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Prevention of depression: The state of the science at the beginning of the 21st Century

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Abstract

Major depression is one of the most prevalent mental disorders and the number one cause of disability worldwide. Once a person experiences a major depressive episode (MDE), the likelihood of recurrence is very high. The prevention of first onset, as well as the protection against recurrence after recovery, are therefore essential goals for the mental health field. By the end of the 20th century, however, most depression research efforts had focused on either acute or prophylactic treatment. In this article, we review USA and international studies that have attempted to reduce incidence of MDE, either 1) to prevent onset in populations of children and adults (including women during the postpartum period) not currently meeting diagnostic criteria for depression, or 2) to prevent a new episode in individuals who have recovered after treatment through protective, but not prophylactic interventions. We identified twelve randomized controlled trials focused on preventing the onset of major depression (both MDE and postpartum depression (PPD)), five randomized controlled trials focusing on preventing relapse, and no randomized controlled trials focused exclusively on preventing recurrent episodes through protective interventions. The review is limited in scope given that depression prevention trials focused on infants, young children, and older adults were not included in the review. The research to date suggests that the prevention of major depression is a feasible goal for the 21st century. If depression prevention interventions become a standard part of mental health services, unnecessary suffering due to depression will be greatly reduced. This review concludes with suggestions for the future direction of depression prevention research.

Prevention of depression: The state of the science at the beginning of the 21st century

At the close of the 20th century, the World Health Organization (WHO) reported that major depression was the number one cause of disability in the world (Murray & Lopez, 1996). The WHO also reported that major depression was the fourth most important disorder in 1990 and would become the second most important by the year 2020 in terms of the global burden of disease as indicated by both disability and mortality (Murray & Lopez, 1996). To reduce the prevalence of major depression, we must reduce its incidence, duration, or both. Treatment interventions are focused on reducing duration of episodes, that is, terminating a current clinical episode as soon as possible. Preventive interventions are focused on reducing incidence, that is, the number of new episodes of major depression. Prevention advocates have long pointed out that, when the prevalence of a disorder is very high, treatment approaches are not

sufficient (Albee, 1985). It is therefore imperative to develop effective preventive interventions for such disorders.

Defining 'prevention of depression'

The word 'prevention' has been used somewhat loosely in the area of mental health. For example, 'preventive interventions' have included identifying individuals in the early stages of major depressive disorders and providing treatment to them. To address this problem and to delineate three levels of intervention, the Institute of Medicine (IOM) released a report in 1994, which proposed the following categorical definitions: *Prevention* refers to interventions occurring before the onset of the disorder and is designed to prevent the occurrence of the disorder. *Treatment* refers to interventions occurring after the onset of the disorder, to bring a quick end to the clinical episode. Treatment can be provided after early case-finding outreach efforts or

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as traditional treatment services, in which patients bring themselves in, or are brought into treatment, once they are afflicted by the disorder. *Maintenance* refers to interventions that occur after the acute episode has abated, in order to prevent relapse, recurrence, or disability in a patient who has received treatment (Muñoz, Mrazek, & Haggerty, 1996).

Within prevention, three additional sublevels have been defined which further delineate the pathway through which prevention efforts are targeted: universal, selective, and indicated (Mrazek & Haggerty, 1994). Universal preventive interventions are targeted at entire communities (e.g., mass media health education campaigns) regardless of risk. Selective preventive interventions are targeted at high-risk groups within a community, chosen by demographic characteristics rather than individual risk profiles (e.g., offspring of depressed parents). Indicated preventive interventions are targeted at individuals with early signs or symptoms but not meeting criteria for major depressive episodes (e.g., subsyndromal). Subclinical depressive symptoms can have a substantial impact on functioning (Wells et al., 1989) and thus can be an important target for preventive interventions.

It is important to highlight that this review is not exhaustive of the depression prevention literature. First, in agreement with the recommendations put forth in the IOM report, it is imperative to develop prevention interventions that target individuals throughout the lifespan. Secondly, the IOM report also highlighted that implementation of preventive interventions must consider issues related to the adaptability and fit of prevention interventions to special populations and within community settings. Although these two points are important for the development of comprehensive and effective prevention efforts, limitations of the research literature limit our ability to discuss these points in detail in this review. Frankly, the field of depression prevention is still in early development. This review will therefore focus on an essential question at this stage of development: Can we prevent the first onset and recurrence of major depressive episodes?

