Global Mental Health 3

Treatment and prevention of mental disorders in low-income and middle-income countries

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We review the evidence on effectiveness of interventions for the treatment and prevention of selected mental disorders in low-income and middle-income countries. Depression can be treated effectively in such countries with low-cost antidepressants or with psychological interventions (such as cognitive-behaviour therapy and interpersonal therapies). Stepped-care and collaborative models provide a framework for integration of drug and psychological treatments and help to improve rates of adherence to treatment. First-generation antipsychotic drugs are effective and cost effective for the treatment of schizophrenia; their benefits can be enhanced by psychosocial treatments, such as community-based models of care. Brief interventions delivered by primary-care professionals are effective for management of hazardous alcohol use, and pharmacological and psychosocial interventions have some benefits for people with alcohol dependence. Policies designed to reduce consumption, such as increased taxes and other control strategies, can reduce the population burden of alcohol abuse. Evidence about the efficacy of interventions for developmental disabilities is inadequate, but community-based rehabilitation models provide a low-cost, integrative framework for care of children and adults with chronic mental disabilities. Evidence for mental health interventions for people who are exposed to conflict and other disasters is still weak—especially for interventions in the midst of emergencies. Some trials of interventions for prevention of depression and developmental delays in low-income and middle-income countries show beneficial effects. Interventions for depression, delivered in primary care, are as cost effective as antiretroviral drugs for HIV/AIDS. The process and effectiveness of scaling up mental health interventions has not been adequately assessed. Such research is needed to inform the continuing process of service reform and innovation. However, we recommend that policymakers should act on the available evidence to scale up effective and cost-effective treatments and preventive interventions for mental disorders.

Introduction

The previous two reviews in this Series on global mental health[5,6] have summarised how mental disorders are related to other health conditions, and described the gap between needs and services for mental health, especially in low-income and middle-income countries. We investigated whether interventions to treat and prevent mental disorders are sufficiently effective and affordable to support a substantial scaling-up of such services in low-income and middle-income countries. Although evidence for the effectiveness of such interventions is robust, most of it has been derived from high-income countries.[7,8] Because differences in sociocultural factors and health systems probably limit the generalisability of evidence to low-income and middle-income countries,[9] we restricted our review to evidence gathered in these countries. We focused on four mental disorders that pose the greatest burden in adults and children: depression, schizophrenia, alcohol-use disorders, and developmental disabilities

Search strategy

We searched the PsiTri database (EU Mental Health library) and the separate registers of trials held by Cochrane groups (Depression, Anxiety and Neurosis Group; Drugs and Alcohol Group; Schizophrenia Group, and Developmental, Psychosocial and Learning Problems Group) for studies of the treatment of mental disorders. We also did a manual search of the online databases PubMed and Medline. We searched for "depression", "schizophrenia", "developmental disabilities", "mental retardation", and "alcohol-use disorders". We selected all randomised controlled trials generated in low-income and middle-income countries, about any treatments for these four key disorders.

Limitations of our review include time delays between identification of a reference in the PsiTri database, obtaining a hard-copy publication, and coding into PsiTri. Second, because the participating countries in multicentre trials are not always listed in Psi Tri, we excluded multicentre trials since we could not select multicentre trials that were conducted solely in low-income and middle income countries. We were also unable to ensure that the large number of Chinese schizophrenia studies excluded duplicates.

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To assess the evidence for cost-effectiveness of interventions for the four disorders, we applied more stringent inclusion criteria to the results of our search. For depression and schizophrenia, we focused on trials that assessed interventions identified by the Disease Control Priorities Project (DCP2)[1] as cost-effective for low-income and middle-income countries. Because the DCP2 project did not include alcohol-use disorders and developmental disabilities, we reviewed all intervention types for these disorders. We only included controlled trials (placebo or usual care) published since the World Health Report in 2001.[2]

To find studies about the prevention of mental disorders, we used the WHO Report on Prevention of Mental Disorders[3,4] and a systematic search of PsycInfo, Medline, Pubmed, and Cochrane databases, with the following keywords: "prevention"; "mental disorders"; specific mental disorders ("depression", "schizophrenia", "developmental disabilities", and "alcohol-use disorders"); and major risk factors ("child abuse and neglect", "violence", "family disruption", "mentally-ill parents", "poverty", and "refugee status").

We used an unpublished systematic search for studies of interventions during and after conflict or disaster situations in low-income and middle-income countries that include quantitative preintervention and postintervention measures. We searched for descriptions of "conflict" ("war", "violence", "refugees", and "torture") and "disaster" ("earthquake", "hurricane", "tsunami", and "volcano") combined with "treatment outcome" and "mental health services".

(cognitive disabilities or mental retardation, attention deficit hyperactivity disorder, and autism). Interventions in conflict or emergency-affected contexts are a special case, but must be considered since they continue to affect vast numbers of people in low-income and middle-income countries. Finally, we consider the implications of evidence for such interventions on policy and practice.

