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Early Intervention to Reduce the Global Health and Economic Burden of Major Depression in Older Adults

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Abstract

Randomized trials for selective and indicated prevention of depression in both mixed-aged and older adult samples, conducted in high-income countries (HICs), show that rates of incident depression can be reduced by 20–25% over 1–2 years through the use of psychoeducational and psychological interventions designed to increase protective factors. Recurrence of major depression can also be substantially reduced through both psychological and psychopharmacological strategies. Additional research is needed, however, to address the specific issues of depression prevention in older adults in low- and middle-income countries (LMICs). The growing number of older adults globally, as well as workforce issues and the expense of interventions, makes it important to develop rational, targeted, and cost-effective risk-reduction strategies. In our opinion, one strategy to address these issues entails the use of lay health counselors (LHCs), a form of task shifting already shown to be effective in the treatment of common mental disorders in LMICs. We suggest in this review that the time is right for research into the translation of depression-prevention strategies for use in LMICs.

INTRODUCTION

LMICs: low- and middle-income countries

HICs: high-income countries

Indicated prevention: intervening to prevent major depression in a person who already has mild, or subthreshold (i.e., subsyndromal) symptoms

LHCs: lay health counselors

In this review, we set forth a case for the public health significance of preventing major depressive episodes in older adults, particularly given the demographic shifts taking place in low- and middle-income countries (LMICs) as well as in high-income countries (HICs). Our literature review of studies conducted in HICs indicates that a reasonably robust evidence base exists for selective and indicated prevention of late-life depression. More recent information from studies in LMICs has shown that lay health counselors (LHCs) can effectively deliver psychosocial interventions in a collaborative, stepped-care framework to treat prevalent cases of common mental disorders (33, 34). Thus, the stage is set for translating depression-prevention strategies to LMICs through lay delivery systems. Here we set forth the objectives of depression prevention, summarize approaches that are promising in 2012, and make recommendations for future depression-prevention research in both HICs and LMICs.

WHY IS PREVENTION OF MAJOR DEPRESSION IMPORTANT, ESPECIALLY IN OLDER ADULTS?

From a public health perspective, prevention of major depression in later life is important for the following reasons (24, 34): First, depressive episodes in older adults are prevalent and disabling (6–10% in primary-care settings, 30% in medical and long-term care settings); second, depression is associated with significant excess mortality after myocardial infarction and stroke as well as for cancer, and it is the major risk factor for suicide in old age; third, available treatments are ~50% effective in achieving and sustaining remission and health-related quality of life, and in averting years lived with disability; fourth, milder or subthreshold (subsyndromal) states increase the risk of developing the full clinical disorder but may be more reversible than the advanced clinical state and may also be associated with neurobiological changes at an earlier and more modifiable stage of development; fifth, the geriatric mental health workforce shortages confronting the world also drive the imperative for devising effective, scalable, depression-prevention models that can be implemented by general medical counselors or LHCs (34) rather than mental health specialty clinicians (26); and finally, preventing depression in older adults may be cost-effective (51).

Two questions provide the organizing framework for depression-prevention research and practice in older adults: Can early, targeted intervention reduce incidence, severity, or duration of incident major depressive episodes to a clinically significant degree among older individuals at increased risk for or already living with subthreshold symptoms of depression, and how do we best organize and implement interventions to prevent major depression in a community-dwelling elderly population?

The goals of research and practice are to improve accuracy in predicting major depression in older adults and their caregivers, to guide the timely introduction of risk-reduction strategies, and to determine any additional health and economic benefits to prevention of major depression in older adults. These could include slower progression of cognitive decline, better control of pain, enhanced cardiovascular and cerebrovascular health, less caregiver burden, and lower cost to the health care delivery system. All these are significant downstream burdens that could be mitigated through prevention of depression in later life.

In addition, however, basic research into the biological and psychosocial processes leading to depression could also help by discovering new possibilities to prevent depression. A heuristically useful example is provided by studies of the pathogenesis of depression in patients exposed to interferon alpha (IFA) for treatment of hepatitis C (29). In such patients, sleep disturbance may increase IFA's depressogenic effects whereas, conversely, improving sleep quality could protect from the development of depression. In a similar vein, more research is needed on the causes of social inequalities in the incidence and prevalence of depression and the

variable distribution of these factors across different societies (1, 8).

