenia and depression. The use of newer atypical antipsychotic drugs for schizophrenia reduces the probability of hospitalization. But the analysis for Brazil found older neuroleptic drugs to be the more cost-effective strategy overall (Lindner and others 2009). For depression, drug costs represent a smaller share of the economic cost and did not affect the cost-effectiveness across competing alternatives. A budget impact analysis suggested that the addition of serotonin-norepinephrine reuptake inhibitors (SNRIs) for treating depression could generate cost savings to the health care system, given the overall lower average cost per patient treated (Machado and others 2007).

In Colombia, a cost-effectiveness analysis of three classes of antidepressants showed that the older tricyclic antidepressants had greater effectiveness and lower costs compared with the newer selective serotonin reuptake inhibitors and SNRIs. Colombia's lower hospitalization costs compared with Brazil's were the more important cost driver, and in this setting, the drug costs had a minimal impact. In summary, the cost-effectiveness of

antidepressants depends on the relative effectiveness of the choice of drugs, but it is likely determined by budget constraints, pricing policies, and relative hospital costs (Machado and others 2008).

In Nigeria, treating schizophrenia had higher costs per treated case; however, given the larger proportion of the population suffering from depression, the total costs for treating depression were higher (Gureje and others 2007). Cost-effective treatment options for schizophrenia include community-based interventions that combine older antipsychotic drugs with psychosocial treatment or case management. The use of newer atypical antipsychotic drugs without supportive psychosocial therapy was found to be the least cost-effective treatment strategy.

The literature offers very little guidance for what may be cost-effective for other MNS disorders in LMICs, such as dementia, drug use disorders, and childhood disorders. The limited economic evaluations for dementia have been conducted in HICs, focusing on burden and mood, with only a few studies capturing health gains expressed as QALYs (Jones, Edwards, and Hounsome 2012). In the United Kingdom, for example, a manual-based coping strategy program for promoting the mental health of caregivers of people with dementia was found to be cost-effective in cost per QALY terms (Livingston and others 2014). For attention-deficit hyperactivity disorder (ADHD), consistent evidence from HICs demonstrates that drug therapy is cost-effective compared with no treatment or behavioral therapy. None of the cost-effectiveness studies were relevant for adults, in whom ADHD is a growing concern, or for long-term cost-effectiveness beyond six months (King and others 2006; Wu and others 2012).

Very little evidence is available for parent training and education programs for childhood disorders, although these may also offer cost-effective solutions for conduct disorder (Dretzke and others 2005). ADHD and dementia are characterized by a high economic burden on care systems and caregivers of children, adolescents, and the elderly. Evidence shows there is an increase in the indirect costs to caregivers in terms of increased absenteeism and lost productivity associated with managing a family member's care (Matza, Paramore, and Prasad 2005). Findings from HICs are not necessarily transferable to LMICs, given the differences in the recognition, diagnosis, and health care system costs. Yet, as demographic and economic transitions occur, dementia and disorders in childhood and adolescence are likely to rise in prominence (Albanese and others 2011).

There is also a dearth of economic evidence to guide and support drug policy and resource allocation decisions. Even in HICs, evidence is restricted to one

or two studies of specific treatment modalities, such as substitution or maintenance treatment of opioid dependence. In Australia, for example, methadone maintenance treatment and buprenorphine maintenance treatment were found to lead to appreciable increases in heroin-free days at an acceptable and not significantly different level of cost-effectiveness (Doran 2005; Harris, Gospodarevskaya, and Ritter 2005). In countries where the spread of HIV is being fueled by injecting drug users, methadone maintenance programs can also be an effective and cost-effective strategy for HIV prevention, as evidenced by a study undertaken in Belarus, where the average cost per averted HIV infection was projected at less than US\$500 (Kumaranayake and others 2004).

### International Studies

Cost-effectiveness modeling has also been conducted at the regional and international levels. Although these levels lack specificity to a national decision-making context, they can inform priority-setting agendas at the national and international levels, including investment decisions by donors and nongovernmental organizations.