	Trials (n=11 501)
Low-income country	104 (0·9%)
Lower middle-income country	1104 (9·6%)
Upper middle-income country	311 (2·7%)
High income country or multicentre trial	9982 (86·8%)

Table 1: **Trials of mental-health interventions by income level of country**

	Trials (n=1521)
Region	
East Asia and Pacific	977 (64·2%)
Eastern Europe and central Asia	242 (15·9%)
Latin America and Caribbean	135 (8·9%)
South Asia	88 (5·8%)
Sub-Saharan Africa	51 (3·4%)
North Africa and middle east	28 (1·8%)
Type of disorder	
Schizophrenia	1137 (74·8%)
Depression	361 (23·7%)
Developmental disabilities	12 (0·8%)
Alcohol dependency or harmful use	11 (0·7%)
Number of trial participants	
<100	1079 (71·3%)
100–499	316 (20·9%)
>500	8 (0·5%)
Not stated	111 (7·3%)

Table 2: **Trials of mental-health interventions in low-income and middle-income countries by region, type of disorder, and number of participants**

Global evidence for clinical treatments

We identified 11 501 trials worldwide that assessed interventions for the treatment or prevention of schizophrenia, depression, developmental disabilities, or alcohol-use disorder. Table 1 shows that most of this evidence is derived from high-income countries.[7,8] Fewer than 1% of identified trials were from low-income countries and only about a tenth of identified trials were from low-income and middle-income countries. Of these trials, about two-thirds (958/1521) were from China, and more than half (834/1521) assessed interventions to treat schizophrenia in China.

Table 2 shows that about three-quarters of all trials in low-income and middle-income countries investigated treatments for schizophrenia, and one-quarter investigated depression. We identified only 11 trials dealing with alcohol dependence or harmful use of alcohol, and 12 trials dealing with developmental disabilities. The most recent trial for mental retardation was in 1994. Over half of all trials in low-income and middle-income countries (838/1521) were published after the World Health Report on Mental Health in 2001.

	Number of trials
Depression	
Psychosocial treatment	37 (10·2%)
Antidepressant drugs	228 (63·2%)
Mood stabilising drugs	64 (17·7%)
Other intervention	32 (8·9%)
Schizophrenia	
First generation antipsychotic	451 (39·7%)
Family or community intervention	97 (8·5%)
Second generation antipsychotic	318 (28·0%)
Psychological therapy	93 (8·2%)
Other intervention	178 (15·7%)

Table 3: **Trials of treatments identified as cost effective by the Disease Control Priorities Project 2**

	High-income countries		Low-income and middle-income countries	
	Evidence	Level of evidence*	Evidence	Level of evidence*
Depression				
Antidepressants	Antidepressants are more effective than placebo[10-12] but similar to psychotherapeutic interventions;[13] a combination of antidepressants and psychotherapy is the most effective treatment[14]	1	Antidepressants, alone or in combination with other treatments, are efficacious.[15-17]	2
Psychological interventions	Brief psychotherapeutic approaches (cognitive behaviour therapy or interpersonal therapy or problem solving) are more effective than placebo for treatment of moderate or more severe depression[18]	1	Individual psychoeducation is more effective than usual care[19] Group interpersonal therapy is more effective than usual care[20,21] and psychoeducational groups, as part of a stepped-care treatment programme, are more effective than usual care[15]	2
Schizophrenia				
First generation antipsychotics	First generation antipsychotics are more effective than placebo[22,23] and as effective as second generation antipsychotics[24-29]	1	First generation antipsychotics are as effective as second generation antipsychotics for treatment of first-episode psychosis[27]	3
Family therapy and community-based interventions	Programmes such as assertive community treatment,[30] supported housing,[31] and vocational rehabilitation[32] are effective for integration of people with schizophrenia within the community	1	Family interventions are effective for reduction of relapse rates and improvement to the lives of people with schizophrenia[33-35]	2
Alcohol misuse and alcohol dependence				
Pharmacological interventions	Naltrexone is effective for reduction of relapse rates and lowered risk of treatment withdrawal.[36,37] Acamprosate reduces drinking frequency[37,38]	1	Acamprosate is associated with significantly higher continuous abstinence time;[39] naltrexone is associated with improved completion rates in outpatient treatment programmes for people with alcohol dependence[40]	2
Psychological interventions	Brief physician-delivered interventions are effective, especially for patients with less severe drinking problems.[41] Brief screening tools are an effective method for detection of drinking problems in primary care[42]	1	Brief physician-delivered intervention is associated with reduced intensity and amount of alcohol consumption, especially in men[43]	2
Developmental disabilities				
Pharmacological interventions	Antipsychotic medication reduces the severity of problem behaviours associated with mental retardation[44,45] and autism.[46] Methylphenidate improves behaviour in children with ADHD[47] and is cost-effective[48]	1,2	A herbal preparation reduces the severity of problem behaviours associated with mental retardation.[49] Methylphenidate improves behaviour in children with ADHD[50]	3
Psychosocial interventions	Functional analysis helps reduce problem behaviours associated with mental retardation.[51] Cognitive-behaviour methods have a modest impact on reduction of aggressive behaviour in the short-term;[52] individual psychological treatments have a modest benefit[53]	1	Interactive group psychoeducation improves parental orientation towards child-rearing, knowledge towards intellectual disability, and attitude towards management of mental retardation[54]	3
Community interventions	Community living offers lifestyle and skill-development advantages associated with improved life quality compared with living in large residential institutions.[55]	4	Community-based rehabilitation improves activities of daily living in adults with mental retardation, and school participation in children with mental retardation[56-58]	4

*Levels of evidence: 1=systematic review; 2=two or more randomised controlled trials (RCTs); 3=one RCT; 4=observational evidence. ADHD=attention deficit hyperactivity disorder.

Table 4: **Evidence for effectiveness of interventions for selected mental disorders by income level of country**

Fewer than 1% of these trials had more than 500 participants; nearly three-quarters had fewer than 100 participants.

