Prevention of Major Depression

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incidence, major depressive episode, major depressive disorder, onset, randomized controlled trial, recurrence

Abstract
Before the 1980s, no randomized controlled trials had been carried out to test whether major depressive episodes could be prevented. In the past 30 years, several trials have reported success in reducing the incidence (the number of new cases) of major depressive episodes. These studies suggest that major depression can be prevented. Given the large burden of disease caused by major depression, it is time for substantial systematic efforts to replicate these studies, carry out multisite trials, and widely disseminate prevention interventions found to be effective. The present review examines the conceptual and practical differences between treatment and prevention trials and the importance of identifying groups at high short-term risk for major depressive episodes to make prevention trials feasible. We also list the randomized controlled prevention trials that have been carried out to date and discuss the need for prevention interventions that go beyond the limits of traditional face-to-face interventions.
INTRODUCTION

Major depression produces the second-largest burden of disease in the world today and is by far the leading cause of disability (World Health Org. Region. Off. South-East Asia 2001). Approximately 1 in 5 women and 1 in 8 men will experience a major depressive episode during their lifetime (Kessler et al. 1994). Most people with depression do not receive treatment, about one-third of those who do receive treatment do not respond to current approaches, and over half of those who experience a first onset of a major depressive episode will experience one or more recurrences. Current clinical practice, generally limited to treating depression in its acute phase, fails to alleviate the disease burden in a significant way at the population level: two-thirds of the disease burden remains intact (Andrews et al. 2004, Chisholm et al. 2004). The disease burden due to depression has substantial economic ramifications. Depressive disorder generates staggering costs in the health care sector, but the costs due to production losses (work loss days and work cutback days) exceed those by a factor of four (Vos et al. 2004).

The Institute of Medicine (IOM) of the United States of America has produced two reports calling for major efforts to develop, evaluate, and implement prevention interventions focused on mental, emotional, and behavioral disorders (Mrazek & Haggerty 1994, Natl. Res. Counc. & Inst. Med. 2009). The IOM reports provide a conceptual, research, and policy framework to guide prevention science and practice; they also highlight major depression as one of the first major mental disorders likely to be prevented.

This article discusses differences between prevention and treatment interventions and reviews depression prevention research and published randomized controlled depression prevention trials. It also underscores the implications of the state of the science of prevention for policy and practice, and the advisability of developing highly scalable prevention methods (such as evidence-based Internet interventions) that can reach people across the globe. We end by envisioning how societies might be transformed if we made concerted efforts to reduce the unnecessary suffering caused by preventable cases of major depression.

DEFINITIONAL ISSUES

The 1994 Institute of Medicine (Mrazek & Haggerty 1994) report argued that one of the obstacles to progress in the prevention of mental disorders was that the word “prevention” was often used to describe treatment research and practice (for example, since treatment of depression prevents many of the sequelae of depression, research on treatment may have been considered as prevention research). This practice not only obscured the nature of prevention,
but it also overestimated the amount of resources allocated to prevention. Therefore, the committee that authored the 1994 report suggested a clear line of demarcation between prevention and treatment: Interventions that took place before the onset of a clinical episode of the target disorder were preventive, and those that took place after clinical onset were in the realm of treatment (Mrazek & Haggerty 1994, pg. 23).

The 2009 IOM report (Natl. Res. Counc. & Inst. Med. 2009) reaffirmed the importance of this key distinction (see Figure 1).

Within the prevention realm, there are three levels of intervention. Universal preventive interventions are targeted to entire populations; selected preventive interventions are targeted at subgroups of the population considered at high risk due to shared characteristics (e.g., poverty, trauma, bereavement); and indicated interventions are focused on individuals who have early signs or symptoms of the targeted disorder but have not crossed the threshold into a clinical episode. In each case, the focus of the intervention is to reduce incidence, that is, the number of new cases of the disorder. In contrast, the goal of treatment is to reduce prevalence, that is, the number of total cases of the disorder. Note that by reducing incidence, one also reduces prevalence.

The 2009 IOM report (Natl. Res. Counc. & Inst. Med. 2009) added promotion as a category of interventions that can precede treatment. As applied to depression, promotion interventions would be focused on producing persistently healthy and resilient mood states. Promotion interventions are not necessarily focused on preventing disorder but are likely to do so as well.
DEPRESSION PREVENTION RESEARCH

Identifying the Target

The first step in prevention research is to define the condition to be prevented. The word “depression” has many meanings, including a mood state, a symptom that is part of many clinical conditions, a syndrome, and a disorder. Studies have been conducted to address all of these phenomena. This article focuses on major depression, as defined by current diagnostic systems, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM; Am. Psychiatr. Assoc. 2000) and the ICD-10 Classification of Mental and Behavioural Disorders (World Health Org. 2007). Specifically, we review studies that recruit participants who do not currently meet criteria for major depressive episodes (the syndrome that is essential in the diagnosis of major depressive disorder) and that are designed to reduce the number of new major depressive episodes in these participants, usually in comparison with a control group.

Prevention research differs from treatment research in several ways. Perhaps the most salient difference is that in treatment research, the participants already meet criteria for the clinical entity being treated (for example, a major depressive episode), and the intervention is intended to produce improvement or remission of this condition faster than if the intervention were not provided. In prevention research, the participants do not meet criteria for the clinical condition upon entry into the study, and the goal is to provide an intervention that will keep participants from developing a clinical episode at rates lower than a comparison group. In practical terms, this difference requires that prevention researchers target individuals who are likely to develop the clinical episode within the study period (for example, one year). If individuals in the control group do not develop the clinical condition at a high enough rate within the study period, it will be difficult to show a lower rate for the experimental group. Over the years, depression prevention studies have progressed from recruiting participants with high lifetime risk to participants with high imminent or short-term risk, say, within the following three to twelve months, that is, from selected to indicated prevention samples.

Identifying High-Risk Groups

In this section, we illustrate why progress in documenting preventive effects is most likely to come from indicated prevention studies. It is entirely possible that, in the long run, universal and selected intervention services may have the highest payoff in terms of reducing population-wide incidence. The immediate problem, however, is that showing reductions in incidence in universal or selected interventions requires very large sample sizes.

To compare the proportion of new cases (incidence) in a group receiving a preventive intervention versus a group not receiving it, the base rate of new cases must be sufficiently high to yield adequate statistical power with a reasonable sample size. In Figure 2, we present the numbers needed in a prevention trial if the preventive intervention would be able to reduce the incidence by 22%, compared to the control group. This reduction of 22% was found in a recent meta-analysis of preventive interventions (Cuijpers et al. 2008). The incidence of major depression in the general population is relatively low. For example, one study found it to be 1.7% per year (De Graaf et al. 2002). In order to be able to show that a universal prevention program has reduced this incidence by 22% (to 1.3%), both the experimental group and the control group would need to consist of 17,253 participants. In Figure 2, we also show how many participants are needed if we would be able to make our preventive interventions twice as effective (in which case they could reduce the incidence by 44%). In that case, we would “only” need 3,933 participants per condition.

If, however, the incidence rate in the target population is higher (which is usually the case in selective and, even more so, in indicated prevention), the number of participants needed in prevention trials becomes smaller. For example,
if the incidence rate in a population is 30% per year, we would need 735 participants per condition in order to be able to show that the incidence was reduced by 22% (to an incidence rate of 23.4% in the prevention group), and 176 to find a reduction of 44% (to an incidence rate of 16.8%).

The large numbers of participants needed in prevention research are a basic problem in the design of prevention research in depression, as well as in other mental health conditions. These large numbers are almost impossible to realize in research examining the effects of universal prevention. A trial of 35,000 participants, who would have to be identified as not having a depressive disorder, and who would all have be interviewed with a diagnostic interview, would be an enormous enterprise.

We should remember, however, that this power problem is also a relative one. With nonpsychiatric conditions, huge groups have been studied in prevention research, as was shown in a review of studies of newborn screening for cystic fibrosis (Southern et al. 2009). In this review, two well-designed trials were found, with a total of 1,124,483 included neonates. So it is possible that the lower priority that mental health issues are assigned in the health field in general (perhaps because of stigma) results in insufficient resources being made available for research on the prevention of mental disorders.

There are several ways to reduce or solve the power problem in prevention research. One important method is to focus on indicated prevention. Indicated prevention is directed at populations who typically have high incidence rates of depression, because many of them are in a prodromal phase of a depressive disorder. Another possibility to increase statistical power is to focus on high-risk groups with multiple risk factors, such as a combination of subthreshold depression and being a child of a parent with a depressive disorder (Clarke et al. 2001, Garber et al. 2009).

Another strategy is to focus on multiple mental disorders and combine interventions aimed at prevention of depression with those aimed at prevention of, for example, anxiety disorders. Many prevention programs at school focus on generic life skills, such as coping skills, social skills, and cognitive skills. These life skills may affect the incidence of depression,
anxiety disorder, and substance use disorder at the same time. Possibly, such programs could affect the incidence of internalizing problems, while other programs could affect the incidence of externalizing problems. Indicated preventive interventions aimed at the prevention of depression could be combined with the prevention of anxiety disorders because the rate of comorbid depression and anxiety is high and because behavioral approaches for prevention could use comparable methods based on cognitive and behavioral psychotherapies. For pioneering work in this area, see the work of Seligman and colleagues (1999, 2007).