The primary source of evidence for MNS disorders to date comes from the WHO-CHOICE program (Chisholm 2005; Chisholm and Saxena 2012; Hyman and others 2006). An advantage of the WHO-CHOICE approach is its application of a consistent methodology, which enables like-with-like comparisons to be made between different disorders and geographical regions. Table 12.1 shows the comparative cost-effectiveness of a range of interventions for addressing MNS disorders in different regions of the world, relative to a situation of no intervention. Because each intervention is compared with a situation of no treatment, the resulting metric is called an average, as opposed to incremental, cost-effectiveness ratio.

The results are reported for six geographically distinct groupings of LMICs that are used by the World Bank for reporting purposes. Inevitably, such country groupings contain substantial sociocultural as well as economic heterogeneity, which limits their applicability to particular contexts or populations. Previously published and updated findings (Chisholm and Saxena 2012; Hyman and others 2006) have been converted here to 2012 US\$ values, based on International Monetary Fund inflation estimates, to enable comparison with other cost and cost-effectiveness information presented in this and other DCP-3 volumes. The exception to this price conversion process relates to newer psychotropic medications, such as fluoxetine for depression or risperidone for

psychotic disorders, which are now produced in several countries under nonbranded, generic licenses and can be purchased for approximately 10 times less than a decade ago.

As long as these lower, generic prices of newer antidepressant and antipsychotic medications are sought out and applied, the previously demonstrated cost-effectiveness superiority of interventions using older drugs for treating schizophrenia and depression essentially disappears, meaning that there is little reason to choose between them on efficiency grounds (see table 12.1). What remains clear, however, is that drug treatment alone does not constitute the most cost-effective option for treating mental disorders; rather, it is the combination of pharmacological and psychosocial treatment that leads to the best overall balance of cost and health outcome for severe mental disorders.

Across the six regions considered, the average cost per healthy life year gained for such a combination strategy—the most cost-effective of the strategies considered—ranges from US\$3,300 to US\$14,000 for schizophrenia and bipolar disorder. For depression, treatment in primary health care on an episodic basis costs between US\$800 and US\$3,500 per healthy life year gained; for a little more cost, as well as more overall health gain in the population, treatment on a proactive, maintenance basis is also a cost-effective alternative, because so many persons experience recurrent episodes (US\$1,300–US\$4,900 per healthy life year gained). Differences in cost per healthy life year gained are largely driven by the cost of labor and contacts with the health care system (relatively higher in Latin America and the Caribbean and relatively lower in Sub-Saharan Africa and South Asia).

Other disorders that can be appropriately managed in nonspecialist health care settings and that have been subjected to economic evaluation cover neurological disorders (epilepsy and migraine) and substance use disorders (harmful alcohol use). WHO-CHOICE analyses conducted for these disorders, again updated to 2012 prices, indicate that they are at least as cost-effective to treat as the aforementioned mental disorders (Chisholm 2005; Linde, Chisholm, and Steiner 2015; Rehm and others 2006). Table 12.1 indicates that a year of healthy life can be obtained for less than US\$1,000 by offering brief interventions to persons with alcohol use disorders, and for between US\$600 and US\$2,500 by treating epilepsy with first-line anti-epileptic drugs. For migraine, a recent multicountry study using WHO-CHOICE methods has been completed and is highlighted in box 12.1.

**Table 12.1** Regional Cost-Effectiveness of Interventions for MNS Disorders  
(cost per disability-adjusted life year averted or healthy life year gained, 2012 US\$)