By preventing depression in older adults, one aims to prevent a downward spiral of depression → disability → death, that is, to enhance and prolong older adults' capacity for independence and improve their quality of life. Because depression diminishes both functional ability and life span, the ultimate goal of depression prevention is to protect and increase both (24, 36).

The doubling of the number of older adults living with a mental disorder by 2030 is only part of the public health challenge of, and rationale for, preventing episodes of major depression in old age. Specifically, older adults of low socioeconomic status have elevated risk for chronic illnesses, including depression. The social worlds that put older adults at risk for depression, especially those living in low-income neighborhoods, also act to reduce the effectiveness of antidepressant treatment (13). Thus, research and practice in depression prevention must also involve socially disadvantaged adults (who are often racial and ethnic minorities). For example, at Pittsburgh, we are currently conducting a randomized controlled trial (RCT) of prevention via problem-solving therapy (PST) to prevent episodes of major depression, diminish disability, and improve health-related quality of life in low-income adults (35% of whom are African Americans) who have risk factors for depression and are already mildly symptomatic (48). The control condition is health education in dietary practices, chosen because of the high rate of obesity among participants and the need to provide an attentional control. Relative to white participants in the trial, black participants have (*a*) lower household income and formal years of education, (*b*) higher rates of major health hazards (obesity, diabetes, hypertension), (*c*) higher rates of physical disability, and (*d*) more frequent histories of alcohol or substance abuse (49). About one-third of both blacks and whites report a remote prior history of major depressive episodes. Subjects are being followed for two years, with booster sessions of PST or of health education every six months. As we review below, the successful conduct of depression-prevention research requires an infrastructure of community partnerships with primary-care and social service agencies that reach the vulnerable populations most in need of preventive interventions. Additional adaptation to the language, culture, and conditions of LMICs will be necessary to advance depression-prevention research and to have an impact on the global burden of depression's illness-related disability. In return, demonstrating the efficacy of a low-cost, task-shifting approach to prevention of depression is relevant to the United States, especially in regions that are in short supply of mental health resources of any kind.

PST: problem-solving therapy

Selective prevention: intervening to prevent major depression in a person who has risk factors for depression but is not yet symptomatic

WHAT ARE THE OBJECTIVES OF DEPRESSION PREVENTION?

Implicit in the discussion of depression prevention in older adults are three underlying objectives: the preemption of incident episodes of depression; the prevention of recurrent episodes of depression; and finally, the protection from depression's medical and psychosocial complications (24, 36).

The Institute of Medicine (IOM) delineated several types of depression prevention in its 1994 (25) and 2009 (27) reports: universal, selective, and indicated prevention. In universal prevention, the entire population base, regardless of whether all individuals in it are at risk for depression, is targeted. An example would be outreach through media to promote protective factors and well-being through exercise and healthy sleep and dietary practices and to educate the general population about the early warning signs of depression, to dispel stigma about depression, and to encourage help-seeking; educational outreach to primary-care physicians, to educate them about the risk factors (such as depression) for suicide in older adults, is another example.

As opposed to this wide-scale intervention, selective prevention focuses on those patients presenting with established susceptibility on the basis of a set of risk factors. For example, in the case of late-life depression, such

NNT: number needed to treat

well-known risk factors include disability, social isolation, bereavement, and chronic insomnia (43, 46). Moving toward greater severity of risk are preventive measures directed toward patients already living with some symptoms of depression, though remaining subsyndromal: so-called indicated prevention (34, 36). To date, most of the published data derive from studies of selective and indicated prevention. The sample size requirements for studies of universal prevention are substantially greater than the samples of 150–300 generally seen in studies of selective and indicated prevention (16–18); thus, this form of large-scale depression prevention research has been very hard to implement both because of the large sample sizes required and the availability of practicable, easily administered interventions. Recently, however, the National Institute of Mental Health has funded the VITAL-DEP study of universal depression prevention; VITAL-DEP is an ancillary study of the efficacy of vitamin D and of fish oils in preventing cancer and cardiovascular disease. VITAL-DEP is described below.

Prevention of depressive disorders is of great public health significance not only in HICs but also in LMICs. The specific concerns regarding late-life depression in LMICs include the rapid demographic transition and aging in countries such as China and India; changing social conditions that are recognized as risk factors (e.g., living alone or living with a chronic disabling condition); and the weak response of the health system to addressing the needs of the elderly (let alone mental health needs), in particular the lack of specialist human resources. Interventions are needed that focus on prevention that can be delivered by nonspecialist and lay workers in nonhealth care, home, or primary-care settings (3, 20, 34, 35).