One more method to reduce the problem of statistical power is to increase the effects of the intervention (Cuijpers 2003). In order to optimize the effect of a program, the goals and design of the program should be based on a theoretical framework, focus on risk and protective factors that are known to be related to the disorder, and meet the needs of the target population. This is why it is important to conduct good risk estimation studies before the evaluation of an intervention. Currently, there is often little evidence that the risk factor an intervention is targeting is indeed a causal factor in the process leading to a disorder; how multiple risk factors work together in the causal path toward a disorder is even less examined. But it is this type of research that is necessary for the further development of effective prevention programs (Cuijpers 2003). As illustrated before, it is extremely difficult to document whether universal interventions have resulted in a significant reduction of new cases of mental disorder, even when the interventions have been designed well. But it may be possible that measuring the impact of universal interventions in selective and indicated populations would permit the detection of significant effects in these smaller and higher-risk subgroups.

There are several other, more statistical and methodological methods to increase the power of prevention studies. It is, for example, possible to extend the follow-up period (although this needs powerful interventions with strong effects) and to use survival analysis rather than fixed incidence counts. Improving the reliability of diagnoses would also increase the power of studies.

If we focus on indicated prevention interventions, in which incidence rates are much higher, the sample sizes become much more feasible. See Table 1 for estimates of sample sizes needed per group given specific incidences in the control versus the experimental group. In examining this table, note the importance of differences in proportions, rather than the absolute difference between incidences, in determining the significance of the effect. For example, a five percent reduction in incidence between an experimental and a control condition may require vastly different samples

<table>
<thead>
<tr>
<th>Experimental group incidence</th>
<th>Control group incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05</td>
<td>0.10</td>
</tr>
<tr>
<td>0.05</td>
<td>466</td>
</tr>
<tr>
<td>0.10</td>
<td>721</td>
</tr>
<tr>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>0.30</td>
<td></td>
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<tr>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>0.45</td>
<td></td>
</tr>
</tbody>
</table>

Note: Assumptions were made in estimating sample sizes based on Fisher’s exact test for difference of two proportions, powered at 0.80 with Alpha = 0.05, two-tailed, with equal N.
depending on the incidence rate in the control condition. Whereas 721 participants per group are needed to attain significant effects when the incidence in the control group is 0.15 and the experimental condition reduces this incidence to 0.10, if the incidence in the control group is 0.50 and the experimental intervention reduces it to 0.45, 1606 participants per group are needed.

If we had an intervention that reduced incidence in half, reducing the incidence of a control group from 0.50 to 0.25 would require 64 participants per group to find significance, whereas as many as 214 per group would be needed to go from 0.20 to 0.10. These examples illustrate why it is necessary to select a group with a substantial base rate of incidence.

The section above emphasizes why the search for screening methods that predict new cases of major depression is an important aspect of prevention science (Le & Boyd 2006). Many of the risk factors for major depression have been known for some time. They include such factors as gender, family history, bereavement in the early years, trauma, and socioeconomic hardship. However, these are lifetime risk factors that may be useful in identifying groups for selected interventions but are not particularly useful by themselves in identifying participants for indicated prevention trials because of the low specificity of most known risk factors for predicting short-term risk. That is, the actual likelihood of developing a major depressive episode starting during the trial period is relatively low.

It is important, as well, to distinguish between risk factors that can be modified and factors that only function as markers. Gender and family history, for example, are not modifiable. Neither are genetic markers. Recent studies reporting higher incidence of major depressive episodes in individuals with one or two short alleles of the serotonin transporter gene who experience stressful life events (Caspi et al. 2003) suggested that the combination of genetic and environmental risk factors may help predict imminent risk. However, a recent meta-analysis (Risch et al. 2009) found no association between the serotonin transporter gene either alone or in combination with stressful life events and incidence of depression. Stressful life events did retain their strong association with incidence. If they are identified, genetic or other biological markers for risk of depression would be very useful in identifying groups for selected interventions in prevention research, and the search for them will undoubtedly continue. Note that such markers need not be associated only with risk for pathology. They could also be associated with protective factors, such as resilience (Feder et al. 2009). Whether genetic traits will ever be safely modifiable is an open and controversial question.

One of the high-risk markers for new major depressive episodes is having a past history of such episodes. Thus, many depression prevention trials include individuals with a history of major depressive episodes but not a current episode. In these individuals, one can prevent recurrence, but, of course, not the first onset. Individuals who have had a major depressive episode but do not currently meet criteria for such an episode may be at risk for relapse or recurrence. Relapse is considered an exacerbation of a major depressive episode that may have been improving but has not fully remitted. Prevention of relapse is part of good treatment for major depression and would generally not be considered a target for trials intended to reduce incidence. Recurrence is considered the beginning of a new major depressive episode after a previous one has fully remitted (defined as, say, 12 months or more without symptoms). The previous episode may have ended with or without formal psychiatric or medical treatment (see figure 1 in Thase & Denko 2008).

High levels of depressive symptoms on self-report scales have been found to be short-term predictors of major depressive episodes (Cuijpers & Smit 2004). Therefore, studies focused on preventing or reducing depressive symptoms currently below the threshold required for a clinical diagnosis are essential precursors to prevention trials focused on incidence. Several investigators have recruited individuals with subthreshold symptoms and
taught them mood management methods of the type found helpful in treatment studies. Participants in such prevention trials are identified as having symptoms above a certain cutoff score on depression symptom scales but not meeting diagnostic criteria for major depressive episode. The logic of the studies is to follow these individuals to determine whether a smaller proportion of those taught mood management methods cross the clinical threshold compared to those who do not get the intervention. Most of these studies have focused on the intervention’s effect on symptoms but have not examined incidence. In their recent review of this literature, Horowitz & Garber (2006) discuss several issues important for prevention research, including whether reductions in subthreshold symptoms should be conceptualized as treatment or preventive effects.

DEPRESSION PREVENTION TRIALS

In the past few decades, hundreds of controlled studies have examined the effects of mental health programs aimed at preventing mental health problems at school (Durlak & Wells 1997, 1998), work-related stress (Van der Klink et al. 2001), distress among caregivers for the elderly (Knight et al. 1993, Thompson & Briggs 2000), and many other conditions (Cuijpers 2003, Mrazek & Haggerty 1994, Natl. Res. Counc. & Inst. Med. 2009). This considerable body of research has shown that some prevention programs in mental health are capable of strengthening protective factors, such as social skills, problem-solving skills, stress-management skills, prosocial behavior, and social support; that these programs can reduce both the consequences of risk factors and psychiatric symptoms; and that they may have positive economic effects. Despite this large body of research, few studies have examined whether these prevention programs are actually capable of reducing the incidence of new cases of major depression or other mental disorders defined according to diagnostic criteria.

In the 1970s, when the first author (RFM), under the mentorship of James G. Kelly, first reviewed the prevention literature (Kelly et al. 1977, Muñoz & Kelly 1975, Muñoz et al. 1979), there were many calls for prevention of mental disorders but no randomized controlled trials testing whether clinical depression could be prevented.

The first randomized controlled depression prevention trials were conducted in the 1980s and 1990s (Clarke et al. 1995; Gillham et al. 2000; Miranda & Muñoz 1994; Muñoz 1993; Muñoz & Ying 1993; Muñoz et al. 1987, 1995; Seligman et al. 1999; Vega et al. 1987). Since then, the number of depression prevention trials has increased rapidly. A recently conducted meta-analysis of these studies (Cuijpers et al. 2008) found a total of 19 studies that fit the prevention paradigm, that is, subjects with a depressive disorder according to DSM criteria at baseline were excluded, and only subjects with no diagnosable depressive disorder were included. The included studies tested whether the incidence rate of mental disorders was reduced in the recipients of preventive interventions compared to subjects who did not participate in such an intervention. Cuijpers et al. (2008) found that the overall incidence rate ratio was 0.78 (95% CI: 0.65–0.93). The incidence rate ratio (IRR) is the incidence rate of developing a depressive disorder in experimental subjects relative to the incidence rate in control subjects. An IRR of 0.78 indicates a reduction of the risk of developing a depressive disorder in the next year of about 22% in participants receiving an intervention compared to people in the control groups. This study indicates that, in addition to treatment of existing depressive disorders, prevention of new cases of depressive disorders seems to be possible and may have become a realistic strategy to reduce the enormous burden of these disorders.

### Table 2: Selected characteristics of representative studies examining the effects of preventive interventions on the incidence of depressive disorders.