Disorder: intervention	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 Pacific
<i>Schizophrenia</i>						
SCZ-1: community-based treatment with older (neuroleptic) antipsychotic drug	8,390	20,465	21,263	13,799	4,915	5,688
SCZ-2: community-based treatment with newer (atypical) antipsychotic drug	7,978	18,961	19,755	12,891	4,718	5,414
SCZ-3: community-based treatment with older antipsychotic drug + psychosocial treatment	6,005	13,858	14,413	11,396	3,490	3,865
SCZ-4: community-based treatment with newer antipsychotic drug + psychosocial treatment	6,014	13,649	14,192	11,233	3,523	3,890
<i>Bipolar disorder</i>						
BIP-1: community-based treatment with older mood stabilizer drug (lithium)	4,571	14,261	12,120	9,999	3,392	4,402
BIP-2: community-based treatment with newer mood stabilizer drug (valproate)	7,930	16,470	13,911	12,339	5,047	5,839
BIP-3: community-based treatment with older mood stabilizer drug + psychosocial care	4,516	13,292	11,440	9,329	3,281	4,136
BIP-4: community-based treatment with newer mood stabilizer drug + psychosocial care	7,583	15,287	13,094	11,426	4,784	5,434
<i>Depression</i>						
DEP-1: episodic treatment in primary care with older antidepressant drug (TCAs)	1,410	3,491	3,171	2,668	786	899
DEP-2: episodic treatment in primary care with newer antidepressant drug (SSRIs)	1,395	3,361	3,057	2,456	788	894
DEP-3: episodic psychosocial treatment in primary care	2,189	4,838	4,594	2,724	1,161	1,223
DEP-4: episodic psychosocial treatment + older antidepressant	2,083	4,427	4,232	2,722	1,128	1,178
DEP-5: episodic psychosocial treatment + newer antidepressant	2,144	4,477	4,285	2,660	1,167	1,218
DEP-6: maintenance psychosocial treatment + older antidepressant	2,461	4,866	4,783	3,225	1,315	1,373
DEP-7: maintenance psychosocial treatment + newer antidepressant	2,532	4,927	4,847	3,137	1,367	1,425
<i>Alcohol use disorders</i>						
ALC-8: brief physician advice in primary care	407	878	—	494	684	332
<i>Epilepsy</i>						
EPI-1: older anti-epileptic drug in primary care	694	1,511	1,450	2,516	600	1,057
EPI-2: newer anti-epileptic drug in primary care	1,884	2,854	2,877	4,115	1,639	2,249

Sources: Chisholm and Saxena 2012; Hyman and others 2006.

Note: MNS = mental, neurological, and substance use; TCAs = tricyclic antidepressants; SSRIs = selective serotonin reuptake inhibitors; — = not available.

## Box 12.1

### Cost-Effectiveness of Interventions for Migraine

A WHO-CHOICE (World Health Organization–CHOosing Interventions that are Cost-Effective) analysis was conducted for a selected core set of interventions for migraine in four countries: China, India, the Russian Federation, and Zambia. The analysis included first-line analgesics, such as acetylsalicylic acid 1,000 milligrams (mg), and second-line medications, such as sumatriptan 50 mg, for acute treatment of attacks. It was assumed that the latter would be used only by nonresponders to first-line medications (a stepped care treatment paradigm). The analysis included prophylactic drugs, such as amitriptyline 100 mg daily. The expected consequences of adding consumer education, in the form of posters and leaflets in pharmacies explaining how to acquire and use these medications, and training for health care providers were also modeled. Compared with no treatment, the cost per healthy

life year gained ranged from less than US\$100 for acute management with simple analgesics to thousands or even tens of thousands of US\$ for treatment of analgesic nonresponders with triptans.

The most cost-effective strategy by far is acute management with simple analgesics; it was less than US\$100 per disability-adjusted life year averted and therefore represents a highly cost-effective use of resources for health. Adding consumer education and improving adherence has a small upward influence on cost-effectiveness. Compared with no treatment at all, this strategy is less than US\$150 per healthy life year gained; compared with use of simple analgesics without consumer education, the incremental cost to be paid to obtain one extra healthy life year rises to US\$600.

*Source:* Linde, Chisholm, and Steiner 2015.

### Specialist Health Care

Specialized mental health care covers hospital-based outpatient and inpatient care for acute and severe episodes or cases of mental disorder. In many LMICs, mental hospitals absorb a disproportionate share of the government mental health budget—over 70 percent in many cases—yet such institutions are commonly associated with isolation, human rights violations, and poor outcomes. Such expenditure patterns also curb the development of more equitable and cost-effective community-based services.

The dramatic deinstitutionalization observed in most HICs in recent decades has been accompanied by a certain amount of economic research into the costs, needs, and outcomes of persons relocated into community-based care. Such research has shown that community-based care is certainly associated with better health and social outcomes, and it is not inherently more costly than institutions, once account is taken of individuals' needs and the quality of care (Knapp and others 2011). New community-based care arrangements could be more expensive than long-stay hospital care, but they may still be seen as more cost-effective because, when appropriately set up and managed, they deliver better health and economic outcomes. Accordingly, such a process of deinstitutionalization should not be predicated on

the basis of expected cost savings; inadequate expenditure on community-based care is quite likely to result in poor outcomes for the individuals and families concerned (Knapp and others 2011).