WHAT ARE PROMISING APPROACHES FOR 2012?

Both randomized prevention trials and epidemiological modeling suggest that prevention of major depression in later life may be most efficiently accomplished by targeting elderly persons who experience risk factors, particularly functional limitations as a result of illnesses such as stroke or macular degeneration, have a small social network, and/or have subthreshold (i.e., subsyndromal) symptoms (41, 42, 46). Efficiency of interventions to prevent depression encompasses both the impact of the intervention and the effort required to implement it. Impact is reflected in the proportion of cases that would be prevented if the adverse effects of the targeted risk factor were completely blocked (attributable fraction). Effort is reflected by the number of persons who would need to receive a depression-prevention intervention to avoid one new case of late-life depression (number needed to treat, or NNT). Schoevers et al. (43) have estimated that the risk factor where preventive interventions would have the highest impact and lowest effort is the presence of subthreshold depressive symptoms (NNT = 3–4 in indicated prevention versus NNTs of 7–9 in selective prevention). That is, preventive interventions may have more impact in older adults with subthreshold symptoms (indicated prevention) than in patients without such symptoms, even though they may have other risk factors such as disabilities from medical illness (selective prevention).

Capturing the state of the field, a meta-analytic review of 19 early-intervention trials with mixed-aged samples reported a pooled incidence rate ratio of 0.78 [95% CI (confidence interval): 0.65–0.93], indicating a reduction in incidence of diagnosable major depression of nearly 20% over 1 year (19). Several published papers support the efficacy of selective and indicated prevention of depression in either at-risk or already mildly symptomatic older subjects. Some of the studies have used as their primary outcome variable the occurrence of major depressive episodes (typically studies of indicated prevention), whereas other studies have encompassed both major and minor depressive episodes as their primary outcome (typically studies of selective prevention). We now present examples of each below.

A study exemplifying selective prevention enrolled patients with recent stroke (41).

Depression occurs in 30–40% of stroke victims, and poststroke depression has been implicated as a contributing factor to impaired recovery of stroke victims, along with increased mortality. In the study, nondepressed patients receiving a placebo were significantly more likely over the course of 12 months to suffer a major or minor depressive episode than were those patients administered an SSRI (selective serotonin reuptake inhibitor) alone (low-dose escitalopram, 5 mg/day) or those who received a course of PST (41). The resulting NNT for this study was ~8. Similarly, a recent review of the literature on depression prevention in patients treated with interferon-alpha for hepatitis C has indicated that pretreatment with selective serotonin reuptake inhibitors halves the incidence of depressive episodes during the interferon-alpha treatment (28).

A recent report from Amsterdam (52) evaluated indicated prevention in Dutch primary-care patients above the age of 75. To determine the efficacy of an indicated stepped-care prevention program, 170 individuals with subthreshold symptom levels of depression or anxiety were followed. Although these individuals did not yet meet the diagnostic criteria for their respective disorders, they were offered either a preventive stepped-care program or usual care. Comprising the intervention program were four sequential steps, each of three months duration: watchful waiting, cognitive behavioral therapy-based bibliotherapy, PST, and referrals to primary care if the patient needed antidepressant medication. In the end, the incidence of major depressive episodes and anxiety disorders was reduced by half over a one-year follow-up period. Thus, ~24% of patients randomly assigned to usual treatment experienced the onset of major depressive episodes or of anxiety disorders, compared with 11% of participants receiving the stepped-care treatment for depression prevention. This stepped-care algorithm was also demonstrated to be cost-effective (51).

Beyond reducing the incidence of major depressive episodes, however, prevention also entails protecting older adults from the downstream consequences of depression (36). One critical downstream consequence is suicide. Evidencing the efficacy of suicide-prevention strategies is the PROSPECT study (2, 10) (Prevention of Suicide in Primary Care Elderly: Collaborative Trial). PROSPECT showed that by exporting depression care management strategies to urban and rural primary-care practices in New York, Philadelphia, and Pittsburgh, a reduction in suicidal ideation was observed over 2 years, from baseline rates of 25–30% to rates at follow-up of ~10–15%. Taken together, the available data, though still limited, suggest the feasibility, efficacy, and safety of selective and indicated depression prevention in other adults.