Our initial assessment of the literature suggests that this is possible. This assessment is accompanied by a caveat, however, given the limitations discussed above. For example, infants, young children, and older adults are often excluded from prevention trials, consequently leading to a limited number of published reports focused on these populations (Castro, Barrera, & Martinez, 2004). Although the literature on late-life depression has grown significantly over the past 15 years, the focus on depression preventive interventions remains limited. In fact, much of the prevention research with older adults has focused on health-related illnesses as the primary intervention

target, while the incidence of depression or depressive symptomatology have typically been the secondary or tertiary prevention outcome targets (Alexopoulos, 2001; Anderson, Jané-Llopis, Hosman, & Jenkins, 2003). Difficulties in the assessment and recognition of depressive symptoms (among both young children and older adults) and the co-morbid presentation of depression with physical ailments (primarily among older adults) may contribute to the dearth of depression prevention trials (Baldwin, 2000; Blazer, 2003). Among infants and young children, prevention intervention trials have focused on teaching depressed parents about the impact of their relationship with their child and on parenting skills (for a review, Le & Boyd, 2006). A number of these reports (e.g., work by Beardslee and colleagues) have been included in this review, though clearly more work with these populations is sorely needed. Despite these limitations, however, and the early stage of the field of depression prevention, the following review should highlight that depression prevention is a reasonable goal warranting further work with a broad spectrum of populations.

In this review, we use the proposed IOM definitions (Mrazek & Haggerty, 1994; Muñoz et al., 1996) to examine the literature on depression prevention investigations. We review randomized control trials (RCT) testing the efficacy of preventive interventions in reducing incidence of new MDEs and address two types of preventive interventions. First, we will address interventions within the first level of interventions, that is, those intended to prevent the onset of new episodes of major depression. Thus, we will exclude studies that select participants because they meet criteria for major depression at the start of the study. Because the field is not yet advanced enough to provide a large number of such RCTs, we will also mention studies which attempt to reduce symptoms, as long as participants were not recruited for the study because they were already 'cases'. Given the growing attention in prevention of depression research toward youths, this section of the report will examine USA and international child, adolescent, and adult investigations, including an examination of the postpartum depression (PPD) literature. Secondly, we will address interventions in the maintenance level of the IOM definition, in this case, interventions provided to adults who have been successfully treated for MDEs, with the goal of preventing recurrences of these episodes. Maintenance interventions can include prophylactic treatments that continue antidepressants or psychotherapy, or protective interventions designed to confer protective effects beyond a more time-limited period, perhaps through the development of new self-regulation strategies. The focus of this section of the review will be on

protective interventions since they represent the leading edge of maintenance intervention strategies. Since very few RCTs address the prevention of recurrence, this review will include relevant RCTs that address the prevention of relapse, a related but conceptually distinct phase of major depression.

Major depressive disorder incidence and recurrence

Incidence rates for MDE are difficult to locate given the longitudinal, prospective research design required in order to identify its course. Among adolescents, one-year incidence rates for major depression were 5.7% for first onset and 17.9% for relapse among a community sample of high school students (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Twenty-month incidence of MDE among German adolescents was 3.4% (Oldehinkel, Wittchen, & Schuster, 1999). Among adults, one-year incidence of MDE was 1.6% in data reported in the Epidemiological Catchment Area study (Eaton et al., 1989), which was higher than previous reports of 0.52% (Hagnell, Essen-Möller, Lanke, Öjesjö, & Rorsman, 1990) and 0.23% (Murphy, Olivier, Monson, Sobol, & Leighton, 1988). The National Comorbidity Survey reported that over 72% of adults with a lifetime history of MDD report a history of recurrent episodes (Kessler, Zhao, Blazer, & Swartz, 1997), while the Collaborative Depression Studies found that 60% of individuals experience a recurrence of MDD with five years of an acute episode of depression (Solomon et al., 2000).

A comprehensive literature search was conducted on PsychINFO and PubMed using the keywords 'randomized control trials', 'randomized trials of psychosocial interventions', 'prevention', 'incidence', 'recurrence', 'relapse' and 'major depression'. The search was limited to articles published no later than 1 November 2006 focused on RCTs examining the prevention of first onset and recurrence of major depression and depressive symptoms. In addition, we examined review articles and the bibliographies of retrieved empirical studies.

Reducing depressive symptoms in children and adolescents to reduce risk of MDEs

Universal interventions. A universal approach to depression prevention is preferable given the reduced stigma associated with participation when compared to indicated or selected approaches. This is likely most true when carrying out empirical investigations in school-based settings and when working with children and adolescents where peer relations are particularly critical. However, it remains to be decided whether the benefits of conducting large universal interventions offset the costs to implement

such a programme. Additionally, data from universal interventions are equivocal.

In 1993, Clarke, Hawkins, Murphy, and Sheeber conducted one of the earliest investigations focused on testing a depression prevention programme among adolescents. The authors set out to examine, among 9th and 10th grade students, the effects of two brief school-based interventions in reducing depressive symptoms when compared to a control condition (Clark et al., 1993). Neither intervention produced lasting changes in depressive symptoms. There were several limitations identified (e.g., self-ratings of depression symptoms, too brief of an intervention), which the authors accounted for in later targeted prevention of MDE trials (Clarke et al., 1995, 2001).

Few investigators have focused prevention efforts exclusively on the growing ethnic minority population of the USA. Cardemil, Reivich, and Seligman (2002) published findings on the impact of the Penn Resiliency Program (PRP) among 5th to 8th grade Latino and African American children. Results indicated lower depressive symptom scores, fewer negative cognitive and hopeless thoughts, and greater self-esteem reported among the Latino children in the PRP at six months post-intervention. However, the significant impact of the PRP failed to extend to the African American children. Two-year follow-up data (Cardemil, Reivich, Beevers, Seligman, & James, 2006) indicated that the positive effects of the PRP were maintained by the Latino children only and were limited to reports of lower depressive symptoms.