Detailed analysis of this kind has not been conducted in the context of ongoing efforts to relocate services in LMICs. However, a simple comparison of the cost of a community-based versus hospital-based service model has been carried out as part of the WHO-CHOICE analysis for schizophrenia and bipolar affective disorder. For schizophrenia, the costs of the hospital-based service model exceeded those of the community-based service model by 33–50 percent, reflecting greater use of resource-intensive services, such as acute and long-term psychiatric inpatient care (Chisholm 2005; Chisholm and others 2008). Even if one assumes no improved outcomes for persons treated under the community-based service model, there is a clear difference in terms of cost-effectiveness; the costs of the community-based service model are 25–40 percent lower.

Relocating services and resources away from long-stay mental hospitals toward nonspecialized health settings is a key financing issue for mental health systems. Efforts to change the balance of mental health care are often hindered by a lack of appropriate transitional funding. Transitional or dual funding is required over a

period of time to build up appropriate community-based services before residents of long-term institutions can be relocated. It is crucial to present an evidence-based case for relocating the locus of care, not only on the grounds of equity, human rights, and user satisfaction, but also on the grounds of financial feasibility over a defined transitional period.

## AFFORDABILITY: COSTS OF INTERVENTION SCALE-UP

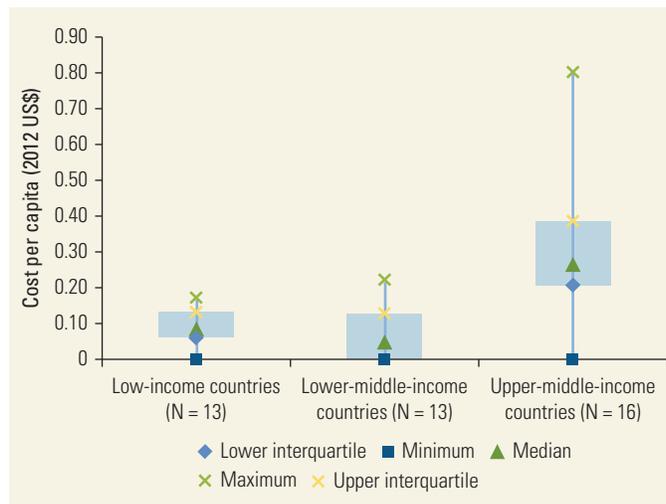
The finding that interventions for the prevention and treatment of a range of MNS disorders have been cost-effective in LMICs does not necessarily translate into their affordability, especially given very low budget allocations for mental health. In addition to evidence on the effectiveness and cost-effectiveness of different policy or treatment options, therefore, information is also needed on the feasibility and acceptability of interventions, including their financial feasibility or affordability. In this section, we provide estimates of the expected costs of scaling up the delivery of a set of cost-effective policies and intervention strategies, including demand reduction measures for harmful alcohol use at the population level, school-based mental health promotion at the community level, and treatment of priority MNS disorders in nonspecialized health care settings.

### Demand Reduction Strategies for Harmful Alcohol Use

The economic evidence presented earlier in this chapter indicates that the most cost-effective strategy for reducing alcohol consumption is raising taxes or prices on alcohol products, followed by banning alcohol advertising, restricting access to alcohol, and enforcing drinking and driving legislation. Analysis of the costs of scaling up these interventions in LMICs was undertaken by the WHO in preparation for the High-Level Meeting on Non-communicable Diseases (WHO 2011). The overall annual cost per capita of implementing the constituent elements of an alcohol demand reduction strategy was estimated for countries with low versus middle incomes. The median cost ranges from less than US\$0.10 per capita for low-income countries (LICs) and lower-middle-income countries to around US\$0.25 for upper-middle-income countries (figure 12.2). These costs are driven by human resource needs for program management and enforcement of alcohol-related laws and policies, as well as media-related expenses.

The variability around the median cost of implementation results from large intercountry differences in the prevalence of alcohol use. Application of the same costing

**Figure 12.2** Cost of Scaling Up Population-Based Alcohol Control Measures in Low- and Middle-Income Countries



Source: WHO 2011.