Meta-analytic reviews of studies in HICs have found that the incidence of new depressive disorders can be reduced by ~25% over 1–2 years compared with usual care (18, 19) through the use of learning-based psychotherapies [such as interpersonal psychotherapy (IPT) and cognitive behavioral therapy (CBT)], and PST administered by mental health professionals and (in the case of PST) general medicine clinicians. A recent study, the MANAS trial conducted in Goa, India (34), demonstrated that the use of LHCs, as part of a collaborative stepped-care intervention, significantly increased recovery rates from common mental disorders (anxiety and depression) in patients of public primary-care facilities. (MANAS means "project to promote mental health" in the local Konkan language.) The MANAS intervention also showed a trendworthy reduction ($p = 0.07$) in the incidence of depressive disorders in patients with subthreshold (subsyndromal) depressive symptoms. Given the shortage of mental health specialists in LMICs, MANAS utilized the strategy of task shifting, that is, the redistribution of tasks among health workforce teams, to make more efficient use of lay human resources for health. Developing models of depression prevention in older adults via lay delivery systems seems especially salient in LMICs but would also clearly have implications for practice and policy in HICs.

IPT: interpersonal psychotherapy

CBT: cognitive behavioral therapy

In our review of prevention trials performed in HICs, we found additional evidence, some from controlled clinical trials and some from open studies, that supports both selective and indicated models of depression prevention in older adults (16):

1. Social support groups and widow-to-widow programs for spousally bereaved individuals (33);
2. Support groups, psychoeducational interventions, respite care and multicomponent interventions aimed at caregivers of frail older patients and dementia caregivers (9, 20, 44);
3. Supportive interventions for nursing home residents (17);
4. PST in older adults with chronic general medical illnesses, such as macular degeneration (42) and stroke (41);
5. Antidepressive medication in high-risk older adults, such as those who are of poststroke status (41);
6. Psychoeducational interventions, such as the Coping with Depression course, a CBT-based intervention (15);
7. Life review and reminiscence (6);
8. Internet-based CBT (47); and
9. Stepped-care models for older primary-care adults with subthreshold depression or anxiety symptoms (51, 52).

With respect to prevention of recurrent major depression, Reynolds, Dew, Anderson, and colleagues (37–39) have shown that maintenance treatment using a variety of psychosocial (e.g., IPT) and pharmacologic interventions (tricyclic antidepressants, SSRIs, and acetylcholinesterase inhibitors) can prevent depression recurrence (NNTs of 4–5) and slow cognitive decline and conversion to dementia in older adults (37–39), in addition to reducing suicide risk in older primary-care adults (10). In addition, Buysse, Reynolds, and colleagues (11) have demonstrated the efficacy of brief behavioral treatment for chronic insomnia (BBTI) in older primary-care adults ($n = 79$): with both a higher response rate of 67% versus 25% in an information control condition and with significantly greater reduction in symptoms of depression and anxiety (11). This work suggests the potential value of treating insomnia as a means of preventing mental disorders such as major depression and anxiety (21).

WHAT IS THE POTENTIAL FOR IMPACT ON GLOBAL MENTAL HEALTH? EXPERIENCE FROM INDIA AND THE NETHERLANDS

Of relevance to LMICs, MANAS LHCs provided psychoeducation to patients who screened positive for common mental disorders and focused on educating the person about their symptoms as well as the need to share emotional symptoms with the doctor and other key people in their social network (34). LHCs taught patients strategies to alleviate symptoms, such as learning breathing exercises for anxiety symptoms, scheduling activities for depression symptoms, and adhering to medication regimens for those patients receiving antidepressants. They also provided information about social and welfare organizations when needed. The MANAS trial used as a control condition enhanced usual care, in which physicians and patients received screening results and were given the treatment manual prepared for primary-care physicians. The intervention and control groups comprised 1,360 and 1,436 participants, respectively. On the basis of intent-to-treat sample completion rates of 85–88%, the intervention had an impact on 6-month recovery rates from common mental disorders [65% versus 52.9% (NNT = 8), with a stronger effect in public facility attenders: 65.9% versus 42.5% (NNT = 4)]. In the subthreshold cases, the study demonstrated a protective effect of the intervention overall in terms of 6-month prevalence rates: 5.63% in collaborative stepped-care versus 7.62% in enhanced usual care (mean difference −1.90, $p = 0.07$). IPT was chosen as the psychological treatment because it was effective for major depressive disorder in trials in Uganda and Chile (4, 7). However, a key finding of MANAS was that IPT was not acceptable or feasible in its original format, and LHCs improvised to deliver an abbreviated form, comprising only

some components of the initial phases of IPT combined with psychoeducation delivered over 1–3 sessions.