Three-quarters (265/361) of all depression trials and half the schizophrenia trials (548/1137) included at least one intervention identified by the DCP2 as a priority intervention for low-income and middle-income countries (table 3).[1] These interventions were psychosocial treatment and antidepressant drugs for depression, and antipsychotic drugs and family or community intervention for schizophrenia. Nine of the 11 trials of treatments for alcohol dependence or harmful use and five of the 13 developmental disability trials assessed pharmacological interventions. Table 3 shows that more than two-thirds (769/1137) of schizophrenia trials that assessed DCP2 interventions were on antipsychotic drugs. Similarly, about four-fifths (292/361) of all depression trials that assessed DCP2 interventions were about either antidepressants or mood-stabilising drugs. A fifth (67/361) of all depression trials compared first and second

generation antidepressants. Table 4 summarises evidence for treatments for these disorders in countries with various income levels.[10–58]

Cost-effectiveness of clinical treatments

We reviewed all controlled trials (placebo or usual care), published since 2001, that assessed cost-effective clinical interventions for treatment of depression and schizophrenia, as described in DCP2.[1] 13 of the 361 depression trials and four of the 1137 schizophrenia trials were included. We included all identified trials of interventions for alcohol misuse and developmental disability in low-income and middle-income countries, since so few of these studies were available and since DCP2 did not assess the cost-effectiveness of treatments for these disorders.

Depression is ranked as the seventh most important cause of disease burden in low-income and middle-income countries.[59] It tends to be disabling, recurring or chronic, and untreated; for example, depression is the leading cause of disease burden in Brazil,[60] and the second leading cause in women in Chile.[61] Because depression typically occurs with anxiety in community and primary-care settings, these are often described as common mental disorders.[62] Table 5 summarises five randomised controlled trials that assessed the efficacy of simple, efficient, and feasible treatments for depression in predominantly poor communities in Uganda,[20,21] Chile,[15] India,[16] Pakistan,[19] and Mexico.[63,64] Most of these trials tested psychological interventions. Two of three trials that assessed group psychological interventions showed efficacy, as did one of the two that assessed individual psychological interventions. Group psychological interventions in low-income and middle-income countries, for example in Latin America[65] and Asia,[66] might be experienced as an extension of traditional social mechanisms, such as support through social networks and collective action.

Antidepressants were tested in two trials: as a discrete treatment in India[16] and as part of a multimodal intervention in Chile.[15] The Indian trial showed that antidepressants were more effective than placebo or usual care, but only in the short term; however, low adherence could have contributed to reduced efficacy in the long-term. In the Chilean study, patients in the intervention group had a higher recovery rate than controls; however, they were also more likely to receive medication, in more appropriate doses, and for longer periods of time than controls. The structured monitoring and support associated with the intervention probably also helped to ensure better compliance with medication.

Eight other trials of a range of psychosocial and pharmacological interventions in low-income and middle-income countries were not included in table 5, either because we could not assess their methodological quality or because sample sizes were small. Some of these trials showed that antidepressants were more effective in combination with psychotherapy than alone.[67–70] Informational support for postnatal depression was effective in the short term,[71] as was sports training with cognitive behavioural therapy for mild depression.[72]

	Setting	Study design	Sample	Intervention	Comparison group	Main results
Uganda[20,21]	Villages	Cluster RCT	248 villagers of both sexes with depression	Group interpersonal psychotherapy	Villages without intervention groups	93·5% recovered with intervention *vs* 45·3% in comparison group at the end of treatment, and 88·3% *vs* 45·1% at 6 months (p<0·001)
India[16]	General medical outpatients at a district hospital	RCT	450 adults with common mental disorders	Fluoxetine or individual problem-solving treatment	Placebo	70% of antidepressant group recovered at 2 months compared to 54% of placebo group (p=0·01); no difference between psychotherapy and placebo
Chile[15]	Primary care	RCT	240 depressed women living in deprived urban areas	Multi-component stepped-care programme including psychoeducational groups for all and antidepressants for more severe only	Usual care	70% recovered with intervention *vs* 30% in usual care at 6 months (p<0·001)
Pakistan Karachi[19]	Urban Community	RCT	366 lower middle class women with depression or anxiety	8 individual counselling sessions at home by minimally trained counsellors	No intervention	Reduction in mean symptom scores (p<0·001) at the end of intervention (8 weeks)
Mexico[63,64]	Community mental-health centres in Mexico City	RCT	135 female patients with depressive symptoms	6 psycho-educational group sessions	One session of information	Both groups improved but no differences between groups at 4 months and deterioration at 2 years (only 39 women included in final analysis)

RCT=randomised controlled trial.

Table 5: **Randomised controlled trials for treatment of depression in low-income and middle-income countries since 2001**

	Setting	Study design	Sample	Intervention	Comparison group	Main results
China[34]	Rural county in China	Cluster randomised trial, 9-month follow-up	326 patients with schizophrenia	Medication and psychoeducation group and group receiving medication alone.	Not offered active treatment	Psychoeducation enhanced relatives' knowledge, caring attitudes, medication compliance (p<0·05) and reduced relapse (p<0·05)
China[27]	Psychiatric hospital in Beijing, China	Randomised controlled trial, 52-week follow-up	160 inpatients with first-episode schizophrenia or schizophreniform disorder	Chlorpromazine (FGA)	Clozapine (SGA)	80% of both groups achieved remission in 1 year, although median time to remission was shorter in those receiving clozapine (p=0·02); by 52 weeks differences were not significant.
China[33]	Psychiatric hospital in Beijing, China	Randomised controlled trial, follow-up 9 months after discharge	101 patients with schizophrenia and their families	Patient and family education (in hospital: 8 and 36 h with patients and families, respectively; in community: 2 h per month for 3 months after discharge)	Usual care	9 months after discharge, patients in the intervention group displayed better overall functioning (p=0·024) and lower clinical severity scores (p=0·008). Rates of relapse in the two groups did not differ.
China[90]	Outpatients, psychiatric hospital, Beijing	Randomised controlled trial, 2 year follow-up	103 patients with schizophrenia	Community re-entry programme	Group psychoeducation	CRP group improved in terms of social functioning (p<0·001) and psychiatric symptoms (p=0·001) compared with the psychoeducation group; re-employment rate was higher and relapse and rates of readmission to hospital were lower in the CRP group

FGA=first-generation antipsychotic. SGA= Second-generation antipsychotic. CRP=community re-entry programme.