Note: N = number.

methods to three illustrative countries from these different income strata—Ethiopia, India, and Mexico—yields similar results (US\$0.06, US\$0.10, and US\$0.24, respectively). Although such per capita costs indicate that these strategies are inherently affordable, total costs can add up quickly. This is particularly the case in larger countries, such as Nigeria, where government policies that increase taxation on alcohol are expected to cost US\$13 million per year, and policies such as roadside breath testing are expected to cost even more (US\$25 million per year at 80 percent coverage) (Gureje and others 2007).

### Social Emotional Learning Programs

As documented in chapter 10 in this volume (Petersen and others 2015), sufficient evidence exists from LMICs and HICs to consider universal and targeted SEL programs as best practice policies for countries to implement. This finding is particularly true when teachers and school counselors can be trained to deliver these interventions by integrating social and emotional learning and life skills development in life orientation curricula.

The cost of implementing school-based SEL interventions in the context of LMICs has not yet been estimated, so an analysis was undertaken for the specific purpose of this volume for a selection of countries—Ethiopia, India, Mauritius, and Mexico—using methods already developed for micro-costing of population-based alcohol control strategies (WHO 2011). In addition, the analysis used data from a psychosocial intervention to prevent depression in adolescents ages 12 to 16 years in Mauritius (Rivet-Duval, Heriot, and Hunt 2011). The Resourceful

Adolescent Programme–Adolescent version (RAP-A) showed that 11 hourly psychosocial sessions led to short-term benefits to depression, hopelessness, coping skills, and self-esteem; benefits to coping skills and self-esteem were sustained at follow-up after six months.

For costing this intervention, we assessed the annual budgetary impact associated with the implementation of the program among all 12-year-olds in the local population, who make up 0.8–1.4 percent of the total population in the selected countries. The health educators, who are teachers, are assumed to work full-time on this program, visiting and delivering the intervention at different schools within municipalities or districts (six sessions per day). If teachers deliver the RAP-A program on a part-time basis, training costs—which include training of trainers at the national level and subnational courses each year for the health educators—will be higher. For every set of 20 health educators, we included one supervisor; central administration and program management costs were also included.

Based on 220 school days per year and 20 students per session, 1.7–2.8 full-time health educators would be needed to deliver the intervention at scale for a district of one million persons (table 12.2). Country-specific unit cost estimates taken from the WHO-CHOICE database (<http://www.who.int/choice/costs>) were used to place a monetary value on these various resource inputs. The resulting cost of implementing this program at full scale (100 percent coverage) ranges from US\$0.03 per head of population in Ethiopia and India to US\$0.11 in Mexico and US\$0.24 in Mauritius, reflecting higher salary and other input costs. These findings indicate that school-based SEL interventions represent a low-cost strategy for promoting adolescent mental health. More information about and evaluation of the long-term effectiveness of programs such as RAP-A is needed.

### Mental Health Care in Nonspecialized Treatment Settings

Successful scaling up of mental health services involves putting together a range of human, physical, and other resource inputs to deliver interventions

and services capable of improving mental health and related outcomes. Accordingly, an essential element of evidence-based mental health service planning and scale-up relates to an assessment of what resources are required to deliver services to the population in need and to meet program goals. However, the lack of complete or reliable local epidemiological and resource data has often thwarted such efforts in many countries, although that is changing with the generation of national mental health profiles (see, for example, WHO’s mental health ATLAS database, <http://apps.who.int/globalatlas>).

Empirical studies offer insights into average treatment costs for depression and schizophrenia, when using medication alone or in combination with psychotherapy (annex 12E). Using older antidepressant drugs and providing stepped care tailored to the needs of patients has relatively low annual costs per case of depression, from US\$107 in India to less than US\$200 in Nigeria (Buttorff and others 2012; Gureje and others 2007). Similarly, the annual cost per treated case of epilepsy is relatively low; in Nigeria, older anti-epileptic drugs are less than US\$100 per patient per year. Schizophrenia is generally more expensive to treat per person, using drug therapy alone, than either depression or epilepsy. Schizophrenia treatment costs are more likely to vary widely across countries, depending on the combination of inpatient and outpatient treatment and the antipsychotic medications used.