The use of the Internet to disseminate depression-prevention strategies is promising and deserves much more study than it has received to date (31). An interesting example is whether improving sleep quality via Internet-based CBT approaches to chronic insomnia could lead to reductions in the incidence and/or severity of common mental disorders (such as depression and anxiety) and substance use disorders. As illustrated by research and clinical experience in the Netherlands, several evidence-based preventive Internet interventions are available for all Dutch citizens at no or minimal cost, including one for older adults (47). To move forward, however, investigation into Internet-based prevention strategies will benefit from the creation of guidelines for reasonable expectations for ethical Internet research, for example, assuring that users know that the Web site cannot provide crisis intervention (31).

In the context of public health impact, the experience of the Netherlands in reaching the target populations is instructive. The Netherlands has one of the world's most efficient and population-oriented health care systems; thus, it is not surprising that the intellectual and health policy leadership for development and dissemination of depression prevention has occurred there probably more than anywhere else in the world. That said, a relatively small proportion of persons living with minor depression take advantage of depression-prevention services offered in the Netherlands (16).

Possibilities to increase participation rates include strategies addressed to patients and to health care and social service organizations. Strategies aimed at potential participants in depression-prevention services could and probably should include media campaigns to reduce stigma ("promotion" and "universal" prevention, to use the IOM's 2009 lexicon), as well as media campaigns stressing the possibility of preventing depression. Organizational solutions would probably include the offering of coping-with-depression courses through the Internet, further embedding preventive services in primary care, and further embedding coping-with-depression courses in broader community interventions. Inevitably, approaches such as these will entail efforts to increase awareness in health professionals about the availability and efficacy of preventive services and systematic screening of potential participants.

RECOMMENDATIONS FOR DEPRESSION-PREVENTION RESEARCH

To move the field forward and to maximize appropriate change in clinical practice and policy, we recommend several strategies: first, use of fewer exclusion criteria to recruit clinically representative participants with medical, neurologic, and/or psychosocial risk factors/comorbidities common in later life; second, partnerships with primary-care practices and community-based agencies reaching low-income adults where public health need is greatest; third, use of lean assessment batteries with low respondent burden that are appropriate for people with little formal education; fourth, specification of prevention-relevant outcomes beyond symptom ratings, such as burden of coexisting medical illness (especially cardiovascular and cerebrovascular illness), degree of cognitive and functional impairment, and caregiver burden; fifth, follow-up periods of at least 12 months and, preferably, 24 months to derive more accurate and clinically meaningful estimates of true incidence reduction; and sixth, use of a structured but flexible and culturally appropriate menu of approaches to be carried out by general medical clinicians (rather than mental health specialists) and/or LHCs. Research projects need to be powered to detect moderately large effect sizes of interventions on the cumulative incidence of major depression over one- and two-year follow-up periods. On the basis of the limited published data, this means sample sizes on the order of 150–300 participants (or 75–150 in each of the experimental and control arms).

General Approach

Because of the diversity of challenges inherent in risk for depression in later life, interventions need to allow for some degree of tailoring to meet the specific needs of the individual and his/her caregiver. Thus, a structured but also tailored approach to delivering the interventions responsive to individual needs is appropriate. Important synergies, for example, can be attained by simultaneously intervening with the caregiver and with the care recipient. That is, dyadic intervention may have greater potential owing to effects on factors such as effective support seeking and support provision within the dyad (45).

Interventions that have already been shown to promote self-efficacy and resilience in prior studies of depression treatment seem to be promising candidates. The focus should be on assessing the value of such strategies before older adults become ill, in the face of the most pervasive risk factors for depression in old age: disabilities related to medical and cognitive impairments, social isolation, caregiving burden, bereavement, and poor sleep (43, 46).