<table>
<thead>
<tr>
<th>Study name</th>
<th>Risk ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allart 2007</td>
<td>1.12</td>
<td>0.57</td>
<td>2.21</td>
<td>0.34</td>
<td>0.73</td>
</tr>
<tr>
<td>Anisman 2009</td>
<td>0.12</td>
<td>0.02</td>
<td>0.93</td>
<td>-2.03</td>
<td>0.04</td>
</tr>
<tr>
<td>Austin 2008</td>
<td>0.95</td>
<td>0.58</td>
<td>1.57</td>
<td>-0.20</td>
<td>0.84</td>
</tr>
<tr>
<td>Brugha 2000</td>
<td>0.51</td>
<td>0.13</td>
<td>1.98</td>
<td>-0.97</td>
<td>0.33</td>
</tr>
<tr>
<td>Clarke 1995</td>
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<td>0.27</td>
<td>1.20</td>
<td>-1.48</td>
<td>0.14</td>
</tr>
<tr>
<td>Clarke 2001</td>
<td>0.31</td>
<td>0.11</td>
<td>0.88</td>
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<td>0.03</td>
</tr>
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<td>Dennis 2009</td>
<td>0.65</td>
<td>0.34</td>
<td>1.23</td>
<td>-1.33</td>
<td>0.18</td>
</tr>
<tr>
<td>Elliott 2000</td>
<td>0.50</td>
<td>0.25</td>
<td>0.98</td>
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</tr>
<tr>
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</tr>
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<tr>
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<td>Priest 2003</td>
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<td>1.25</td>
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<td>Robinson 2008</td>
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<td>1.12</td>
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<td>1.63</td>
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<td>1.45</td>
<td>-0.58</td>
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<td>0.64</td>
<td>1.72</td>
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<td>0.23</td>
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<td>Stice 2008 SET</td>
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<td>1.32</td>
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<td>Wileness 2004</td>
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<td>1.39</td>
<td>-0.95</td>
<td>0.34</td>
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<td>Van’t Veer 2009</td>
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<td>0.31</td>
<td>1.21</td>
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<td>Young 2006</td>
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<td>0.65</td>
<td>0.85</td>
<td>-4.32</td>
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</tbody>
</table>

### Figure 3
Relative risk ratios for incidence of depressive disorders.

Toward Evidence-Based Preventive Interventions

The majority of studies examining prevention of depressive disorders have used cognitive behavioral interventions, and a few have examined interventions based on problem-solving therapy, interpersonal psychotherapy, or another type of intervention.

**Prevention based on cognitive behavior therapy.** Cognitive behavioral interventions largely focus on the effect of dysfunctional thoughts and activity levels on current behavior and future functioning. These interventions are aimed at teaching patients to evaluate,
Table 2  Description of randomized controlled trials, interventions tested, incidence rates, and relative risk

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Target Population</th>
<th>Inclusion criteria</th>
<th>Conditions</th>
<th>N</th>
<th>n (FU)</th>
<th>Intervention</th>
<th>FU (mn)</th>
<th>Exp</th>
<th>Control</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allart et al. 2007</td>
<td>Ind</td>
<td>Adults with sD</td>
<td>BDI ≥ 10; no current MDD</td>
<td>1. CBT</td>
<td>68</td>
<td>42</td>
<td>12 CBT grp sessions (CWD)</td>
<td>12</td>
<td>27.3</td>
<td>25</td>
<td>1.12</td>
</tr>
<tr>
<td>Arnarson &amp; Craighead 2009</td>
<td>Ind</td>
<td>Adolescents</td>
<td>CDI = 75th–90th percentile or CASQ ≥ seventy-fifth percentile; no current DD</td>
<td>1. Eclectic</td>
<td>81</td>
<td>90</td>
<td>14 eclectic grp sessions</td>
<td>6</td>
<td>1.6</td>
<td>13.3</td>
<td>0.12</td>
</tr>
<tr>
<td>Austin et al. 2008</td>
<td>Sel</td>
<td>Antenatal women</td>
<td>Risk for depression (EPDS &gt; 10 and/or ANRQ &gt; 23 or hx of DD)</td>
<td>1. CBT</td>
<td>191</td>
<td>86</td>
<td>6 CBT grp sessions + 1 booster</td>
<td>5–10</td>
<td>20</td>
<td>21</td>
<td>0.95</td>
</tr>
<tr>
<td>Brugha et al. 2000</td>
<td>Sel</td>
<td>Primiparous women</td>
<td>Risk factor for depression</td>
<td>CBT</td>
<td>103</td>
<td>106</td>
<td>6 CBT + problem solving social support grp sessions</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>0.51</td>
</tr>
<tr>
<td>Clarke et al. 1995</td>
<td>Ind</td>
<td>Adolescents (15–16)</td>
<td>CESD ≥ 24; no current MDD/DYS</td>
<td>CBT</td>
<td>76</td>
<td>74</td>
<td>15 CBT grp sessions (CWD)</td>
<td>12</td>
<td>14.5</td>
<td>25.7</td>
<td>0.57</td>
</tr>
<tr>
<td>Clarke et al. 2001</td>
<td>Ind</td>
<td>Adolescents (13–18)</td>
<td>CESD ≥ 24; ≥ 1 DSM-IV criteria; parent with MDD</td>
<td>CBT</td>
<td>45</td>
<td>49</td>
<td>15 CBT grp sessions (CWD)</td>
<td>24</td>
<td>9.3</td>
<td>28.8</td>
<td>0.31</td>
</tr>
<tr>
<td>Dennis et al. 2009</td>
<td>Ind</td>
<td>New mothers (2 weeks postpartum)</td>
<td>High-risk mothers (EPDS &gt; 9)</td>
<td>PS</td>
<td>349</td>
<td>352</td>
<td>Telephone-based support by peers with hx of PPD</td>
<td>3</td>
<td>5</td>
<td>7</td>
<td>0.65</td>
</tr>
<tr>
<td>Elliott et al. 2000</td>
<td>Sel</td>
<td>Pregnant women</td>
<td>Vulnerable (LQ)</td>
<td>PE</td>
<td>47</td>
<td>52</td>
<td>11 PE sessions + mutual support</td>
<td>3</td>
<td>19</td>
<td>39</td>
<td>0.50</td>
</tr>
<tr>
<td>Garber et al. 2009</td>
<td>Ind</td>
<td>Adolescents (13–17) of parents with depression</td>
<td>Parent: Hx of MDE; Adolescent: CESD &gt; 20 or 2 mn remission from MDE or both</td>
<td>1. CBT</td>
<td>159</td>
<td>157</td>
<td>8 CBT grp sessions + 6 continuation sessions</td>
<td>9</td>
<td>21.4</td>
<td>32.7</td>
<td>0.66</td>
</tr>
<tr>
<td>Gillham et al. 2006</td>
<td>Ind</td>
<td>Early adolescents (11–12)</td>
<td>CDI ≥ 7.9; no current MDD DYS</td>
<td>1. CBT</td>
<td>147</td>
<td>124</td>
<td>12 CBT grp sessions</td>
<td>24</td>
<td>21</td>
<td>36</td>
<td>0.57</td>
</tr>
<tr>
<td>Hagan et al. 2004</td>
<td>Sel</td>
<td>Mothers of very preterm babies</td>
<td>No current DD</td>
<td>1. CBT</td>
<td>101</td>
<td>98</td>
<td>6 CBT grp sessions + PE</td>
<td>12</td>
<td>29</td>
<td>26</td>
<td>1.13</td>
</tr>
<tr>
<td>Study</td>
<td>Type</td>
<td>Condition</td>
<td>Inclusion Criteria</td>
<td>Control Group</td>
<td>Intervention Group 1</td>
<td>Intervention Group 2</td>
<td>Interventions</td>
<td>Follow-up</td>
<td>Effect Size (Hedges' g)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Konnert et al. 2009</td>
<td>Ind</td>
<td>Nursing home residents (over 60)</td>
<td>No MDE, GDS ≥ 9</td>
<td>1. CBT</td>
<td>2. CAU</td>
<td></td>
<td>13 CBT sessions</td>
<td></td>
<td>6.0</td>
<td>8.7</td>
<td>0.23</td>
</tr>
<tr>
<td>Lara et al. 2009</td>
<td>Ind</td>
<td>Pregnant women in Mexico</td>
<td>CES-D ≥ 16 and/or self-report hx of MDD</td>
<td>1. PE</td>
<td>2. CAU</td>
<td></td>
<td>8 PE grp sessions</td>
<td>4-9</td>
<td>10.7</td>
<td>25.0</td>
<td>0.43</td>
</tr>
<tr>
<td>Martinovic et al. 2006</td>
<td>Sel</td>
<td>Adolescents (13–19) with epilepsy</td>
<td>sD, no current DD</td>
<td>1. CBT</td>
<td>2. CAU</td>
<td></td>
<td>12 CBT grp sessions</td>
<td>9.0</td>
<td>0.15</td>
<td>0.03</td>
<td>0.14</td>
</tr>
<tr>
<td>Muñoz et al. 1995</td>
<td>Sel</td>
<td>GM patients (minority; chronically ill)</td>
<td>No MDD in past 6 mn</td>
<td>1. CBT</td>
<td>2. CAU</td>
<td></td>
<td>8 CBT grp sessions</td>
<td>(CWD)</td>
<td>12.0</td>
<td>5.0</td>
<td>0.54</td>
</tr>
<tr>
<td>Muñoz et al. 2007</td>
<td>Ind</td>
<td>Pregnant Latina women</td>
<td>CES-D ≥ 16; hx of MDD</td>
<td>1. CBT</td>
<td>2. CAU</td>
<td></td>
<td>12 CBT grp sessions</td>
<td>(CWD)</td>
<td>12.4</td>
<td>25.0</td>
<td>0.57</td>
</tr>
<tr>
<td>Priest et al. 2003</td>
<td>Sel</td>
<td>All women, after delivery</td>
<td>No other inclusion criteria</td>
<td>1. Debrief</td>
<td>2. CAU</td>
<td></td>
<td>8 CBT grp sessions</td>
<td>(CWD)</td>
<td>12.4</td>
<td>18.0</td>
<td>10.02</td>
</tr>
<tr>
<td>Robinson et al. 2008</td>
<td>Sel</td>
<td>Post-stroke patients</td>
<td>No current DD (major or minor), HAM-D &lt;11</td>
<td>1. ADM</td>
<td>2. PST</td>
<td>3. Placebo</td>
<td>6 PST sessions + 6</td>
<td>12.0</td>
<td>23.0</td>
<td>35.0</td>
<td>0.51</td>
</tr>
<tr>
<td>Rovner et al. 2007</td>
<td>Sel</td>
<td>Older patients with neovascular macular degeneration</td>
<td>No current DD</td>
<td>1. PST</td>
<td>2. CAU</td>
<td></td>
<td>6 indv PST sessions</td>
<td></td>
<td>6.0</td>
<td>28.4</td>
<td>0.84</td>
</tr>
<tr>
<td>Seligman et al. 1999</td>
<td>Sel</td>
<td>Undergraduate students</td>
<td>ASQ = bottom quartile, no current MDD</td>
<td>CBT</td>
<td>CAU</td>
<td></td>
<td>8 CBT grp sessions</td>
<td></td>
<td>36.0</td>
<td>40.0</td>
<td>0.83</td>
</tr>
<tr>
<td>Seligman et al. 2007</td>
<td>Sel</td>
<td>Undergraduate students</td>
<td>Mild to moderate depressive sx (BD I = 9–24)</td>
<td>CBT</td>
<td>CAU</td>
<td></td>
<td>8 CBT grp sessions + homework, one ftf meeting with grp leader + Web booster and email coach</td>
<td>6.0</td>
<td>26.0</td>
<td>27.0</td>
<td>0.95</td>
</tr>
<tr>
<td>Sheffield et al. 2006</td>
<td>Uni, Ind</td>
<td>All students of 36 schools</td>
<td>High-symptom students (top 20% of CDI and CES-D), no current MDD/DYS</td>
<td>1. CBT-Uni</td>
<td>2. CBT-Uni</td>
<td>3. CBT-Uni+Ind</td>
<td>8 CBT + PST grp lessons</td>
<td>18.0</td>
<td>18.0</td>
<td>20.0</td>
<td>0.85</td>
</tr>
<tr>
<td>Spence et al. 2003</td>
<td>Uni</td>
<td>All students of 18 high schools</td>
<td>No specific inclusion criteria</td>
<td>1. CBT</td>
<td>2. CAU</td>
<td></td>
<td>8 grp lessons of CBT + PST</td>
<td></td>
<td>12.0</td>
<td>10.0</td>
<td>1.06</td>
</tr>
<tr>
<td>Study</td>
<td>Type</td>
<td>Target Population</td>
<td>Inclusion criteria</td>
<td>Conditions</td>
<td>N&lt;sup&gt;a&lt;/sup&gt;</td>
<td>n (FU)</td>
<td>Intervention</td>
<td>FU (mn)</td>
<td>Incidence (%)</td>
<td>Exp</td>
<td>Control</td>
</tr>
<tr>
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</tr>
<tr>
<td>Stice et al. 2008</td>
<td>Ind</td>
<td>High school students</td>
<td>CESD ≥ 20, no MDE</td>
<td>1. CBT</td>
<td>89</td>
<td>81</td>
<td>1. 6 CBT grp sessions</td>
<td>6</td>
<td>7</td>
<td>13</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. SET</td>
<td>88</td>
<td>82</td>
<td>2. 6 SET grp sessions</td>
<td>7</td>
<td>7</td>
<td>3</td>
<td>0.51</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3. CBBT</td>
<td>80</td>
<td>76</td>
<td>3. Feeling Good (Burns 1980)</td>
<td>7</td>
<td>7</td>
<td>3</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4. CAU</td>
<td>84</td>
<td>77</td>
<td></td>
<td>7</td>
<td>7</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>van’t Veer-Tazelaar et al. 2009</td>
<td>Ind</td>
<td>Older adults in primary care</td>
<td>No current MDE; CESD ≥ 16</td>
<td>1. CBBT +PST</td>
<td>86</td>
<td>62</td>
<td>3 months CBBT + calls/visits from nurse, then 7 PST sessions</td>
<td>12</td>
<td>12</td>
<td>24</td>
<td>0.61</td>
</tr>
<tr>
<td>Willems et al. 2004</td>
<td>Ind</td>
<td>Adults (18–65)</td>
<td>One MDD core symptom, no MDD in</td>
<td>1. CBT</td>
<td>107</td>
<td>83</td>
<td>Minimal indiv CBT contact (CWD); 1 ftf contact + self-help book + 6 short telephone</td>
<td>12</td>
<td>12</td>
<td>18</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>past 6 mn</td>
<td>2. CAU</td>
<td>109</td>
<td>94</td>
<td>consultations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young et al. 2006</td>
<td>Ind</td>
<td>Adolescents (15–16)</td>
<td>CESD ≥ 16; 2 symptoms; no current MDD/DYS</td>
<td>1. IPT</td>
<td>27</td>
<td>27</td>
<td>2 indiv + 8 IPT grp sessions</td>
<td>6</td>
<td>3.7</td>
<td>28.6</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. CAU</td>
<td>14</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zlotnick et al. 2001</td>
<td>Sel</td>
<td>Pregnant women</td>
<td>At least 1 of 4 risk indicators of PPD, no current MDD</td>
<td>IPT CAU</td>
<td>37&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17</td>
<td>4 IPT grp sessions</td>
<td>3</td>
<td>0</td>
<td>33</td>
<td>0.08</td>
</tr>
<tr>
<td>Zlotnick et al. 2006</td>
<td>Sel</td>
<td>Pregnant women</td>
<td>High score on risk survey, no current MDD</td>
<td>IPT CAU</td>
<td>53</td>
<td>46</td>
<td>4 IPT grp sessions</td>
<td>3</td>
<td>4</td>
<td>20</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Abbreviations: ADM: antidepressive medication; ANRQ: Antenatal Risk Questionnaire; ASQ: Attributional Style Questionnaire; BDI: Beck Depression Inventory; CASQ: Children’s Attributional Style Questionnaire; CAU: care-as-usual; CBBT: cognitive-behavioral bibliotherapy; CBT: cognitive behavior therapy; CDI: Children’s Depression Inventory; CESD: Center for Epidemiological Studies–Depression; CWD: Coping with Depression; Debrief: debriefing; DD: depressive disorder; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, fourth edition; DYS: dysthymia; EPDS: Edinburgh Postnatal Depression Scale; Exp: experimental condition; ftf: face-to-face; FU: follow-up; GDS: Geriatric Depression Scale; GM: general medicine; grp: group intervention; HAM-D: Hamilton-17 Depression Rating Scale; Ind: indicated prevention; Indv: individual intervention; IPT: interpersonal psychotherapy; LQ: Leverton Questionnaire; MDD: major depressive episode; MDE: major depressive disorder; mn: months; PE: psychoeducation; PPD: postpartum depression; PS: peer support; PST: problem-solving therapy; RR: relative risk; Sel: selective prevention; SET: supportive-expressive therapy; sD: subthreshold depression; sx: symptoms; Uni: universal prevention.