In Nigeria, treating schizophrenia with older antipsychotic drugs falls between US\$200 and US\$300; newer antipsychotic drugs cost more than US\$6,000 per year. In Brazil, treatment with older, first-generation antipsychotic drugs is as low as US\$120 per patient per year; second-generation drugs cost more than US\$4,000 per person annually (Lindner and others 2009). In Thailand, direct medical costs for drug treatment in combination with family interventions are US\$764 per patient per year. The variability in costs per person treated is in part due to the small number of studies that have explored the costs of different combinations of interventions and are not necessarily comparable. Accordingly, the studies are not particularly useful for estimating the total cost of an essential package of mental health services. Total costs also

**Table 12.2** Cost of Implementing Resourceful Adolescent Programme–Adolescent Version in Four Countries

Cost item	Ethiopia	India	Mexico	Mauritius
Total population age 12 years (%)	1.4	1.1	1.0	0.8
Health educators needed per 1 million population (at 100% coverage)	2.8	2.3	2.1	1.7
Cost per head of population at 100% coverage (US\$)	0.03	0.03	0.11	0.24

Source: World Health Organization, CHOICE (database), <http://www.who.int/choice/costs>.

vary considerably among countries, given their different epidemiological mental health profiles, national policies, and access to health care.

Analytical tools and methods for financial planning have been developed for many disease areas and programs; these have been used to estimate the cost of significantly scaling up the delivery of a specified package of mental health care in LMICs (Chisholm, Lund, and Saxena 2007). These authors carried out a financial analysis to estimate the expenditures needed to scale up over a 10-year period the delivery of a specified mental health care package, comprising pharmacological and/or psychosocial treatment for schizophrenia, bipolar disorder, depression, and hazardous alcohol use. Current service levels in 12 selected LMICs were established using the WHO-AIMS (Assessment Instrument for Mental Health Systems) assessment tool.

The analysis estimated the costs to meet the specified target coverage levels of 80 percent of cases with psychosis and bipolar disorder, and 25–33 percent of cases with depression and risky drinking. Spending for this package would need to be approximately US\$2.00 per capita in LICs (compared with current spending of US\$0.10–US\$0.20), and US\$3.00–US\$4.00 in middle-income countries. For a middle-income country of 50 million people, total annual spending on the package would amount to between US\$150 million and US\$200 million. A subsequent, updated assessment of the comparative cost-effectiveness analysis of 44 neuropsychiatric interventions in two WHO subregions (one in Sub-Saharan Africa, the other in South Asia) estimated that the annual cost of delivering a defined package of interventions for schizophrenia, depression, epilepsy, and alcohol use disorders would be US\$3–US\$4 per capita (Chisholm and Saxena 2012).

This approach to service costing has been applied more recently to the subnational context of scaling up mental health services in LMICs, as part of the PRogramme for Improving Mental health carE (PRIME) study being conducted at the district level in Ethiopia, India, Nepal, South Africa, and Uganda (Lund and others 2012). The costing analysis was carried out to inform local PRIME country teams about the expected resource implications and financial feasibility associated with the implementation of their respective district mental health care plans (Chisholm, Burman-Roy, and others 2015). The results indicated that, starting from a generally very low base of mental health service coverage and expenditure, the cost of scaled-up provision in nonspecialist health care settings of an evidence-based package of care that included psychosis, depression, alcohol use disorders and, in some countries, epilepsy, range from US\$0.25 to US\$0.70 per capita in four of the five districts

assessed (figure 12.3). For a district with a total population of one million persons, therefore, an annual outlay of US\$250,000–US\$700,000 would be required to reach the specified target coverage levels. The outlier is South Africa, where the prevailing price and quantity of health care service inputs are much higher. The cost per capita of delivering the specified care package at target coverage levels in the South African district approaches US\$2.50 per capita; this is higher than in the other countries but relatively low in the context of current health spending levels in South Africa.