Promising Interventions

Simple, brief, learning-based approaches, already shown to have efficacy in the treatment of depressive disorders, pain, or insomnia disorders, seem promising to address the mandate of the *NIMH Strategic Plan* (Strategy 2.3) to develop and test innovative interventions to reduce risk and positively alter trajectories of illness (32). Although antidepressant medications are the most widely used modality for treating prevalent cases of major depression, their use in subthreshold depression may be ill-advised owing to a lack of evidence for efficacy in mild depression, as well as adverse effects, such as hyponatremia, risk for falls, bone demineralization, and cataracts, in older adults (22). Psychological interventions may be preferable for reasons of safety and patient preference. PST, in which behavioral activation is an important component, has been used in depression-prevention studies successfully (12, 42, 52), is more easily utilized than IPT or CBT, and can be embedded within a clear service model (5). Teaching coping skills may diminish the sense of loss of control (feeling trapped or helpless) at the core of depression. Similarly, teaching strategies for better sleep (because poor sleep is a known and well-established risk factor for depression) may diminish affective reactivity and enhance cognitive flexibility on the part of both care recipients and caregivers (11, 23). In this context, BBTI seems particularly promising because it has been shown to improve sleep quality and reduce symptoms of depression and anxiety (23). Moreover, learning-based interventions are effective for prevalent cases of depression and insomnia. Interventions such as PST and BBTI are also practicable, i.e., safe, cheap, deliverable by general medical clinicians (including nurses, social workers, and potentially LHCs), and more likely to be acceptable to older adults than would be the use of antidepressant medication before major depression is diagnosable. An important caveat in this discussion, however, is demonstrated by data showing that SSRI pharmacotherapy is effective in the prevention of recurrent episode depression, an enormously important clinical issue in the care of older adults (38).

Given their very low cost, desirable safety profile, and general acceptability, the use of nutriceuticals also holds promise as an approach to preventing depression in old age, particularly in LMICs. In this context, the VITAL-DEP trial (VITamin D and OmegA-3 TriaL-Depression Endpoint Prevention, R01-MH091,448), which is presently getting under way, is poised to make an important contribution. Led by Olivia Okereke at Harvard Medical School, VITAL-DEP is an ancillary study integrated with VITAL (U01-CA138,962), a National Institutes of Health–sponsored trial of cancer and heart-disease prevention. Using long-term (5-year) vitamin D_3 and marine omega-3 fatty-acid supplementation in a 2×2 factorial RCT design among a well-characterized,

community-dwelling cohort of 10,000 men (aged ≥60) and 10,000 women (aged ≥65), VITAL-DEP will estimate these agents' effects on depression risk and mood symptoms. Furthermore, the trial will test the impact of the agents on depression risk among African Americans, who will comprise ~25% of the study population. Finally, a random subset of 1,000 men and women will be recruited to local clinical trial centers for detailed, in-person neuropsychiatric assessments; among these participants the trial will test effects of the agents on reducing the risk of depression among those with high-risk factors (43, 46) (selective prevention) and of major depression among those with subsyndromal symptoms (indicated prevention). Thus, VITAL-DEP is the first randomized trial with scale and statistical power sufficient to incorporate universal, selective, and indicated approaches to late-life depression prevention.

Important Measurement Domains

The literature suggests a core of shared measurement domains in keeping with the general logic model articulated here: depression and anxiety (both categorical measures and dimensional measures of severity), comorbid medical burden, social and physical disability, insomnia, pain, cognitive status, social isolation/support, caregiver burden, self-efficacy, problem-solving skills, and promising biopredictors of depression (e.g., proinflammatory cytokines) (28, 48, 49). Biopredictors of depression may enable depression prevention to focus on individuals at highest risk and offer guidance about when and where in the pathway to depression one might best intervene.

Need to Personalize Depression-Prevention Strategies

Because most older adults do not become depressed after a disabling medical event or negative life event such as bereavement, the efficiency of depression-prevention efforts needs to be further enhanced. To address the question of which patients are most likely to benefit from depression-prevention efforts, it seems important to investigate both profiles of social worlds and biosignatures of depression risk and of response to prophylactic interventions (e.g., mRNA transciptomes, cytokine activity, sleep). That is, the field should seek to understand biological correlates of the likelihood of depression, time period of risk, and risk reduction using psychosocial or biological strategies. This is in keeping with the general goal of research: to develop ways of estimating depression risk (using sociodemographic, clinical, and biological variables easily obtained in community settings), based on models of pathogenesis, to guide the rational, timely, and clinically appropriate introduction of risk-reduction strategies to persons who need them most.