Table 6: **Intervention studies for the treatment of psychotic disorders in low-income and middle-income countries since 2001**

One trial, from Mexico, reported that the effects of psychotherapeutic, pharmacological, and placebo treatments for mild to moderate depression were similar at 33 weeks.[73] A Sri Lankan pilot trial[74] assessed the effectiveness of cognitive behaviour therapy for reduction of medically unexplained symptoms, which are a frequent presentation of depression and anxiety. The intervention, consisting of six sessions of cognitive behaviour therapy over three months, reduced symptoms, visits, and distress, and increased patient satisfaction in the short term.[74]

Schizophrenia is a psychotic disorder of low prevalence, which is often chronic and very disabling. Although effective treatments for schizophrenia are available, the accessibility, equity, and acceptability of services that deliver such interventions are inadequate in countries of all income levels. Rates of dropout from treatment programmes are high,[75] and people with schizophrenia have increased rates of death,[76] comorbid substance abuse,[77] and social dislocation, all of which contribute to poor outcomes. Thus, services for people with schizophrenia are most effective when they are organised to ensure early recognition, adequate outreach and engagement, promotion of human rights, and provision of individualised care through a range of flexible health-care and social interventions.[78] Increasingly, psychosocial interventions have been adopted and consumers and carers have helped to improve the acceptability of services.[79,80]

Antipsychotic medications are the mainstay of treatment for schizophrenia. Many practitioners prescribe second generation antipsychotics, even though they are far more expensive than older antipsychotics, and do not ensure better outcomes for people with schizophrenia.[75,81] Results from research in China accord with these results.[27] In low-income and middle-income countries, where resources for interventions in mental health are scarce, the treatment gap for schizophrenia is already large[82] because mental health systems are absent or poorly developed, and mental health is prioritised below competing health needs.[83] Absence of mental health services delays treatment for schizophrenia, which in turn worsens long-term outcomes.[84] The direct and indirect costs of treatment with antipsychotic drugs are high,[85] and long-term outcomes for those in low-income and middle-income countries with chronic psychotic disorders can be poor.[86–88] Work begun in the 1990s[89] suggested that clinical and social outcomes for people with schizophrenia can be improved by involvement of families and communities in interventions aimed at reduction of discrimination, improved adherence to medication, and strengthening of social integration (table 6).[33,34,90]

Alcohol abuse is growing rapidly in low-income and middle-income countries, especially in men, and contributes to the burden of disease both as a disorder and as a risk factor for more than 60 other health problems, especially injuries.[91] Many people with alcohol-use disorders might not seek health care for their alcohol problem, because of shame, low awareness, or scarcity of established services.[92] Recognition of alcohol-use disorders tends to be poor in primary-care settings despite the availability of screening instruments that have been validated for use in low-income and middle-income countries.[93] Advice and brief counselling delivered by physicians and primary health workers has been shown to reduce consumption and intensity of drinking in men with alcohol-use disorders, especially those who are hazardous drinkers, although its effectiveness for treatment of alcohol dependence, the most severe form of alcohol-abuse disorder, is less certain.[40,42,91,94] People with alcohol dependence who seek

timely help from specialised treatment programmes, such as inpatient management of withdrawal from alcohol, rehabilitation treatment, and mutual help organisations (eg, Alcoholics Anonymous), have been shown to have better outcomes than those who do not seek help.[91] This evidence, which is almost entirely from high-income countries, does not show that any one intervention approach (for example, pharmacotherapy compared with psychotherapy) is more effective than others.[94] Opioid antagonists (such as naltrexone) and acamprosate produce a moderate reduction in the rate of relapse to heavy drinking.[94] A meta-analysis showed that acamprosate produced an overall 13% improvement in 12-month continuous abstinence rates in alcohol-dependent patients.[37] Two small randomised controlled trials in low-income and middle-income countries have shown the efficacy of these drugs for the management of alcohol dependence.[38,39]

Although children comprise between a third and a half of the population in low-income and middle-income countries, little research has focused on interventions for developmental disabilities in childhood, such as mental retardation, autism, and attention deficit hyperactivity disorder.[95] However, in high-income countries, pharmacological and psychosocial treatments for developmental disabilities including attention deficit hyperactivity disorder,[46,47,96] mental retardation,[43,44,51] and autism[45] have been shown to be effective. A clinical trial from India showed the efficacy of a herbal preparation for management of behavioural and cognitive deficits in children with mental retardation,[48] and a trial from Brazil showed that methylphenidate was effective for attention deficit hyperactivity disorder.[49] Although community-based rehabilitation programmes have been actively promoted as feasible and affordable models for treatment of developmental disabilities in low-income and middle-income countries,[97] trial evidence is scarce and such programmes can only be accessed by 2% of people in these countries.[98] Uncontrolled trials of community-based rehabilitation in low-income and middle-income countries show that participants have improved levels of independence (eg, as measured by school attendance).[55]

Prevention

Preventive strategies aim to reduce: the incidence, prevalence, and recurrence of mental disorders; the time spent with symptoms; the risks for such mental illnesses; and the effects of illness on affected people, their families, and society.[3] Meta-analytic reviews of controlled trials, almost exclusively from high-income countries, have showed substantial mean effect sizes for preventive trials targeted at depressive symptoms.[99–101] In school-aged children and adolescents, preventive interventions targeted at use of alcohol and drugs are effective.[102] Small to moderate effect sizes have been reported for stress management,[103] child abuse prevention programmes,[104] and interventions to reduce aggressive behaviour[105] and eating pathology.[106] Group-based parenting interventions are effective for improvement of emotional and behavioural adjustment in children aged under 3 years.[107] Outcome indicators for these studies are mostly observational evidence-based risk factors, psychiatric symptoms, and pathological behaviour.