Limited positive findings have been reported in school-based interventions delivered outside of the USA. Yu and Seligman (2002) demonstrated that the PRP was effective in reducing depressive symptoms in a sample of adolescents in China. A 10-week programme delivered in a German middle school (Pössel, Horn, Groen, & Hautzinger, 2004) had a preventive effect on participants assigned to the intervention who reported, at study entry, minimal or subsyndromal levels of depressive symptoms when compared to their counterparts in the control condition whose scores remained unchanged. Researchers in Australia have developed, modified, and tested a school-based cognitive-behavioural (CBT) and interpersonal (IPT) prevention intervention programme for adolescents, the Resourceful Adolescent Programme (RAP). Thus far, all versions of the RAP (e.g., adolescent) have demonstrated to have preventive effects on symptom reduction when compared to control conditions (Merry, McDowell, Wild, Bir, & Cunliffe, 2004; Sochet et al., 2001).

Targeted interventions. Beardslee and colleagues have taken the lead in conducting multiple family-based

interventions to prevent depression in children of parents affected by depressive disorders. The interventions were comprised of two cognitive-based interventions – a clinician-facilitated 6–10 session psycho-education programme that included parent, child, and family sessions, and a 2-session lecture intervention delivered in a group format to the parents only (Beardslee & Gladstone, 2001). Both interventions have produced positive changes in parents and children, with greater changes in communication and understanding of the depressive illness reported by participants in the clinician-facilitated intervention (Beardslee et al., 1993); the positive effects of this intervention were sustained for up to three years post-intervention (Beardslee, Wright, Rothberg, Salt, & Versage, 1996). In a more recent report, Beardslee, Gladstone, Wright, and Cooper (2003) demonstrated that over a 2.5-year follow-up, children in both interventions reported a decrease in internalizing symptoms. This family-based intervention was adapted for delivery to low-income, culturally diverse urban families (Podoresfksy, McDonald-Dowdell, & Beardslee, 2001), but has yet to be tested in RCTs.

The Penn Depression Prevention Program (PPP) was effective in significantly reducing symptoms of depression among children with elevated levels of depressive symptoms and who were exposed to parental conflict (Jaycox, Reivich, Gillham, & Seligman, 1994). Reductions in depressive symptoms were not retained, however, at the 3-year follow-up (Gillham & Reivich, 1999). The PPP underwent minor language adaptations and was tested in a sample of 7th grade rural children residing in Western Australia (Roberts, Kane, Thomson, Bishops, & Hart, 2003). The intervention was effective in reducing anxiety but not depressive symptoms at the post-intervention and 6-month follow-up. In both the intervention and the control groups, participant depressive symptom scores were reduced, with intervention participants reporting non-significantly lower scores.

In a recent trial comparing multiple brief prevention interventions among adolescents with elevated depressive symptoms, Stice, Burton, Bearman, and Rhode (2006) demonstrated that alternative (e.g., supportive-expressive group) active interventions, including CBT (Clarke et al., 1995), can prevent the worsening of depressive symptoms. Immediate and 1-month, but not 6-month, significant depressive symptom score reductions were demonstrated among participants who were assigned to the CBT intervention when compared to waiting-list control participants. Exploratory analyses of the onset of severe depressive symptoms at any point in time during the 6-month follow-up indicated that rates of severe depressive pathology (BDI > 30) were lower but not significantly different among participants assigned to any of the active interventions when compared to the waiting list condition.

Preventing incidence of major depressive episodes

Few investigators have focused their efforts on examining the impact of prevention interventions in the reduction of MDEs. As of this writing, there have been twelve RCTs designed to test prevention of MDEs, of which five published studies (Clarke et al., 1995, 2001; Chabrol et al., 2002; Elliott et al., 2000; Zlotnick, Johnson, Miller, Pearlstein, & Howard, 2001) have reported significant reductions in incidence of MDEs (Table I).

Depression prevention in adolescents

One of the first successful prevention intervention trials targeting major depression and dysthymia for at-risk adolescents was conducted by Clarke and colleagues (1995). The high-risk sample was defined as 9th and 10th grade adolescents reporting elevated (≥24) scores on the Center for Epidemiologic Studies-Depression scale (CES-D) (Radloff, 1977) and who did not meet DSM-III-R criteria for a current depressive disorder. One hundred and fifty adolescents were randomized to the intervention condition, a 15-session CBT group intervention (coping with stress course), or to a 'usual care' control condition. Survival analyses across the 12-month follow-up period revealed that participants in the intervention reported fewer depressive disorder episodes (MDE and dysthymia) than their peers assigned to the control group, 14.5% versus 25.7%, respectively. There were no significant differences in CES-D scores between the conditions across the entire follow-up period; however, significantly lower pre- to post-intervention CES-D scores were reported among the intervention participants. A later study by Clarke et al. (2001) examined the effectiveness of the same intervention in reducing the incidence of depressive disorders among high-risk adolescents defined as those reporting subsyndromal levels of depressive symptoms and having parent(s) in treatment for depression. There was a significant reduction in CES-D scores over the 12-month follow-up period for participants in the intervention. At the 12-month follow-up, the incidence of MDE was also significantly lower for adolescents assigned to the intervention compared to those in the usual-care control condition (8.0% versus 24.7%, respectively); although the lower rate of depressive episodes was maintained at the 18- and 24-month follow-up by the intervention condition, the strength of this effect diminished.