As suggested above, an important dimension of risk for depression and anxiety is poor sleep (21). Insomnia is known to be a potent risk factor for depression and anxiety, not simply a prodrome. What is not yet known is whether protecting sleep or improving sleep quality prevents depression in older adults. Poor sleep is also highly prevalent in later life, especially among those living with social and financial strain, those living with chronic pain and related medical disabilities, and those with mild cognitive impairment and progressive cognitive disability. Poor sleep in the care recipient also affects caregivers, often leading to a decision to place a family member in long-term care. Furthermore, there appears to be a bidirectional relationship between poor sleep and increase in proinflammatory cytokine activity. Both appear to be depressogenic (29). Thus, improving sleep fits well into the conceptual framework of depression prevention articulated here (23). Good sleep is important to regulating affect, decreasing stress reactivity, and helping to mitigate chronic pain. It is also essential to information processing, cognitive flexibility, and problem solving. Insomnia is a modifiable precursor and risk factor for depression occurrence and reoccurrence. Teaching people

healthy sleep habits, getting them to understand and experience firsthand how changing behavior affects health, is a unique entree into sustainable, health-promoting life styles. In this context, we have recently published clinical trial data showing that curtailing time in bed and allowing less sleep is associated with poorer health outcomes in adults 75 and older over a 30-month period of observation (40). There appear to be close relationships between sleep duration/quality, health span, and life span.

Finally, we recommend that depression-prevention research adhere to the U.K. Medical Research Council (MRC) guidelines for developing and evaluating complex interventions (14). These guidelines underscore the importance of a good theoretical understanding of how interventions cause change (or protect, in the case of prevention) so that weak links in the causal chain of pathogenesis can be identified and strengthened. In addition, MRC guidelines emphasize that lack of effect may reflect implementation failure rather than genuine ineffectiveness, hence the need for a thorough evaluation process to identify implementation problems. Finally, the guidelines emphasize the importance of adequate sample sizes to take account of variability in outcome, a range of outcomes to optimize data use, and adaptation to local settings.

SUMMARY POINTS

1. The number of older adults in LMICs, including India and China, will grow substantially in the next few decades. According to the U.S. Census National Database (50), the age 60+ population in India is ~99.4 million persons in 2011 (9%). The projections for 2030 are 192.7 million (14.3%). In China, the comparable numbers are 178 million (13%) and 350 million (25%) in 2011 and 2030, respectively. There is thus an urgency to develop innovative and cost-effective interventions to meet the need for mental health care delivery in older adults.
2. Major depressive episodes in older adults are prevalent and disabling (6–10% in primary-care settings; 30% in inpatient medical and long-term care settings). Incidence rates are about half of prevalence rates (36).
3. The disorder often runs a relapsing or chronic course, and social factors, particularly related to economic or social disadvantages such as low education and violence, are major determinants (13, 38, 39).
4. The condition is often comorbid with other chronic conditions such as diabetes and is responsible for much of the disability associated with these conditions (10, 30, 43).
5. Depression is associated with worse physical health, for example, cardiovascular or HIV outcomes, by undermining treatment adherence and healthy lifestyle choices (10).
6. Depression is associated with excess mortality after myocardial infarction, stroke, and cancer diagnosis and is the major risk factor for suicide in old age (36).
7. Available pharmacologic and psychosocial treatments are only partially satisfactory in reducing symptom burden, sustaining remission, and averting years lived with disability; hence, effective preventive interventions are needed (5, 16).
8. The treatment gap for people with mental disorders has been extensively documented, especially in LMICs, where close to 90% of people with mental disorders do not receive cost-effective treatments (34).

9. The great scarcity of mental health specialists in most countries and the inequity of the distribution in these specialists are major barriers to closing the treatment gap (20, 26, 34). The existence of the treatment gap and the attendant workforce issues underscore the need for developing effective models of depression prevention that can be implemented by health workers with shorter training and fewer qualifications to make more efficient use of the available human resources for health (3, 35).
10. Preventing depression in older adults may be cost-effective (46, 51) by preventing the downward spiral of depression → disability → death and prolonging older adults' capacity for independence.

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The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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