<sup>a</sup>randomized.
<sup>b</sup>unable to determine; exact number not reported by authors.
<sup>c</sup>high-symptom group.
<sup>d</sup>counseling.
challenge, and modify their dysfunctional beliefs (cognitive restructuring), with the further aim being to change behavior. Therapists also emphasize homework assignments designed to increase the frequency of outside-of-session pleasant and rewarding activities. Therapists exert an active influence over therapeutic interactions and topics of discussion, use a psycho-educational, collaborative approach, and teach patients new ways of coping with stressful situations. Cognitive behavior therapy demonstrates the strongest empirical evidence for the treatment of depression, is the most studied preventive intervention for depression, and is found to be effective in treating many other problems and disorders (Cuijpers et al. 2009).

Within the “family” of cognitive behavioral interventions, the “Coping with Depression” course (CWD) developed by Peter Lewinsohn and colleagues (Lewinsohn et al. 1984, 1992) is the most commonly used preventive intervention for depression (Cuijpers et al. 2009). The CWD is a cognitive behavioral intervention for depression using a psychoeducational format. In this approach, participants work through a standardized protocol. The CWD is usually conducted in a group format, as an indicated preventive intervention. The psychoeducational approach implies that the therapist works more in the role of an instructor than a therapist, and the patient is more of a student than a traditional patient. Another characteristic of the CWD is the “toolbox” idea, that is, participants learn practical skills intended to help them cope with and overcome depressive feelings. These include social skills, cognitive restructuring, and behavioral activation to increase pleasant events (“activity scheduling”) (Lewinsohn et al. 1992). Preventive versions of the CWD typically reduce the number of sessions and offer simplified materials (Muñoz & Ying 1993, appendix A). For example, the “Coping with Stress” course for prevention of depression in adolescents has fewer sessions than the treatment version of the CWD and focuses on cognitive restructuring (Clarke et al. 1995, 2001; Garber et al. 2009).

The theoretical basis for the CWD is social learning and social cognitive theory (Bandura 1977, 2001), according to which treatment for depression involves increasing self-efficacy related to mood management, using such skills as increasing pleasant and decreasing unpleasant person-environment interactions (Lewinsohn et al. 1985).