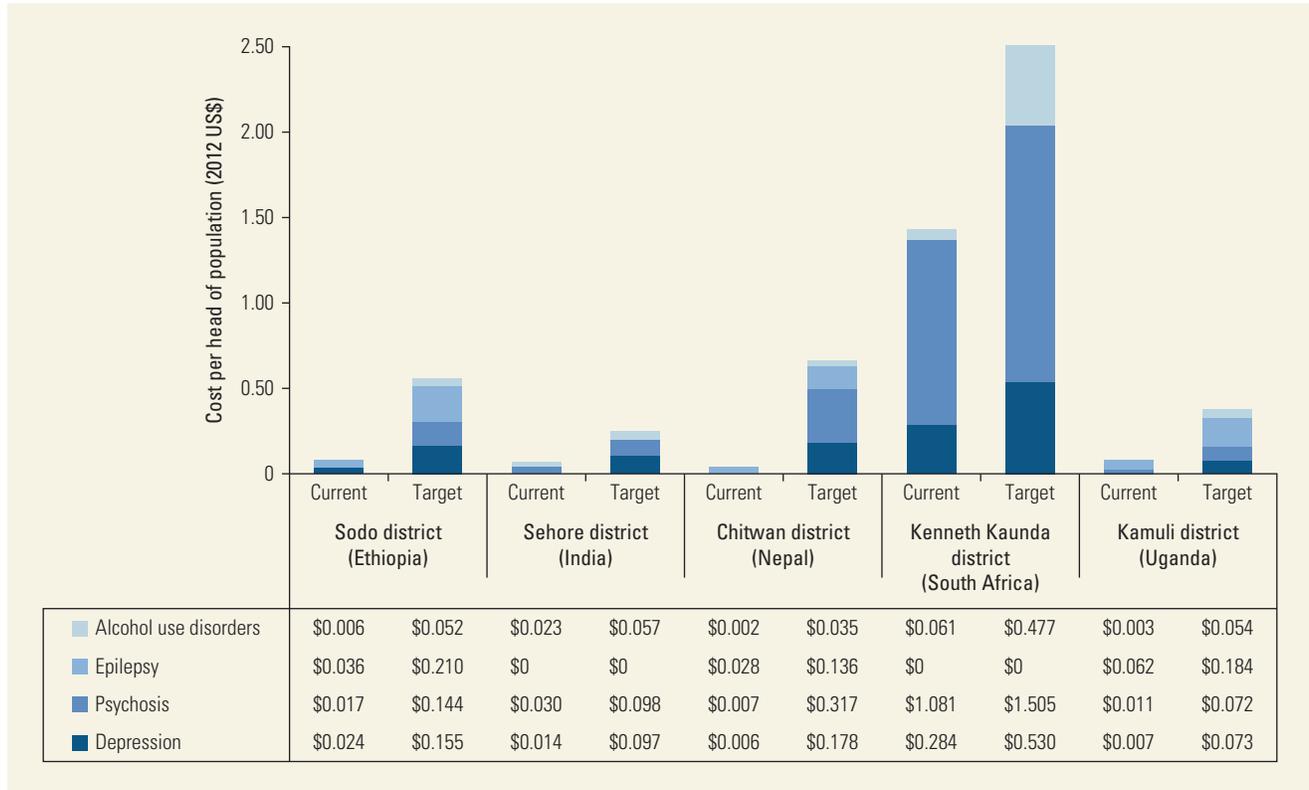
Getting to target levels of annual spending in each district would necessitate a steady budgetary increase, estimated at US\$0.02–US\$0.11 extra per head of population per year if a 10-year period is used. Extending the cost estimation to take into account program management and some utilization of specialist, hospital-based services by the district population increases these baseline cost projections, substantially so in India and South Africa (by at least 100 percent) and modestly so in the other three sites (by approximately 20 percent). These upper cost estimates amount to only 1 percent of total current health spending per capita in South Africa and up to 7 percent in Ethiopia.

A limitation of the costing methods used for this recent analysis is that they are unable to take proper account of critical health system constraints to service scale-up, such as midterm expenditure caps, supply-side bottlenecks in recruiting staff or accessing essential medicines, and inadequate referral and supervision mechanisms. Such constraints can substantially alter the actual level of program implementation or achievement. Even if such supply-side factors were managed successfully, there is the additional concern that demand for and actual uptake of available services do not match the desired levels of effective coverage, for example because of the influence on help-seeking behaviors of stigma around mental illness. Broader environmental and political factors can likewise impact the success or efficiency of implemented strategies of care or prevention.