Table 1. Randomized controlled trials aimed at the prevention of Major Depressive Episode onset.

Study	Participants	Intervention	Depression measure(s)	Findings
Children and Adolescents				
Clarke et al., 1995	150 9–10 grade high school students with elevated depression scores	15 session after-school CBT group *vs.* usual care	CES-D, KSADS	Lower incidence of depressive episodes (MDD and dysthymia) at 1 year f/u for experimental condition (14.5%) *vs.* control (25.7%)
Clarke et al., 2001	94 13–18 year olds with subsyndromal depressive symptoms and offspring of parents with MDD	15 CBT group sessions; 3 parent information meetings *vs.* usual care	CES-D, HDRS, KSADS	Lower incidence of MDE at 1 year for experimental group (8%) *vs.* control (24.7%); effects persisted at 2 year f/u
Gillham et al., 2006	271 11–12 year old youths whose parents were members of an HMO	12 CBT group sessions *vs.* usual care	CDI, DICA-R, KSADS	PRP reduced depressive, anxiety, and adjustment disorders when combined; non-significant lower incidence of MDE at 2 years among high symptom youths in PRP (21%) *vs.* control (36%)
Sheffield et al., 2006	2479 year 9 students from 36 schools in Australia; 521 (21%) high-symptom (CES-D + CDI =) top 20% of full sample	Universal (8 50-min CBT. classroom sessions, teacher-led) *vs.* Indicated (8 90-min. CBT group sessions, clinician-led, high symptom students) *vs.* Universal + Indicated *vs.* Assessment only control	CDI, CES-D, ADIS-C, LIFE	Non-significant difference in MDE incidence at the 18 month f/u; Among high symptom participants incidence for MDE was 18.1% universal *vs.* 21.4% indicated *vs.* 17.8% universal + indicated *vs.* 20.4% control condition
Spence et al., 2003, 2005	1500 grade 8 students in public and private schools in Australia	School-based Problem-Solfing for Life (combination of CBT and problem-solving)	BDI, DY, ADIS-C	Non-significant reduction of MDE incidence between PSFL (9.9%) *vs.* control (8.4%) over 4 years
Adults				
Chabrol et al., 2002	258 French women	1 hour CBT session during days 2 and 5 postpartum *vs.* usual care condition	EPDS	Probable PPD incidence was lower for the experimental group *vs.* the usual care condition, 30% *vs.* 48%, respectively
Elliot et al., 2000	99 pregnant women with first or second child	11 session psychoeducation group *vs.* control condition	PSE	19% incidence of PPD among first time mothers in experimental *vs.* 39% in control condition
Muñoz et al., 1995	150 low income, ethnic minority, primary care patients	8-session CBT course *vs.* control condition	DIS	Non-significant incidence of MDE between the experimental (3%) *vs.* control (5.6%) conditions at 1 year
Muñoz et al., 2007	41 pregnant women with a history of MDD or current elevated depressive symptoms	12-sessiongroup CBT and mood-management course	CES-D, EPDS, MMS	One year incidence of MDD was 14% for the experimental *vs.* 25% for the comparison condition ($h = 0.28$)

(Continued)

Table 1. Continued.

Study	Participants	Intervention	Depression measure(s)	Findings
Seligman et al., 1999	255 college students with elevated pessimistic explanatory style	8-week CBT workshop vs. assessment-only control condition	BDI, LIFE, SIGH-D, SCID	Lower incidence of moderate MDE at 3 years for the experimental condition at 3 years; however the difference was not significantly different (40% experimental vs. 48% control, $p < .08$)
Stamp et al., 1995	139 women in their first pregnancy	2 session prenatal and 1 session postnatal support group vs. routine care only	EPDS	No significant differences in incidence at 6, 12, and 24-week postpartum; lower incidence rates were reported at 6- and 12-weeks by the experimental condition
Zlotnick et al., 2001	35 low-income pregnant women	4 session antenatal care implementing interpersonal therapy principles vs. usual antenatal care	SCID (MDE module)	Zero incidence of PPD among experimental condition vs. 33% in usual antenatal care condition at 3 months postpartum