In a recent meta-analysis of studies examining the effects of the CWD on the incidence of depressive disorders in adolescents and adults, it was found that the six studies aimed at prevention of new cases of major depression resulted in a reduced risk of developing major depression of 38% (incidence rate ratio was 0.62; Cuijpers et al. 2009). Other studies using cognitive behavioral interventions are not formally based on the CWD, although they usually focus on modifying the three key targets of the CWD: activities (behavioral activation), thoughts (cognitive restructuring), and people (interpersonal skills training).

Prevention based on interpersonal psychotherapy. In recent years, several preventive interventions have been examined which are based on interpersonal psychotherapy (IPT). Interpersonal psychotherapy is a brief and highly structured manual-based form of psychotherapy that addresses interpersonal issues in depression. In the initial phase of IPT, the depressive symptoms are explored and psychoeducation about depression is given. The interpersonal context of the patient is explored and depressive symptoms are linked to recent interpersonal events. There are four possible treatment focuses: complicated grief, interpersonal conflict, role transition, and interpersonal deficits (van Schaik et al. 2006). IPT stems from the work of Harry Stack Sullivan, Adolf Meyer, and John Bowlby (Weissman & Markowitz 2002). The late Gerald Klerman and Myrna Weissman developed the current form of the treatment in the 1980s (Klerman et al. 1984).

Trials of IPT-based interventions for prevention of depressive disorders have found very strong effects of IPT on the incidence of depressive disorders in adolescents (Young et al. 2006) and women during the postpartum period (Zlotnick et al. 2001, 2006). Although these
studies should be considered as pilot projects and should be regarded with caution, these positive effects certainly warrant further research on IPT as preventive intervention.

**Prevention based on problem-solving therapy.** Another type of intervention that has been used recently in prevention trials is based on problem-solving therapies (PST). In PST, the patient systematically identifies his or her problems, generates alternative solutions for each problem, selects the best solution, develops and conducts a plan, and evaluates whether this has solved the problem. PST as a treatment can range from a more intensive “social problem-solving therapy” (D’Zurilla & Nezu 1982, Nezu & Perri 1989) to more brief versions, which can be applied by nurses in primary care (Mynors-Wallis et al. 1995). It can be applied both individually and in a group format.

**Prevention via the Internet.** A new development, which may be important for prevention of depression, is the introduction of Internet-based interventions in recent years (Barak et al. 2008, Griffiths & Christensen 2007). Preventive and early interventions for depression are becoming increasingly easy to access through the Internet. Internet-based cognitive-behavioral interventions appear to be effective (Spek et al. 2007) and have several other advantages: They allow participants to work at their own pace, abolish the need to schedule appointments, and save time traveling. Furthermore, Internet interventions may advance research into the outcome of interventions because every keystroke of users can be recorded for subsequent analysis (Marks et al. 2007). Several cognitive-behavioral systems aimed at depression are already available, and a meta-analysis showed that these systems are effective in reducing depressive symptoms (Spek et al. 2007). Although most of these systems are aimed at the treatment of depression, there is no reason to assume that they cannot be used as (indicated) preventive interventions. Future research should focus on whether it is possible to implement preventive interventions on a larger scale through the Internet (Christensen & Griffiths 2002).

**Target Groups and Settings**

**Universal, selective, and indicated prevention.** The groups targeted for preventive interventions greatly depend on the type of prevention. Few studies have examined the effects of universal prevention on the incidence of depressive disorders, and the few studies that did failed to find evidence that these interventions are effective in reducing incidence (Sheffield et al. 2006, Spence et al. 2003), probably because of limitations in statistical power (see Cuijpers 2003 and Horowitz & Garber 2006 for a discussion of statistical considerations). As noted above, the difficulties of showing that universal interventions reduce incidence do not necessarily mean that universal interventions are not effective. Rather, it means that detecting differences between experimental and control conditions requires sample sizes that are usually impractical or prohibitively expensive with traditional research methods. Selective and indicated preventive interventions have been examined in a variety of different target groups. These trials are described below.

**Adolescents.** There are a number of important reasons to target adolescents for preventive interventions. First, depression in children and adolescents is a critical problem from a public health perspective. With an estimated prevalence of up to 2.8% in children and up to 8.3% in adolescents, depression is a frequent condition in underage groups, with high recurrence rates, often poor psychosocial and academic outcomes, and an increased risk for other mental disorders (Birmaher et al. 1996a,b; Costello et al. 2006; Steinhausen et al. 1998).

Second, if prevention interventions are effective during adolescence, then they are more likely to prevent first onset. Depression rates begin to rise in early adolescence, until they have reached adult levels in late adolescence (Lewinsohn et al. 1993). It is well established that most adults with recurrent depression have
their initial depressive episodes as teenagers (Pine et al. 1998).

The age of onset for major depressive disorder symptoms has been estimated to be 19.1 years for 20% of those ever suffering from major depressive disorder, and 25.8 years for 50% of those ever suffering from major depressive disorder (Mrazek & Haggerty 1994). The age of first diagnosis, however, has been estimated to be 25.3 years for 20% of those ever suffering major depressive disorder and 38.8 years for 50% of those ever suffering major depressive disorder. This means that many people who eventually develop a major depressive disorder have subthreshold symptoms of depression for several years. During this window of risk between onset of symptoms and the first clinical episode (often during adolescence or young adulthood) preventive interventions may be able to reduce the risk of developing depressive disorders and averting the often chronic and recurrent course of major depression.

A more practical reason to develop preventive interventions for adolescents is that they can be approached through the school system. Virtually all children and adolescents can be screened at school, and the school offers a setting in which preventive interventions can be administered readily. Consequently, a large proportion of studies on preventive interventions for adolescents have been conducted at schools (e.g., Arnarson & Craighead 2009, Stice et al. 2008). Most trials have used an indicated prevention approach to target adolescents with elevated symptoms of depression and have tested cognitive-behavioral interventions (Clarke et al. 1995, 2001; Garber et al. 2009; Gillham et al. 2006; Martinovic et al. 2006; Stice et al. 2008), interpersonal psychotherapy (Young et al. 2006), or a combination of CBT with another approach such as problem-solving therapy (Sheffield et al. 2006, Spence et al. 2003). A recent trial by Arnarson & Craighead (2009) examined an eclectic intervention based on developmental and psychosocial approaches.

Some studies have focused on adolescents whose parents suffer from a depressive disorder (Beardslee et al. 2003, 2008). Parental depression is one of the most potent and clinically salient risk factors for the development of depression in youth (Beardslee et al. 1998, Garber et al. 2009). Offspring of depressed parents are at a two- to threefold increased risk of developing depressive disorders (Weissman et al. 2006). Two of the most successful prevention trials have focused on prevention of depression in this group of adolescents (Clarke et al. 1995, 2001). The cognitive-behavioral intervention tested in these trials has now been successfully tested across several sites (Garber et al. 2009). This type of systematic development exemplifies what is needed to bring the depression prevention field to the level of evidence-based interventions that could then be disseminated widely. Incidence of major depressive episode in trials with significant preventive effects ranged from 1.6% to 21.4% in the experimental intervention compared to 13% to 32.7% in the control (see Arnarson & Craighead 2009; Clarke et al. 1995, 2001; Garber et al. 2009; Stice et al. 2009).

**Postpartum women.** Another important target group for preventive interventions is women at risk for postpartum depression (PPD). PPD is a depressive disorder with the same characteristics as other depressive disorders except that it occurs within four weeks postpartum (O’Hara 1997). About one in every seven new mothers is affected by PPD (Wisner et al. 2006), resulting in an overall prevalence rate of 13% (O’Hara & Swain 1996). Postpartum mood disorders represent the most frequent form of maternal morbidity following delivery (Stocky & Lynch 2000).

PPD is an important public health problem (Cuijpers et al. 2008). Apart from the direct suffering caused by PPD in the patient and the increased risk of hospitalization (Dennis 2004a,b), several areas in the life of a patient can be adversely affected. PPD has been reported to result in an increased risk of marital stress and divorce (Holden 1991), an increased risk of child abuse and neglect (Buist 1998), and sometimes even in maternal suicide and infanticide (Sit et al. 2006). PPD can also
have serious consequences for the children of affected mothers, in the short term and in the long term (Murray et al. 2003). The negative effects of maternal depression on children include an increased risk of impaired mental and motor development, difficult temperament, poor self-regulation, low self-esteem, and long-term behavioral problems (Beck 1999, Goodman & Gotlib 1999, Orvaschel et al. 1988, Wisner et al. 2006). It can also result in insecure attachment (Hipwell et al. 2000, Murray 1992), social interaction difficulties (Davies & Cummings 1994; Dennis 2004a,b), and increased cognitive difficulties (Whiffen & Gotlib 1989), and can interfere with expressive language development (Cox et al. 1987).

PPD often goes undetected due to lack of proper screening and to the sense of shame that often makes a woman hide PPD from her loved ones as well as from health professionals (Murray & Cooper 1997). Untreated PPD often remits spontaneously after four to six months (O’Hara 1997), but can in some cases easily last much longer, causing prolonged suffering (Cooper & Murray 1998). Because it often remains undiagnosed and untreated while causing considerable distress and disruption to the women and their families, effective prevention would be preferable to treatment (Cooper et al. 2003). Research on prevention of PPD is made more feasible by the fact that, at least in developed countries, health professionals see most new mothers regularly during pregnancy.