We excluded six of the 26 primary prevention trials identified in low-income and middle-income countries because information about their outcomes was inadequate. Table 7 shows four randomised controlled trials for prevention of anxiety and depression.[108–111] In China, a depression prevention programme that educated schoolchildren in positive thinking, conflict management, and decisionmaking skills was effective for reduction of depressive symptoms.[109] A school-based physical exercise programme in Chile reduced anxiety

	Design	Sample	Intervention	Comparison group	Results
Chile[108]	Controlled trial with classes randomly assigned to conditions	198 adolescents from a low socioeconomic status area	Structured school-based physical activity programme, over 1 year, three sessions a week, designed jointly by students and teachers (adult learning approach)	Adolescents of same age, following standard exercise class once a week	Anxiety decreased more in intervention group than controls (13·7 % *vs* 2·8%, p<0·01) and self-esteem increased 2·3% *vs* −0·1% (p<0·0001). No change in depression score
China[109]	Randomised controlled trial	220 school children at risk for depression, mean age 11·8 (SD 1·69) with subclinical depression	Penn Optimism Programme, 10 weeks of 2 h sessions	No intervention	Children with intervention showed fewer depressive symptoms at post-test (p<0·001) at 3 months (p<0·001), and at 6-months (p<0·001) of follow-up.
Iran[110]	Randomised controlled trial	100 nursing students	Educational counselling sessions every week for 12 weeks to reduce anxiety	No intervention	At follow-up intervention nurses showed lower anxiety than controls (p=0·003). Self esteem decreased in control nurses and increased in intervention nurses (p<0·001)
Nigeria[111]	Randomised controlled trial	33 surgical patients	Self-instructional training (SIT), or rational emotive therapy (RET)	No intervention	SIT reduced anxiety (p<0·05) and RET reduced depression (p<0·05) in comparison to no intervention

Table 7: **Trials of interventions for prevention of depressive and anxiety disorders and symptoms in low-income and middle-income countries since 2001**

levels, but not depression.[108] One trial, targeted at Iranian nursing students, reported that a one-semester programme of educational counselling every week reduced anxiety in the long term.[110] The implications of prevention of work stress and related depression and anxiety problems in nurses in low-income and middle-income countries could be important for health systems in these countries. Another randomised controlled study, of prevention methods in adults at risk for depression and anxiety such as surgical patients,[111] also reported beneficial effects.

Suicide is a leading cause of death in low-income and middle-income countries, especially in young people.[5] Controlled studies of suicide prevention in low-income and middle-income countries are scarce.[112] In Sri Lanka, a country with very high suicide rates,[113] a community-befriending programme in a rural village[114] decreased suicidal behaviour in the intervention village from 13 suicides during the 6-year preimplementation period to no suicides at the end of the time-series trial;[114] however, suicides also decreased in the comparison village. Self-poisoning with pesticides is common in low-income and middle-income countries, with estimates of 300 000 deaths a year in the Asia-Pacific region alone.[115] However, so far the feasibility or effectiveness of reduction of access to pesticides, or improvement of medical care for pesticide poisoning in low-income or middle-income countries have not been assessed in controlled studies.[116] Figures from Argentina, Philippines, and Sri Lanka showed that the number of suicides fell after pesticides were banned or imports were reduced.[117] We have reported on the results of a modelling exercise that estimated the number of deaths that could be averted by improvement of depression treatment in China.[5]

We did not identify any trials for the prevention of schizophrenia or other psychotic disorders in low-income or middle-income countries. Although alcohol and drug-misuse are rapidly growing health problems, we identified only one controlled prevention study.[118] In China, an unblinded matched community-based trial showed that a programme of participation and action by various community sectors and leaders, which included education in schools, literacy improvement, and employment opportunities, reduced the incidence of drug abuse.[118] Control strategies, such as a programme in South Africa consisting of random breath testing and higher taxation, have been shown to be cost-effective for prevention of alcohol abuse.[91] In high-income countries a 10% increase in price can reduce the long-term consumption of alcohol by about 7%, and some data suggest that in low-income countries it could be reduced by about 10%.[119] An uncontrolled trial of a community-based programme in rural India that emphasised education and awareness building, action against drunken men, advocacy to politicians to limit the sale and distribution of alcohol in bars and shops, and mass oaths for abstinence reported a 60% reduction in alcohol consumption.[120]