Notes: ADIS-C-Anxiety Disorders Interview Schedule for Children; BDI-Beck Depression Inventory; CDI-Children's Depression Inventory; CES-D-Center for Epidemiologic Studies-Depression Scale; DICA-R- Diagnostic Inventory for Children and Adolescents; DIS-Diagnostic Interview Schedule; DY-Four questions to screen for dysthymia based on DSM-IV; EPDS-Edinburgh Postnatal Depression Scale; HDRS-Hamilton Depression Rating Scale; KSADS-Schedule for Affective Disorders and Schizophrenia for School-Age Children; LIFE-Longitudinal Interval Follow-Up Evaluation; MMS-Maternal Mood Screener; PSE-Present State Examination; SIG-H-Structured Interview Guide for the Hamilton Depression Rating Scale; SCID-Structured Clinical Interview for DSM-IV Diagnoses

Gillham, Hamilton, Freres, Patton, & Gallop (2006) tested the effectiveness of the Penn Resiliency Program (PRP) in reducing the incidence of clinical depression among 11 to 12 year olds. High-risk participants were defined as youths with Children's Depression Inventory (CDI; Kovacs, 2001) scores at or above 7 (girls) and 9 (boys) whose parents were members of a large health management organization. The intervention was delivered over the course of 12 90-minute group sessions and was comprised of CBT concepts. Over the course of the study, lower incidence of combined depressive, anxiety, and adjustment disorders were found among the high symptom (CDI $\geq$ 13) participants assigned to PRP (36%) when compared to the control condition (56%). When the affective disorders were examined separately, PRP failed to significantly prevent the onset of depressive disorders specifically; however, lower incidence rates of depressive disorders were reported for high symptom youths in the PRP condition (21%) than those in the control group (36%). During the 2-year follow-up period, PRP effectively improved explanatory styles for positive events. Explanatory styles for negative events and depressive symptoms, however, were moderated by sex such that girls assigned to the PRP intervention reported reductions in explanatory styles for negative events and depressive symptoms.

Spence, Sheffield, and Donovan (2003) conducted a large-scale school-based prevention intervention among 8th graders in Australia. The intervention, implemented by teachers, focused on the delivery of CBT and problem-solving techniques (problem-solving for life (PSFL)) to reduce the incidence of depressive disorders and self-reported depressive symptoms. Survival analyses to examine the incidence of depressive episodes among the high-risk group of participants at the 12-month follow-up revealed a non-significant difference between the PSFL and control conditions (9.9% versus 8.4%, respectively). Long-term examination of the intervention effects revealed that 25% of participants in both conditions reported a depressive episode at some point during the 4-year follow-up period (Spence, Sheffield, & Donovan, 2005). At post-intervention high-risk participants (BDI > 13) in PSFL demonstrated greater reductions in BDI scores when compared to the control participants. Although both groups reported a reduction in BDI scores, only scores reported by PSFL participants reached the normal range (BDI < 13).

In a large school-based cluster, stratified randomized trial, Sheffield and colleagues (Sheffield et al., 2006) set out to evaluate the differential impact of a CBT prevention programme using a universal, indicated, and combined approach pitted against a no-intervention control condition. Adolescents were 9th graders from thirty-six schools in Australia. Twenty-one per cent of the full sample were identified as 'high-symptom' (combined CDI and CES-D scores within the top 20% of the full sample). Only high-symptom participants were randomized to all four conditions. For the full sample, there were no significant differences in MDE incidence and among high-symptom participants approximately 20% experienced a MDE over the 18-month duration of the study (regardless of condition). For this sub-sample, the incidence was 18.1% universal, 21.4% indicated, 17.8% combined, and 20.4% in the control condition; the MDE incidence between the four conditions was not significantly different.

Depression prevention in adults

Fewer investigators have focused on prevention of first onset of depression among adults. The dearth of such investigations is likely due to the fact that depression onset typically occurs during the adolescent and young adulthood years (Kessler et al., 2005). Efforts to prevent major depression among adults have focused primarily on individuals who demonstrate characteristics shown to increase the risk of MDE onset or recurrence, such as women, divorced individuals, individuals from low socioeconomic groups, persons identifying with an ethnic minority group, etc. Muñoz and colleagues (Muñoz & Ying, 1993; Muñoz et al., 1995) conducted the first RCT to prevent MDD among adults in 1983. We will describe the study in some detail because it offers several lessons regarding prevention trials. The high-risk group was defined as low-income, primarily minority, English and Spanish speaking primary care adult patients attending a public sector hospital in San Francisco. To ensure that this was a preventive trial, participants were screened so none met criteria for any depressive or other psychiatric disorder at initial contact. Those in the intervention condition received the 8-session depression prevention course (Muñoz, 1984) in a small-group format. The control group received treatment as usual, namely routine medical care. Of 150 randomized participants, 139 were contacted at one year. Of these, six met DSM-III criteria for MDE during the last year. Four of the cases occurred in the control group (5.6% incidence) and two in the experimental condition (3% incidence). Both of the latter were dropouts who did not receive the intervention. Differences in incidence were not significant. However, participants in the intervention condition reported significantly lower depressive symptom scores when compared to participants in

the control condition. This early investigation demonstrated that even with an incidence of 5.6% in the control group, which is 10 times greater than the rate of 28 out of 31 studies reported by Boyd and Weissman (1982), and three and a half times greater than the 1.6% rate found in the ECA (Eaton et al., 1989), the sample size was insufficient for adequate power. Note that the incidence was reduced by approximately half in a straight comparison between randomized groups and that none of the participants who received the intervention developed a MDE. An important lesson from this study is that selective interventions may not yield high enough incidence rates to document preventive effects, and targeted interventions may be more likely to do so.