In the past decades, a considerable number of studies has examined the possibilities of preventing PPD (Dennis 2005, Dennis & Creedy 2007), but most of these studies have not used diagnostic criteria to exclude women who already have a depressive disorder at study entry and to examine the effects of prevention on its incidence at study completion. Most studies have used self-report measures and have only examined whether the level of depressive symptoms has decreased in the prevention groups compared to control groups. Many of these studies have used cognitive behavioral interventions (Austin et al. 2008, Brugha et al. 2000, Hagan et al. 2004, Muñoz et al. 2007), although other studies have used psychoeducational interventions (Elliott et al. 2000, Lara et al. 2009), debriefing (Priest et al. 2003), peer-to-peer telephone support (Dennis et al. 2009), and interpersonal psychotherapy (Zlotnick et al. 2001, 2006). In these trials, the incidence of PPD was lower for women assigned to the experimental condition; however, significant preventive effects were demonstrated only in the studies that examined psychoeducational interventions (Elliott et al. 2000, Lara et al. 2009) and interpersonal psychotherapy (Zlotnick et al. 2001, 2006). PPD incidence was 11% to 19% in the experimental groups versus 18% to 39% among those assigned to the control conditions.

A recent meta-analysis that included some of these studies did not find clear evidence that preventive interventions during pregnancy may reduce the incidence of postpartum depression (Dennis & Creedy 2007). This meta-analysis, however, contained studies that did not exclude those women meeting diagnostic criteria for a depressive disorder at study entry and that did not necessarily establish incidence of depression in treatment and control groups according to diagnostic criteria.


Much of the research on prevention of depressive disorders among individuals suffering from medical disorders has focused on stroke patients. It is widely acknowledged that depression is an important complication of stroke that may impede rehabilitation, recovery, quality of life, and caregiver health (Hackett et al. 2005, Parikh et al. 1990). Furthermore, stroke-associated depression is associated with lower recovery rates, reduced survival rates,
and increased risks of recurrent vascular events (House et al. 2001, Morris et al. 1993).

In a recent meta-analysis of studies on prevention of post-stroke depression, five small randomized controlled trials were found that examined the number of patients meeting criteria for depression at the end of treatment (Anderson et al. 2004, Hackett et al. 2005). All studies examined the effects of treatment with antidepressant medication, and none used a psychological intervention. Although positive effects were found in most studies, the authors state that there is no conclusive evidence that antidepressant medication prevents the onset of post-stroke depression.

In one large, recent trial, the possibility to prevent the onset of depression using PST and pharmacotherapy was examined, and PST was found to reduce the incidence of depressive disorders (Robinson et al. 2008). Other studies have examined CBT-based preventive interventions focused on adolescents with newly diagnosed epilepsy (Martinovic et al. 2006) and on nursing home residents (Konnert et al. 2009); a six-session individual PST intervention was tested in older patients with neovascular macular degeneration (Rovner et al. 2007).

**Other target groups and settings.** Several prevention-of-depression studies have focused on primary care patients. The advantage of the primary care setting is that many patients with subthreshold depression visit their general practitioner, either for their depressive symptoms or for other reasons. Several studies have used the infrastructure of primary care to recruit participants and to deliver preventive interventions using cognitive-behavioral techniques (Miranda & Muñoz 1994, Muñoz et al. 1995, Willems et al. 2004, van’t Veer-Tazelaar et al. 2009).

A growing number of studies has also focused on older adults. Depression in late life is a highly prevalent condition (Beekman et al. 1999) and has an unfavorable prognosis (Beekman et al. 2002) as well as a considerable impact on the quality of life of patients (Doraiswamy et al. 2002) and their relatives (Hinrichsen et al. 1992, Leinonen et al. 2001). It is associated with a significantly increased mortality rate (Cuijpers & Schoevers 2004) and incurs considerable economic costs (Katon et al. 2003). It is not surprising, therefore, that several studies have been conducted to examine the possibilities to prevent depression in older adults (Breckenridge et al. 1987, Burns et al. 2007, Konnert et al. 2009, Rovner et al. 2007, van’t Veer-Tazelaar et al. 2009).

Prevention studies have been conducted in several other target groups and settings that do not fit into one of the categories described above. For example, two studies recruited adults with subthreshold depression from the general population (Allart-Van Dam et al. 2007, Vega et al. 1987), whereas other studies focused on university students (Seligman et al. 1999, 2007).

**FUTURE PREVENTION RESEARCH**

Given that large-scale interventions for depression are hard to fund, the use of naturalistic opportunities to examine preventive effects should be considered more often. For example, based on epidemiological evidence that poverty is a risk factor for depression and other mental disorders (Bruce et al. 1991, Costello et al. 2001), the IOM 2009 report on prevention (Natl. Res. Counc. & Inst. Med. 2009) suggested that interventions focused on reducing poverty be tested.

The Committee was aware that it would be difficult to convince policy makers to carry out such studies. However, natural experiments are possible. For example, Costello et al. (2003) found that a longitudinal epidemiological study could be used to determine the impact of a casino opening in an Indian reservation, which gave every American Indian an income supplement, moving 14% of study families out of poverty. This increase in income was associated with a reduction in conduct and oppositional defiant disorders, but not with a reduction in anxiety and depression.

Another study took advantage of the television broadcast (during the daily news programs)
of a series of ten four-minute segments teaching cognitive-behavioral mood management skills of the type taught in the Coping with Depression course (Lewinsohn et al. 1992). A pre-post phone assessment of a representative sample of San Francisco residents showed that among those with initially high depressive symptoms, those who watched the segments had significantly lower symptom levels at post test (Muñoz et al. 1982). Though studies such as these are not randomized controlled trials, they take advantage of naturally occurring events to study their impact on depression on entire communities.

Because the likelihood of randomized controlled trials of community-wide interventions is likely to remain low, the field needs to focus on the most cost-effective methods to test prevention interventions. Many people are exposed to risk factors that predict onset of depressive disorder. Many others manifest subclinical depressive symptom levels that may spiral into full-blown depressive disorder if left unattended. However, not all people who are at elevated risk can be offered preventive interventions. That would be logistically too demanding and economically too costly, even in resource-rich countries. Moreover, from a medical ethics perspective it may be undesirable to “medicalize” subclinical symptom levels of depression. After all, not all will develop the disorder, and not all recipients of a preventive intervention will be guaranteed to stay depression free. It is therefore important to select target groups for depression prevention while adhering to the following principles. Prevention ought to be offered when the following conditions are met:

1. People are judged to be at risk of developing major depression in the near future
2. The population-level health gains are as large as possible
3. The costs of offering the interventions are as low as possible
4. Preventive interventions are likely to be as efficient as possible.

Criterion 1 is invoked to put the interest of the patient up front. Criteria 2 and 3 are needed to be realistic from a societal cost-effectiveness point of view. Criterion 4 is implied by 2 and 3, but it deserves attention in its own right. Selecting target groups such that these criteria are optimized is not straightforward because there are trade-offs between generating large health gains (criterion 2) and keeping costs low, including the opportunity costs of provision of other services (criterion 3).

Methods for Identifying High-Risk Groups

The above four criteria can be translated into the following epidemiological indices:

1. Incidence rate ratio (IRR)
2. Population-attributable fraction (AF)
3. Exposure rate (ER)
4. Number needed to be treated (NNT).

The aim is to select the risk factor that is associated with the largest impact on the risk of becoming depressed (large IRR), the largest health gain at population level (large AF), for the lowest effort, hence in the smallest population segment (small ER) and with the greatest efficiency (small NNT). Such indices could be best estimated from population-based cohort data with a set of putative risk factors at baseline and diagnostic status of depressive disorder at both baseline and follow-up. Analyses are restricted to the cohort at risk, that is, the group without depressive disorder at baseline and hence at risk of becoming depressed later. Using conventional statistical analyses one can then obtain the IRR, AF, ER, and NNT for each of the risk factors and thus select that risk factor with the most optimal values for these indices. This process of optimizing health gains and minimizing effort and concomitant costs can be extended in a multivariate way. In other words, it is possible to move beyond a single risk factor and evaluate risk profiles of several risk factors that jointly help to minimize and maximize the indices in their respective directions. This optimization process can be aided visually by generating tree-like graphs (dendrograms),
which makes it easier to follow the optimizing/minimizing process.

To illustrate, in a large sample of people aged 55–85 years, the IRR of developing a depression within a year was 2.18 when they already had some depressive symptoms (Smit et al. 2006b). The IRR is almost doubled (IRR = 4.25) in people who in addition present with two or more chronic illnesses, functional limitations, and have a small social network. Expanding the risk profile with more risk indicators thus helps to increase the IRR. In the same vein, expanding the risk profile amounts to a drop in the NNT from 16 to 4, thus considerably increasing the efficiency of prevention. However, there is some trade-off. Expanding the risk profile with more risk indicators is usually associated with a lower health gain at population level because fewer people will then be targeted for prevention: the AF drops from 40.3% to 19.7%. As said before, cost-effectiveness is expected when IRR and AF are as high and NNT as low as possible. The expanded risk profile tries to reconcile these criteria in an optimal way. For other illustrations on how several risk profiles for late-life depression can be identified in this way, see Schoevers et al. (2006), Smit et al. (2006b), and Smit et al. (2008). All of these risk profiles contained at least some of the following risk factors: anxiety, chronic illnesses, functional impairment, low sense of internal locus of control (mastery), small social networks or living without a partner, and low education, especially when present in women. It should be mentioned that this selection of risk factors stems from a much larger list of putative risk factors. It is also worth noting that these studies were based on different samples and employed different analytic strategies, but collectively they offered converging evidence that attests to the robustness of these risk profiles.