DCP2[2] summarised evidence for the effectiveness of a range of interventions for primary prevention of childhood developmental disabilities, such as rubella vaccination; fortification of food with iodine and folic acid; prenatal screening for Down's syndrome; prevention of maternal alcohol abuse; and interventions to reduce child abuse.[98] A meta-analysis showed that iodine supplementation increased IQ level by an average of 12·2 points.[121] An uncontrolled Turkish observational study reported that a short-term mass-media education programme encouraged consumption of iodised salt in regions with high rates of iodine deficiency.[122] Most prevention studies from low-income and middle-income countries focused on early psychosocial stimulation.[123] Five randomised controlled trials in Bangladesh,[124] Bosnia and Herzegovina,[125] Jamaica,[126–128] and Turkey[129] and two non-randomised controlled trials in Cyprus and Serbia[130] and Mauritius[131] reported positive outcomes from interventions that aim to enhance early mother-child interaction, parenting, and child mental development through group sessions or home visits. Outcomes with relevance to mental health included improvements in maternal responsiveness, child psychophysiological functioning, cognitive development, problem solving, and self esteem, and reductions in parental distress and maternal depression. Studies in Jamaica showed that addition of psychosocial stimulation to a nutritional intervention not only reduced the development of long-term disabilities in undernourished infants and young children but also prevented the development of depressive and anxiety symptoms in adolescence.[126,127,128] Nutritional and psychosocial interventions targeted to populations that are vulnerable to developmental disorders, such as undernourished children living in poverty, can help to prevent developmental delays and behavioural disorders in childhood and adolescence.

Mental health interventions during and after emergencies

Although mental disorders are commonly encountered in emergency situations associated with conflict or natural disaster, research about the outcome of interventions done in the midst of such emergencies is rare. Humanitarian agencies now recommend implementation of mental health interventions and psychological support during and after emergencies.[132] Most research on mental health interventions during acute emergencies has focused on post-traumatic stress disorder. However, there has been much debate about whether it is appropriate to focus on this disorder ahead of other social and mental health problems,[133,134] such as the problems of people with severe pre-existing mental disorders.[135,136]

Small-scale studies of discrete traumatic stressors in high-income countries indicate that cognitive behaviour interventions can prevent at least post-traumatic stress disorder.[137] Similarly, a small study from the midst of a large emergency in Northern Uganda suggested that

	Treatment setting	Treatment coverage (target)	Intervention	Cost-effectiveness range (US$ per DALY averted)*
Schizophrenia	Hospital outpatient	80%	Older (neuroleptic) antipsychotic drug	$US 2499–7230
			Newer (atypical) antipsychotic drug	$US 16 174–20 583
			Older antipsychotic drug+psychosocial treatment	$US 1743–4847
			Newer antipsychotic drug+psychosocial treatment	$ US 10 232–14 481
Bipolar affective disorder	Hospital outpatient	50%	Older mood stabiliser drug	$US 1587–5295
			Newer mood stabiliser drug	$US 2943–6386
			Older mood stabiliser drug and psychosocial treatment	$US 1545–4928
			Newer mood stabiliser drug and psychosocial treatment	$US 2765–5908
Depression	Primary health care	50%	Episodic treatment with older (tricyclic) antidepressant drug (TCA)	$US 478–1288
			Episodic treatment with newer antidepressant drug (SSRI; generic)	$US 1003–1771
			Episodic psychosocial treatment	$US 537–1611
			Episodic treatment with older antidepressant drug+psychosocial treatment	$US 627–1586
			Episodic treatment with newer antidepressant drug+psychosocial treatment	$US 1140–2101
			Maintenance treatment with older antidepressant drug+psychosocial treatment	$US 749–1760
			Maintenance treatment with newer antidepressant drug+psychosocial treatment	$US 1449–2459
Panic disorder	Primary health care	50%	Benzodiazepines	$US 572–1075
			Older (tricyclic) antidepressant drug (TCA)	$US 305–619
			Newer antidepressant drug (SSRI; generic)	$US 567–865
			Psychosocial treatment	$US 338–927
			Older antidepressant drug and psychosocial treatment	$US 443–977
			Newer antidepressant drug and psychosocial treatment	$US 671–1188

DALY=Disability-adjusted life-year. *Range reported for six low-income and middle-income regions.[156]

Table 8: **Interventions for reduction of mental disorders in low-income countries**

behavioural therapy could be effective to treat post-traumatic stress disorder.[138] Moreover, a programme of early childhood care and education for 5 and 6 year old Bosnian children and their mothers was shown to have many positive effects, including weight gain and improvements in psychosocial functioning in the children.[125] We need to investigate whether these findings can be extrapolated and used effectively in large-scale emergencies, and especially in low-income settings with few mental health professionals.[139] A review of qualitative social-science research[140] suggested that various emergency social interventions, which are more easily made available to large numbers of people than are psychological interventions, can be effective. We expect that emergency interventions such as organisation of family reunification, and facilitation of engagement in cultural mourning ceremonies could protect mental health; we need to know whether they could prevent diagnosable mental disorders. Studies in high-income countries suggest that single-session psychological debriefing for post-traumatic stress disorder immediately after trauma is ineffective,[141] and a non-randomised controlled study of 69 teenage refugees in Gaza showed that post-traumatic and depressive symptoms did not improve with seven sessions of clinician-facilitated group crisis intervention based on a psychological debriefing protocol.[142] For people in severe acute distress, so-called psychological first aid (consisting of protection from harm, solutions for basic needs and concerns, and provision and raising of social support) has been recommended immediately after trauma.[143,144] However, research into the outcomes of such interventions is scarce.

Interventions implemented months or years after acute emergencies have been better studied, although not all have been shown to be effective.[145,146] Studies more than a year after a large earthquake, in Turkey, showed that brief behaviour therapy reduced post-traumatic stress disorder and depression.[147,148] Moreover, symptoms of post-traumatic stress disorder were reduced in adolescents after an earthquake in Armenia, and in those in post-conflict Bosnia who received school-based psychotherapy for trauma and grief.[149,150] Importantly, most studies during and after emergencies tend not to assess the effect of the interventions on daily functioning, an outcome variable of key interest to rural communities, in which members typically need to contribute to the community.[151] Despite increasing international consensus on good practices,[132,134] evidence for mental health interventions during and after emergencies needs to be strengthened.