Seligman, Schulman, DeRubeis, and Hollon (1999) conducted an 8-session CBT depression and anxiety prevention programme among at-risk (defined as most pessimistic explanatory style) college students. The authors report moderate success in reducing the incidence of MDEs over a three-year period. Among the 225 students randomized, there was a trend towards lower incidence of moderate depressive episodes reported by those in the intervention (40%) when compared to students in the control condition (48%; $p < 0.08$). Students in the intervention condition also reported significantly lower rates of generalized anxiety disorder and significantly fewer self-reported symptoms of depression and anxiety.

Depression prevention during the postpartum period

Prevention efforts to reduce the incidence of depression among women during the childbearing period have long been a focus of research investigations (e.g., Gordon & Gordon, 1960). However, despite great efforts and often promising effects, such investigations continue to produce mixed results (see Austin, 2003, Dennis, 2004). While many investigations demonstrate some reduction in depressive symptoms following the completion of the intervention, few have reported significant, long-lasting intervention effects. In a sample of 99 women expecting their first or second child, Elliott et al. (2000) demonstrated that an 11-session psycho-education group intervention was effective in reducing PPD. Lower rates were reported among first time mothers randomly assigned to the brief intervention when compared to women not invited to participate (19% versus 39%). Zlotnick and colleagues (2001) demonstrated that a 4-session intervention based on IPT principles reduced the occurrence of PPD among pregnant women receiving public assistance who had at least one depression risk factor (e.g., $BDI \geq 10$). Of the women randomized to the intervention, none of them developed PPD within the 3-month follow-up period. In contrast, 33% in the treatment-as-usual condition developed PPD.

The *Mamás y Bebés*/Mothers and Babies Course is an intervention developed in Spanish and English that uses a cognitive-behavioural mood management framework, and incorporates social learning concepts, attachment theory, and socio-cultural issues (Muñoz et al., 2001). It was designed to prevent the onset of MDEs during pregnancy and postpartum and was pilot tested at a public sector women's clinic. Forty-one pregnant women at high risk for developing MDEs were randomized to the intervention ($n = 21$) or a comparison condition ($n = 20$). High risk was defined as a self-reported history of MDEs and/or high current depressive symptom scores, based on a previous study to ascertain the predictive value of these criteria (Le, Muñoz, Soto, Delucchi, & Ippen, 2004). One-year incidence rates were 14% for the intervention condition versus 25% for the comparison condition (Muñoz et al., 2007). These represent a small effect size ($h = 0.28$) that will be further examined in a larger scale study.

Thus, there is evidence to suggest that targeting at-risk pregnant women is a viable means toward reducing the incidence of PPD. In doing so, researchers are likely to identify women who are already experiencing elevated levels of depression reflective of a MDE during the perinatal months that warrants treatment and not preventive efforts. Chabrol and colleagues (2002) addressed this predicament by designing a programme that targeted both prevention and treatment of symptoms of PPD among at-risk (Edinburgh Postnatal Depression Scale – EPDS ≥ 9) women. In their study, 258 French women were randomly assigned to a 1-hour CBT session during days two and five postpartum, or to a usual-care control group. During weeks 4-6 postpartum, women in the intervention group who reported elevated depressive symptoms and who endorsed a MDE were invited to participate in a five to eight week one-hour weekly home visit session. During a ten to twelve week period, participants in the prevention group reported a significant reduction in probable depression (EPDS ≥ 11), such that 30.2% in the prevention condition (versus 48.2%) endorsed elevated rates of depressive symptoms.

Other studies aimed at reducing the incidence of PPD symptoms among pregnant women have not reported significant intervention effects. As in the trials led by Elliott and Zlotnick, the following investigations focused their efforts on pregnant women who were at greater risk for PPD. Stamp, Williams, and Crowthers (1995)

employed a 2-session prenatal and 1-session postnatal group intervention for 'more vulnerable' women. Although the intervention did not demonstrate a significant effect on depressive symptoms, fewer women assigned to the intervention reported elevated EPDS (>12) scores at the 6- and 12-week follow-up (13% vs. 17% and 11% versus 15%, respectively); this non-significant finding was not replicated at the 6-month follow-up. Similarly, a randomized trial of a 6-session antenatal group intervention conducted among women in their first pregnancy who reported one of six depressive symptoms at baseline did not yield any significant differences on depression scores at three months postpartum when compared to women assigned to their usual antenatal care (Brugha et al., 2000).