**Issues in Risk Identification Methods**

The identified risk profiles help to select target groups for prevention of major depression. This approach will help to reduce the risk of developing a depressive episode in those people most in need of it, and at economically affordable costs.

The risk profiles also give guidance on the type of intervention that needs to be offered to (or designed for) the intended target group. After all, some risk factors (low mastery or antecedent anxiety disorder) can be ameliorated via psychological interventions, whereas other risk factors cannot be changed, but their adverse effects can be contained by improving coping styles. Finally, there are risk factors that cannot be manipulated in any way but that help to identify the target groups. Appropriate interventions may need some tailoring to better fit the special requirements of that target group.

Selection of high-risk groups is desirable when available preventive interventions are costly, labor intensive, and not easy to scale up. However, selection becomes less relevant when low-cost preventive interventions can be offered on a wide scale, for example, as self-help interventions over the Internet. Countries such as Sweden, the United Kingdom, the Netherlands, and Australia are increasingly taking this e-mental health approach. However, in countries that do not offer e-mental health interventions, careful selection of target groups may make the difference between managing a successful prevention program and not having one at all.

Most risk factors are generic rather than disease specific, and this introduces a bonus: The risk profiles for depressive disorder are quite similar to the risk profiles for anxiety disorders (Smit et al. 2007). As a possible benefit, preventive interventions directed at the risk factors of depressive disorder may also have favorable impacts on the risk of developing an anxiety disorder (see Seligman et al. 1999, 2007). The reverse should also be true.

**Public Health Implications**

Only about 20% to 30% of the years lived with disability due to depression is averted by current treatments (Andrews et al. 2004, Chisholm et al. 2004). The implication is that the
burden of disease due to depression remains largely intact and is not adequately addressed by current health care regimes. This underscores the importance of a health care system capable of not only offering adequate treatment of acute depressive disorder, but one that is also in possession of the following flanking preventive strategies:

1. **Raising public awareness about depression**: what it is, how it can be recognized, how people can cope with its early and subthreshold manifestations, and to whom they should turn to when self-help fails.

2. **Better tools for early recognition** that can be systematically applied in community settings. These may include routine screenings in primary care, the workplace, faith communities, and so on.

3. **Provision of preventive interventions on a large scale**. School-based prevention efforts may be the most feasible; aside from reliably capturing much of the population, interventions directed at teens or adolescents may prevent the first episode, thus possibly preventing a lifetime of depressive episodes. Mass media, such as radio and television, have been found useful for other public health goals (Bandura 2006), and there is some evidence that they could have an impact on depressive symptoms (Muñoz et al. 1982). Many of these preventive interventions could be offered online (via the Internet and other new media) in a self-help format (Griffiths & Christensen 2007).

4. **A more systematic approach toward preventing relapse and recurrence**. Such an approach would be closely connected to the treatment system, targeting individuals with successfully treated depression for maintenance interventions (see Figure 1) to reduce risk of relapse or recurrence.

**Stepped-care approaches.** Preventive interventions may help to improve population health, as a modeling study indicates (Vos et al. 2004). An important development in the area of prevention of depression is stepped-care interventions. These interventions are especially important as indicated prevention, in which subjects do have some depressive symptoms but no depressive disorder according to diagnostic criteria. In such a stepped-care approach, the first step is watchful waiting. This means that no specific intervention is conducted for six to eight weeks because many subclinical depressive symptoms recover spontaneously without intervention. In the second step, a guided self-help intervention is provided to patients. Guided self-help has been proven to be effective in the reduction of depressive symptoms (Cuijpers 1997) and may be sufficient for some patients. If the guided self-help is not sufficient and patients continue to have depressive symptoms, a brief psychological intervention is provided, such as a problem-solving or brief cognitive-behavioral intervention (for example, the “Coping with Depression” course). When this is not enough, patients are referred to specialized mental health care, where they receive intensive treatment with antidepressive medication. Benefits of this preventive approach include nonpathologizing of normal mood fluctuations, customization to the needs of individual patients, and overall reduction in negative side effects as more-intrusive treatments (e.g., medications) are only used in the case of failure of less-intrusive ones. One recent stepped-care trial showed that the incidence of major depression was reduced by 50% in older primary care patients with subthreshold depression, compared to care as usual (van’t Veer-Tazelaar et al. 2009).

**Making Widespread Implementation Feasible**

**Consumable interventions.** One of the obstacles in the implementation of preventive services is cost. Many health systems have inadequate levels of treatment services, and the individuals in charge do not feel they can redirect part of their budget to prevention. Thus, they continue to provide consumable
interventions, which, once used, can never be used again, thus continually depleting their health resources. For example, when a psychologist provides group therapy for depression, after a group session, no other patient can benefit from the hour spent. The therapeutic value of that hour has been consumed. The same is true for the use of medications: Once a pill has been swallowed, no other patient (or even the patient himself or herself) can ever benefit from that pill. It, also, has been consumed.

We need to develop and test nonconsumable interventions. For example, self-help automated Internet interventions, once developed and tested, can be used again and again, by literally thousands of people, without losing their preventive or therapeutic power. Unlike traditional face-to-face interventions, they are available at any time and in any place with access to the Web.

Transcending time and space. Telemedicine interventions have allowed health care providers to transcend the limits of space. A provider geographically separated from the patient, whether across town, across a region, or across the world, can now interact with the patient via television setups that allow, for example, consultation by a specialist who can advise a local primary care provider how to best address a difficult case. However, such arrangements do not transcend the limits of time. The time spent in a telemedicine consultation certainly benefits the distant patient. Nevertheless, that time has been taken away from local patients who could also benefit from the provider’s attention. Evidence-based automated self-help Internet interventions can transcend both time and space. Once they are available online, they can be accessed simultaneously by people anywhere, 24 hours a day. The professional who created the site does not have to be present. The user can decide whether, when, and where to use the site.

Marginal cost. Another advantage of Internet interventions is that, unlike traditional interventions, which have a per-use cost that cannot be reduced beyond a certain point (the time of the provider, the cost of the medication dose), Internet interventions, because they can be delivered by the server relatively cheaply, eventually approach a marginal cost of zero. That is, the cost of providing the Internet intervention to one more person (say, after the first 10,000), becomes negligible. This advantage means that after the initial investment to create and test the site, public health institutions could maintain the site for a modest fixed cost and yet disseminate the intervention widely at very little or no additional cost per additional individual served.

Think globally, act locally, share globally. Depression is a global problem. Nevertheless, health care agencies need to address the needs of their local populations. But, many urban areas have diverse populations composed of people from different cultures, who speak many languages. As local health systems develop Internet interventions adapted to the language and culture of its constituents, they could easily share these interventions with similar individuals in distant settings where local agencies have not created such offerings. This means that agencies could share their evidence-based intervention without taking anything away from their local communities.

To increase the likelihood that prevention interventions for depression will reach the large number of people who need them, we must consider these concepts carefully. These ways of thinking go beyond traditional consumable interventions, which are limited in terms of geography and time. Once developed, self-help automated interventions can be realistically shared globally. We envision systematically filling in a grid of interventions in which the columns depict health problems to be prevented, and the rows the most common languages, and then sharing the evidence-based interventions defined by each cell with people everywhere, at no cost to the users.

The accessibility of interventions that can be provided via mobile devices is increasing at a very fast rate. As of 2007, mobile teledensity (the number of mobile phones per 100 people)
went above 100% in Europe. Surprisingly, countries in the developing world are not far behind. For example, South Africa and Ghana passed the 100% mark in January 2009, and Kenya and Tanzania are expected to get to 100% by 2013 (Micklethwait 2009). It is likely that Internet accessibility will come to most of the world’s population via mobile broadband. Small communities might gain access via either public health clinics with Internet Health Resource Rooms or, for those too far from clinics, via Internet-kiosk operators who would obtain netbooks or other Web-enabled mobile devices and provide access to their neighbors for a small fee.

Envisioning a society with routine preventive services. A review of the depression prevention literature suggests that interventions to prevent clinical episodes are feasible. What is needed now is a systematic test of these interventions. Ideally, the best tested interventions would be implemented first in communities that are willing to cooperate with formal evaluations. One imagines a number of locations (cities, counties, perhaps even states) that would agree to be chosen at random to be administered the interventions at predefined time periods. This type of time series design would help determine whether incidence of depression (and resulting prevalence) in the communities receiving the interventions is significantly reduced compared to those not yet receiving them. Cost-benefit studies examining not only mental health outcomes but also outcomes in the general health, educational, justice, and occupational systems would be informative in terms of health policy.

What Might a Community Look Like if It Provided Preventive Services to Its Members?