Investment in mental health interventions

Decisions about investment in mental health systems can be based on at least three economic criteria: the economic consequences of no investment; the amount of investment needed to address identified needs; and the cost-effectiveness of investment in relation to competing public-health needs. Moreover, non-economic criteria, such as equitable access to health care, human rights protection, and poverty reduction, might be at least as important within the broader process of setting priorities in mental health.[152] The economic consequences of mental disorders include lost production, premature mortality, and expenditures on ineffective or inappropriate

care outside the formal health-care system. Low levels of health-care coverage and insurance in low-income and middle-income settings mean that these costs fall largely on households. For example, a substantial proportion of the direct and indirect costs of schizophrenia, including treatment with antipsychotic drugs,[84] are borne out of pocket by families in low-income and middle-income countries.[153] Excessive health expenditure is strongly associated with depression in women.[154] The economic consequences of not treating mental disorders have only rarely been analysed in low-income and middle-income countries, but a useful indication can be gleaned from baseline assessments carried out as part of a prospective study. For example, three separate mental health economic studies in India showed that most out-of-pocket medical expenses were for informal care sector visits, informal caregiving by household members, and other time and travel costs, and that these costs exceeded the subsequent costs of targeted clinical interventions by public heath-care providers.[16,155,156]

Because mental health expenditure in most low-income and middle-income countries is very low, the cost of dramatic increases to provide appropriate care or prevention to populations in need will be large, and a process of gradual, stepwise increase is likely to be economically more feasible. We have estimated the financial costs of scaling-up effective interventions for mental health care in low-income and middle-income countries in another article in this Series.[157] The DCP2 report[1] identified a basic mental health care package, which consisted of outpatient-based treatment of schizophrenia and bipolar disorder with first generation antipsychotic or mood stabilising drugs and adjuvant psychosocial treatment; proactive care of depression in primary care with generic selective serotonin reuptake inhibitors (SSRIs) and maintenance treatment of recurrent episodes; and treatment of panic disorder in primary care with generic SSRIs (table 8).[158] The report estimated the cost of such a package per head of population per year as US$3–4 in sub-Saharan Africa and south Asia, and $7–9 in Latin America and the Caribbean. The addition of brief interventions by primary care physicians for high-risk alcohol users was estimated to cost an additional 0·04$ per head in south Asia and sub-Saharan Africa and 0·36$ per head in central Asia and Latin America.[91] Available data are not sufficient to allow estimation of the costs of treatment for child mental disorders in low-income and middle-income countries.[98]

In India, two separate studies estimated the cost of episodic treatment of depression with antidepressants in primary care to be equivalent to about US$20–40 for a 6-month treatment episode.[16,155] An analysis for the southeast Asian region put the 6-month cost of treatment at $30–60 for tricyclic antidepressants and $60–80 for SSRIs,[159] although the price of generic SSRIs has fallen since then. Investment for treatment and care of severe mental disorders is expected to be greater (at least $25 per person per month, even with low-cost treatment strategies[158]).

Returns on actual or potential investment are usually expressed in terms of improvements in health (with occasional references to non-health benefits such as increased rates of employment or productivity) and cost

***Panel 1:* A model of community-based rehabilitation for chronic schizophrenia in rural India[168]**

Community-based rehabilitation addresses the needs of people with disabilities as an integral part of overall community development efforts. Its goal is the rehabilitation, social inclusion, and equalisation of opportunities for people with disabilities, and it is implemented through the combined efforts of disabled people; their families and communities; and the appropriate health, vocational, and social services. The principles of community-based rehabilitation, specifically the use of local human resources and involvement of patients, families, and local communities, were adapted to complement the specialist services for psychotic disorders to improve access, equity, and acceptability of the interventions in a very disadvantaged part of rural India.[168] Local members of the community were trained as community-based rehabilitation workers to deliver comprehensive, home-based services, such as identification of people with chronic schizophrenia; access to the clinical team in outreach clinics (figure 1); regular follow-up; monitoring compliance; education for disabled people and their families (figure 2); and planning of rehabilitation interventions. In addition, concerted efforts were made to promote awareness, address stigma, and facilitate economic and social rehabilitation. In most villages, families of mentally ill people and other concerned members also formed self-help groups to promote the social and economic reintegration of local members with severe mental disorders. The clinical and disability outcomes for clients within the community-based rehabilitation programme were better compared to clients who received outpatient care alone; superior medication compliance played an important role in mediation of these effects. This approach to service delivery had a focus on empowerment of clients, mobilisation of existing community resources, intersectoral linkages (welfare, local government, and health sectors), and a human rights perspective. The success of community-based rehabilitation has prompted the district-health committee of the district government, in partnership with a non-governmental organisation, to include mental-health services in their planning and budgeting exercise with a view to scaling up the programme to the entire district.