## CONCLUSIONS

This chapter reviewed the available evidence concerning the cost and cost-effectiveness of interventions for the protection, prevention, and treatment of MNS disorders. The review has shown that there is a considerably greater economic evidence base now than there was when *Disease Control Priorities in Developing Countries*, first edition, was published (Jamison and others 1993). Seminal clinical trials of the treatment of common mental disorders in LMICs have included a cost-effectiveness component. Country- and regional-level economic

**Figure 12.3** Costs of Scaling Up a Mental Health Care Package in Nonspecialized Health Care Settings in Five Low- and Middle-Income Country Districts



Source: Chisholm, Burman-Roy, and others 2015.

modeling studies have been conducted for a range of disorders, permitting comparison of relative cost-effectiveness with other DCPs. Arguably, there is now sufficient evidence to counteract or debunk the overgeneralized claim that treatment of mental disorders is not a cost-effective use of scarce health care resources.

As with any other area of health, the reality is that the range of possible interventions varies a great deal with respect to their cost-effectiveness. An analysis of 500 single and combined interventions assessed by the WHO-CHOICE project for the prevention and control of noncommunicable diseases and injuries in two LMIC regions found that costs differed by at least three orders of magnitude (from a few cents to more than US\$10 per capita), as did cost-effectiveness (from US\$10 to more than US\$100,000 per healthy life year gained) (Chisholm and others 2012).

In the economic analysis for MNS disorders in this series, Chisholm and Saxena (2012) found a very substantial range of cost-effectiveness, with alcohol control measures, drug treatment for epilepsy, and depression treatment identified as offering the best value for money in the two WHO subregions assessed (one in Sub-Saharan

Africa, the other in South-East Asia). This wide range of cost-effectiveness points to the importance of carefully evaluating and choosing an appropriate set of interventions for scaled-up investment and implementation; selecting an inefficient set will waste money and limit potential health gains. Unfortunately, however, a high proportion of mental health budgets is being used in the provision of the least cost-effective interventions, such as long-term inpatient treatment of severe mental disorders in mental hospitals. Very little is invested in more cost-effective strategies, including the community-based provision of adjuvant psychosocial treatment for severe mental disorders, and measures to reduce access to or marketing of alcohol.

Ultimately, policies are enacted and resources allocated at the level of individual countries. It is important that more economic evidence be generated alongside clinical trials or other evaluations at the national level, rather than relying on international estimates that may lack sensitivity to local priorities or health system characteristics. Our review highlighted several cost-effectiveness studies from high as well as lower-income country settings to show

the informational and policy value of such evaluations. Such studies are particularly needed in areas where there is currently a dearth of evidence, including prevention and treatment of childhood disorders, drug use disorders, community-based parenting programs, suicide prevention, and dementia care. The use of comparable costing methods and outcome measurements, that should ideally also incorporate the impact of interventions on income, employment, or poverty, will greatly serve to build up a cogent international evidence base for greater investment in the care and prevention of MNS disorders.

Similarly, the use and application of available tools and methods for costing interventions can help to articulate in budgetary terms the scaling-up or universal coverage goals that a country has set for itself and place financial planning on a firmer footing. Costing analysis to date, including that presented in this chapter, has indicated that significantly scaled-up delivery of a prioritized, evidence-based set of interventions is actually far from being unaffordable in absolute terms. What remains strikingly high is the funding gap between what is needed and what is available, and it is this fact that can make the *relative* increase in budgetary allocations appear daunting in many LICs. Scaling up needs time, not only to build human resource and system capacity, but also to allow for the reallocation of resources away from less efficient uses (including mental hospitals) and the allocation of new domestic or international resources for mental health system development.

## ANNEXES

Annexes to this chapter are as follows. They are available at <http://www.dcp-3.org/mentalhealth>.

- Annex 12A. List of Search Terms
- Annex 12B. Flow Chart and Search Statistics of Identification, Screening, and Eligibility of Included Studies for Mental, Neurological, and Substance Use Disorders
- Annex 12C. List of Studies for Costs and Cost-Effectiveness
- Annex 12D. Cost-Effectiveness Results by Intervention
- Annex 12E. Cost Estimates by Intervention

## NOTES

Disclaimer: Dan Chisholm is a staff member of the World Health Organization. The author alone is responsible for the views expressed in this publication, and they do not necessarily represent the decisions, policy, or views of the World Health Organization.

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.

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