Preventing subsequent episodes of depression: Relapse versus recurrence

Preventing the first onset of major depression would necessarily avert one of its more troubling outcomes: a protracted course of recurrent MDEs (Boland & Keller, 2002). Such a course is not an inevitable outcome, since only 50% of individuals who have experienced one episode of depression go on to experience a second, but becomes increasingly likely with more recurrences: 90% of individuals who have had three prior episodes go on to experience four or more (APA, 2000a). This change in the risk of recurrence may possibly reflect an increased vulnerability to the disorder over time. Recent research on life stress and depression suggest that as the history of depressive episodes increases, so does the vulnerability to future depressive episodes (Kendler, Thornton, & Gardner, 2000, 2001; Monroe, Torres, Guillaumot, Harkness, Roberts, et al., 2006), with some evidence suggesting that these changes in sensitivity may occur as early as the second or third episode of depression (Monroe, Slavich, Torres, & Gotlib, 2007). Both the epidemiological and life stress research suggest that an opportunity may exist to avert a recurrent course of major depression, before the risk of recurrence increases propitiously. This opportunity hinges on the ability to prevent subsequent episodes following the resolution of an acute episode of major depression.

The typical approach is prophylactic treatment with antidepressant medication, with an implication that continuing, perhaps indefinite treatment is required in order to maintain gains in symptom reduction (APA, 2000b). The epidemiological evidence, however, clearly indicates that recurrent depression is not inevitable following a first or even third episode of major depression. Therefore, if recurrent major depression is not inevitable, then

it may be preventable and indefinite treatment may not always be required. If new episodes of major depression can be averted early in the history of illness, then it may be possible to prevent a protracted, recurrent course and the accompanying changes in vulnerability that appears to occur with a greater history of depressive episodes.

The conceptual distinction made between recurrence and relapse by Frank and colleagues is critical for the development of protective interventions targeting recurrence (Frank et al., 1991b). A recurrence is a new episode of depression that occurs during recovery, while a relapse is the resurgence of an episode that had gone into remission, or in other words had temporarily subsided (Frank et al., 1991b; Rush et al., 2006). Key to the distinction between relapse and recurrence is the distinction between remission and recovery, which is conceptually linked to the presence or absence of an active episode, and operationally linked to the period of time one has remained asymptomatic. Frank and colleagues had suggested that remission be defined as at least a two-week period below a cut-off point on depression symptom measures, and that recovery be defined as beginning after two months below this cut-off (Frank et al., 1991b). These definitions have been widely adopted, but not always consistently used; more importantly, almost no studies have empirically validated these operational definitions (for an exception, see Riso et al., 1997), introducing a core ambiguity into all research attempting to reduce relapse and recurrence, particularly when the distinction between relapse and recurrence is not explicitly made (Rush et al., 2006). These conceptual issues should be held in mind as a caveat while considering the research investigating the prevention of subsequent episodes of depression once an acute episode of depression has responded to treatment.

Maintenance interventions could therefore prevent recurrence through ongoing, prophylactic treatment, or more time-limited treatments that confer protective effects beyond the active period of intervention. This distinction is similar to the distinction between prophylactic treatment with antiviral drugs in order to prevent symptomatic outbreaks and protective treatment using vaccination. The categories of prophylactic treatments and protective interventions will be used to organize research on preventing a recurrent course of depression. The bulk of research on the prevention of recurrence falls squarely within a prophylactic treatment approach, which will be briefly reviewed here. The main focus of this section of the review will be on the handful of clinical RCTs that have investigated protective interventions, though to our knowledge, no study has specifically investigated the impact of protective interventions

on recurrence. Therefore the studies reviewed here primarily address the prevention of relapse, though a few have provided suggestive results that are relevant to the prevention of recurrence.

Prophylactic treatments

Current guidelines for psychiatric practice recommend that active medication be generally continued for at least 4–6 months at the same dose used to treat patients to remission (APA, 2000b; Geddes et al., 2003). A number of antidepressant agents have been shown to be effective for maintenance treatment, following an early landmark study which clearly demonstrated the effectiveness of imipramine for protecting patients from relapse and recurrence (Frank et al., 1990; Geddes et al., 2003; Kennedy, McIntyre, Fallu, & Lam, 2002). In addition, ongoing IPT, CBT, and CBASP (cognitive behavioural analysis system of psychotherapy) have also been shown to be effective as maintenance treatments, demonstrating that psychotherapy alone or in combination with medication can be used to protect patients from relapse and recurrence (Frank, Kupfer, Wagner, McEachran, & Cornes, 1991; Hollon, Stewart, & Strunk, 2006; Klein et al., 2004). Pharmacotherapy maintenance, however, does not appear to provide protective benefits beyond active treatment, even after 3 years of active maintenance (Geddes et al., 2003; Kupfer et al., 1992). Indeed, relapse is very likely within four months of the cessation of maintenance medication (DeRubies et al., 2005; Kupfer et al., 1992). Psychosocial interventions, on the other hand appear to show enduring effects beyond active, ongoing treatment, so appear to confer a different type of protection against depression than medication; these interventions are reviewed below.