Figure 1: **An outreach camp at a local primary health subcentre**

Figure 2: **Mental health workers meet with patients and their families**

effectiveness (such as the cost per day or year of healthy life gained by implementation). For example, a Chilean trial[15] calculated with 90% probability that the incremental cost of an extra depression-free day with an intervention to treat depression would not exceed the equivalent of US$1·04.[160] Economic analysis can provide decisionmakers with information to support prudent investment choices, whether for the mental health system or for the health sector in general. For example, the higher cost of new antipsychotic drugs means they are less cost effective than the equally effective older drugs in low-income and middle-income countries. Pharmacological treatment for depression is estimated to yield 20–22 disability-free days or 0·06 disability-adjusted life-years for each treated 6-month episode.[159] Based on treatment costs of $30–60, the cost-effectiveness ratios for low-income settings are about US$500–1000 per averted disability-adjusted life-year. This amount of investment for a healthy year of life seems unfavourable relative to, for example, vaccination programmes or tuberculosis control, but when compared with interventions for other chronic disorders, treatments for common mental disorders are about as cost-effective as antiretroviral treatments for HIV/AIDS, secondary prevention of hypertension, or glycaemic control for diabetes. These findings do not incorporate other economic benefits of mental health care such as reductions in inappropriate use of health care, absence from work due to sickness, and premature mortality, which could even outweigh the investment costs.[161]

Panel 2: Scaling-up a primary care depression programme in Chile

Depression is common in Chile, especially in women and the poor.[170–172] A treatment programme for depressed women in primary care[15] was shown to be efficacious and cost effective, and has been adopted for Chile's national primary care programme. The number of patients treated in this programme has increased exponentially, and reached 141 000 in 2005.[173] The programme has a low rate of referrals to secondary mental-health care, even though about 80% of cases of depression treated in primary care present with moderate or severe depression. The number of psychologists working in primary care has increased almost four-fold, which has begun to redress socioeconomic inequalities in the provision of mental-health services.[174] In 2005, the Chilean government introduced a new initiative—the Universal Access and Explicit Guarantees—to ensure that all people with depression, irrespective of their health insurance, would be entitled to a basic treatment package.

Implications for policy and practice

We conclude that effective, locally feasible, and affordable treatments for depression and schizophrenia in low-income and middle-income countries do exist; however, less evidence exists for the effectiveness of interventions to treat developmental disabilities in childhood or alcohol-use disorders. Evidence suggests that social interventions to support mental health in the midst of emergencies might be effective, as might social interventions for the prevention of depression, substance abuse, and delays in child development. However, most of the evidence for the prevention of mental disorders in adults is from high-income countries.

Although many mental health programmes have incorporated such evidence and achieved local success, few have been systematically scaled up to serve the needs of regional or national populations and even fewer have undergone systematic assessments of their effectiveness in the real world. Thus, despite the increasing array of treatments for mental health, evidence for their feasibility and effectiveness when integrated into routine care settings in low-income and middle-income countries is lacking.[162] Furthermore, most available evidence does not reflect the burden of disease or cost-effectiveness: tables 1, 2, and 3 show that the smallest evidence base comes from the poorest countries, most trials focus on a narrow range of mental disorders, and most assess only pharmacological interventions. Thus, most of the evidence is of limited relevance for mental health care in low-income and middle-income countries. A small, but important and growing, evidence base supports the effectiveness of integration of mental health care into routine health-care programmes, such as primary care[163–167] and extension of community care[156,168] (see panel 1), though more evidence is needed. Most mental health systems in the world are dominated by large custodial psychiatric hospitals that squander resources on ineffective and inappropriate interventions. Furthermore, attempts to create national integrated primary care or community-care programmes have often not lived up to initial expectations.[82,167]

We recommend that, at the very least, governments should consider scaling up the coverage of mental health interventions for which there is credible evidence of effectiveness.[157] The process of scaling up such interventions in poorly resourced settings will be hindered by barriers such as scarce financial, human, and technical resources and other health needs (eg, HIV/AIDS, tuberculosis, and malaria) that compete for priority.[169]

Optimism arises from examples such as the intervention used in the treatment of depression in primary health care in Chile,[15] which has become the model for a national depression treatment programme (panel 2).[173] The programmes of non-governmental organisations (NGOs), such as the Schizophrenia Research Foundation and Basic Needs, provide integrated models for care of people with schizophrenia.[175] WHO projects in a number of countries are developing accessible mental health services as a vehicle to deliver effective interventions.[176,177]

One of the three strategies we call for is research to inform the scaling-up of interventions for mental disorders in low-income and middle-income countries.[157] Such research needs to be retargeted to the needs of low-income and middle-income countries, not only to inform health policy in these countries, but also to demonstrate to high-income countries that interventions that rely on non-specialist health workers and low-cost technologies and strategies can deliver equally effective mental health interventions.[178] Future research should examine not only the clinical benefits of such interventions for individuals and families, but also operational factors that affect their delivery and their effects on the wellbeing of entire communities; for example, by improvements to performance of schoolchildren, reduction of suicide rates, or reduction of inappropriate use of health services.[179] We must take seriously the need for evidence that mental health services represent a social investment and not simply another expense item on a health budget.

The need for more research must not be used as an excuse to delay scaling-up of mental health systems. We believe that the old pretence that overstretched and inefficiently used resources can take on a greater burden of care by integration of mental health into primary care must be abandoned. We must explore radical options such as the recruitment of a new group of health workers whose role is to facilitate the detection of chronic diseases, including mental disorders, and the delivery of psychosocial interventions. In addition, we need arguments for the moral or ethical imperative to extend mental health care services, based on human rights and social responsibility.[180] Put simply, people are entitled to receive help when ill. We have identified good evidence for what that help might comprise for people with poor mental health.

Contributors
All authors have participated in the data analysis and reporting stage of this manuscript, and seen and approved the final version.

Conflict of interest statement
We declare that we have no conflict of interest.

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For more on **these NGOs** see www.scarfindia.org and www.basicneeds.org

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