Prevention is usually described as a very logical idea. One of the reasons it is not implemented widely is because few have envisioned its potential effects on the daily life of our societies. In its 2009 report on the prevention of mental, emotional, and behavioral disorders, the IOM presents a table (Natl. Res. Counc. & Inst. Med. 2009, table 13-1, p. 389) that describes what our society might be like if prevention services were widely available. In this section, we describe and expand on this table.

Pregnant women would be routinely screened for risk of depression. If identified as at risk, they would receive preventive interventions to reduce the likelihood of developing a clinical depression during pregnancy and postpartum. Pregnancy, postpartum, and the first years of life would be considered a critical developmental stage during which the health of the mother and the child would be a top priority for societal resources. Interventions such as mood management training, home visitation, parenting skills, nutritional counseling, early childhood education, and economic supports as needed would be routinely available for new parents and their families.

Early problems in bonding would be screened for and addressed. Parents would be taught alternative methods of interacting with their children that lead to more positive feelings of caring for each other and that will make discipline easier to apply as the child grows.

Screening for normal development would be offered during well-baby care and at the preschool and early school levels. Remedial interventions would then be offered to reduce the likelihood of failure at school and, later, in the work environment. All children would be provided with experiences (such as Head Start) that expose them to supportive educational environments, contact with children from different backgrounds, good nutrition, and a chance to build the skills needed to succeed in school and social interactions. A large proportion of children provided with these services would develop a healthy sense of competence, which would translate to a better chance of success in school. This, in turn, would serve as a protective factor not only for depression, but
also for anxiety, substance abuse, and conduct disorders.

Family and school interventions would be provided to support children so they are more likely to succeed in school, in learning self-regulation of emotions, and engaging with other youth and adults; to increase nurturance and decrease punitive experiences from parents, teachers, and peers; and to teach children to recognize early signs of emotional and behavioral problems, so they learn skills to manage these early symptoms and so they can ask for help when appropriate.

Young people who are at risk, as indicated by academic difficulties and/or problems with peers, are identified and effective school and family interventions are provided that prevent the development of deviant peer groups and the onset of behavior and academic problems. Most young people leave middle school with the social and academic skills they need to be successful in high school and in their relationship with peers. The health care system is brought into play: adolescent children of parents receiving treatment for depression are taught about the disorder. Those found at high imminent risk are provided preventive interventions. The goal of these interventions is to reduce the proportion of adolescents who develop clinical depression. For every year that we prevent new cases of depression, we provide adolescents with the chance of developing more life skills, with the goal of getting them through this critical developmental period unscathed. Even if the final outcome is delaying rather than permanently preventing major depressive episodes, the later the onset of the disorder, the better the premorbid functioning. This means that if young people eventually develop the disorder, it will be easier for them to return to independent functioning.

Screening and intervention services are readily available to help couples plan for when to get pregnant, how to prepare for the coming of the new baby, and how to increase the likelihood that their relationship will remain strong through the process. Unplanned pregnancies are reduced to the minimum. Child development information and child raising methods that have been found to be related to healthy children are provided to families. Tools to screen for risk are taught to parents, and interventions to reduce risk for the children and the family are implemented. The goal: to reduce the incidence of emotional and behavioral disorders in families and reduce family dysfunction that can increase this risk.

**CONCLUSION**

**Recommendations for the Field**

Depression is estimated to become the mental disorder that causes the greatest burden of disease and disability worldwide. It is also one of the mental disorders that is most preventable. Our review of the literature indicates that at least 22% of cases could be prevented each year (Cuijpers et al. 2008) and, with a very systematic approach, as many as 50% of cases (van’t Veer-Tazelaar et al. 2009). Doing so would have a major impact on the health status of our populations. Not only is depression a major source of human suffering, sometimes leading to suicide, but it also has major impact on other mental, emotional, and behavioral disorders. It is related to substance abuse, including alcohol abuse and smoking (e.g., Davis et al. 2008, Khaled et al. 2009), to morbidity and mortality in heart disease (e.g., Doering et al. 2009, Frasure-Smith & Lespérance 2006), and to earlier experimentation with multiple sex partners and the dangers of sexually transmitted diseases and unwanted teenage pregnancies (and subsequent higher risk for depression in the babies) (e.g., Kessler et al. 1997, Lee et al. 2007, Pilowsky et al. 2006, Shrier et al. 2009). Moreover, depression has a major impact on the ability to function adequately both at home and at work. It affects marital and parenting behavior, placing children at higher risk for depression. It affects work, resulting in high levels of absenteeism or reduced productivity.

Treatment services, even in wealthy countries, do not sufficiently reduce the prevalence of major depression because persons with
depression are often not identified, treatment does not help a large proportion of those who receive it, and, once the first episode occurs, depression often becomes recurrent or chronic.

Prevention services for major depression need to become routinely offered in the health care system. In the Netherlands, preventive interventions aimed at the prevention of depressive disorders in people with subthreshold depression are available for the general population and are covered by all health insurances. Preventive services in mental health could be conceptualized similarly to efforts to control hypertension and cholesterol levels. We know that borderline hypertension places people at risk for serious hypertension and associated risk for cardiovascular disease and catastrophic events (e.g., heart attack and stroke). Therefore, maintaining blood pressure within normal limits has become a basic intervention in primary care. Similarly, depressive symptoms are known to place people at risk for major depressive episodes. Therefore, maintaining mood levels within a healthy range ought to become a recognized public health goal. Major depressive episodes can produce massive dysfunction in terms of personal suffering, family harmony, and occupational performance. The most severe cases produce major disability and can lead to suicide attempts and completed suicides. Thus, the impact of the disorder is not only on the afflicted person, but also on their loved ones, their community, and their coworkers. The health care system needs to incorporate depression prevention services just as it has incorporated prevention services focused on physical markers for risk.

At the same time, evidence-based depression prevention services need to be readily available to the general population. The Internet provides one medium that is growing in availability each year. It can now provide not only text-based interventions, but also video and sound-based materials that could reach even individuals with low or no literacy. The development of well-tested interventions in several languages could also make such interventions available to anyone in the world who speaks such languages. Other mass media outlets, such as television and radio, are also accessible globally and have been shown to be effective tools for effecting change in health behaviors at national levels (Bandura 2006).

We envision the creation of a central location, perhaps hosted by the World Health Organization or other trusted and objective institution, that systematically catalogs automated self-help evidence-based preventive interventions, provides a summary of their efficacy, and makes the interventions available to anyone via the Web or satellite systems for mass media dissemination at no cost to them. Public health clinics throughout the world could provide their communities with access to these interventions so that individuals with no personal access to the Web could benefit from them. Eventually, having an Internet Health Resource Room would be as routine a part of public health clinics as having a pharmacy. Countries with the resources to do so could add to the self-help automated offerings additional support, including email guidance, telephone coaching, telemedicine-like video interaction with individuals, and, of course, traditional face-to-face services.

The promise of prevention is now becoming actualized. Before the 1980s, there were visionaries pointing the way to prevention interventions, but no randomized controlled trials testing whether major depressive episodes could be prevented. During the past 30 years, many such trials have taken place. The state of the science as we begin 2010 suggests that it is indeed possible to prevent a sizable proportion of cases of major depression. The tasks for the next stage in the growth of the field are to develop the political will to devote significant resources to additional empirical tests of preventive interventions, to begin to put into practice the interventions that have been shown to be effective, to include these interventions in routine health care, and to develop highly scalable versions of these interventions that could be accessed by anyone in the world, anytime, anywhere. We believe this goal is a worthy objective for the twenty-first century.
SUMMARY POINTS

1. Prevention interventions target individuals or groups prior to the onset of the disorder to be prevented to reduce incidence, that is, the number of new cases of a disorder.

2. Treatment interventions target individuals after onset of the disorder to be treated.

3. Universal preventive interventions target entire populations.

4. Selective preventive interventions target subgroups of the population who are considered at greater risk due to psychosocial or biological markers.

5. Indicated preventive interventions target individuals who show early signs or symptoms of a disorder but do not yet meet criteria for the disorder, with the goal of preventing the onset of a full-blown disorder.

6. There are now several randomized controlled trials that have yielded significant reductions in incidence of major depressive episodes when compared to control groups.

7. Prevention of major depression could significantly reduce the burden of disease due to this highly common and disabling disorder.

8. To disseminate evidence-based preventive interventions for depression, we must develop highly scalable methods that go beyond the current emphasis on face-to-face interventions, such as Internet and mass media interventions.

FUTURE ISSUES

1. We must continue to develop methods to identify individuals at high imminent risk for major depressive episodes in order to be able to carry out randomized trials with reasonable sample sizes.

2. Identification of psychosocial and biological markers of risk would help advance depression prevention research.

3. Replications of successful randomized trials need to be carried out by teams other than those who carried out the original trials.

4. There is a need to train more prevention intervention researchers.

5. Cost effectiveness measures need to be included in future depression prevention trials.

6. Depression prevention trials need to be conducted with different cultural and ethnic groups and in several languages.

7. Depression prevention trials should include individuals across large geographical areas, including participants from more than one country.

8. Once evidence-based depression prevention interventions are sufficiently developed, we will need to make coverage for such interventions routine.
DISCLOSURE STATEMENT
The authors are advocates for the advancement of depression prevention research and practice and are contributors to the literature in this field. They are not aware of additional sources of bias that might have affected the objectivity of this review.

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