Protective interventions: Preventing relapse

In contrast to the apparently palliative effect of maintenance medication, psychosocial treatment approaches appear to confer protective effects beyond active treatment. In particular, it appears that treatment with cognitive therapy (CT) may be particularly effective in providing effective protection against relapse beyond the period of active treatment (Evans et al., 1992; DeRubies et al., 2005; Simons, Murphy, Levine, & Wetzel, 1986). However, these studies were naturalistic follow-up studies, subject to a 'differential sieve' effect, where retention effects and differential response to treatment are confounded with the treatment groups themselves; thus protective effects may be confounded with these differential selections within groups (Hollon et al., 2006).

Five other studies, however, have been identified that may address this potential differential sieve by randomizing participants after response to treatment (Fava et al., 1998, 2004; Ma & Teasdale, 2004; Paykel et al., 1999; Teasdale et al., 2000). The general finding is that protective treatment nearly halves the risk of relapse within the first year after the intervention (Table II). The protective treatments ranged from a novel, theoretically based intervention specifically designed to reduce relapse and recurrence (Ma & Teasdale, 2004; Teasdale et al, 2000) to the continuation or the addition of CT beyond an acute treatment phase (Fava et al., 1998, 2004; Paykel et al., 1999).

In the Paykel study, 158 patients were treated with medication, along with clinical management sessions, during an acute, 20-week treatment phase, as well as during a 48-week follow-up maintenance phase (Paykel et al., 1999). Half of the sample also received 16 sessions of CT during the acute phase, with two additional booster sessions (6 and 14 weeks later). The results of the study are impressive: only 29% of the individuals who also received CT during acute treatment relapsed 48 weeks after acute treatment ended, whereas 47% of the individuals who were treated only with medication and clinical management had relapsed. Thus acute treatment with CT conferred protective effects against relapse, above and beyond that provided by ongoing maintenance medication.

The Fava studies used a different approach, where all patients were treated to remission with medication, then randomized to either 10 sessions of CBT or 10 sessions of clinical management (CM), while their medications were tapered to placebo (Fava et al., 1998, 2004). At one-year follow-up, 15% of the CBT versus 45% of the CM patients had relapsed, and at two years 25% of the CBT versus 80% of the CM patients had relapsed (Fava et al., 1998). The protective effect of this brief course of CBT following acute treatment with medication persisted for 6 years, by which time 90% of the CM patients had relapsed, compared to only 40% of the CBT patients.

Finally, two studies compared Mindfulness-Based Cognitive Therapy (MBCT), a novel treatment specifically designed to prevent relapse and recurrence to treatment-as-usual (TAU) following acute treatment for depression (Ma & Teasdale, 2004; Teasdale et al., 2000). In both the initial and the replication studies, MBCT clearly protected individuals from relapse, but only if they had three or more prior episodes of depression and not if they had less than three. In these two studies, of individuals with three or more prior episodes of depression, 36–37% of individuals receiving MBCT had relapsed versus 66%–78% of the TAU participants over 60 weeks of

Table 2. Randomized controlled trials aimed at the prevention of relapse/recurrence of Major Depressive Disorder.

Study	Participants	Intervention	Depression measure(s)	Follow-up period*	Findings
Paykel et al., 1999	158 partially remitted patients (HRSD ≥ 8, BDI ≥ 9 for ≥ 8 weeks, but below DSM-III-R MDD criteria for past 2 months) on active amitryptiline (treatment & maintenance)	CT (16 sessions over 20 weeks) + Clinical management vs. Clinical management	DSM-III-R MDD, HRSD	48 weeks	Relapse rate: 20 wks 10% CT vs. 18% Control. 68 weeks: 29% CT and 47% control. Remission criteria rates 20 wks: 24% CT vs. 11% control group. Mean symptoms 20 wks: No significant differences (HRSD 8.58 vs. 9.40, BDI 13.46 vs. 16.06)
Fava et al., 2004	40 patients with recurrent depression, treated to recovery	Modified CT (10 sessions every 2 wks) + medication (tapered) vs. Clinical management + medication (tapered)	RDC	6 years	Relapse rate 6yrs: 40% CT vs. 90% CM
Fava et al., 1998	40 patients with recurrent depression, treated to recovery	Modified CT (10 sessions every 2 wks) + medication (tapered) vs. Clinical management + medication (tapered)	RDC	2 years	Relapse rate 1yr: 15% Ct vs 45% CM Relapse rate 2yrs: 25% CT vs. 80% CM
Ma, & Teasdale, 2004	125 recovered patients	MBCT vs. TAU	DSM-IV MDD, HRSD, BDI	1 year	Relapse rate 1yr: 36% MBT vs 78% TAU, for those with 3 + episodes; 20% MBT vs 50% TAU, for those with 3 + episodes
Teasdale et al., 2000	145 recovered patients	MBCT vs. TAU	DSM-III-R MDD, HRSD, BDI	1year	Relapse rate 1yr: 35% MBT vs 66% TAU, primarily for those with 3 + episodes

Notes: *Beyond active treatment; BDI-Beck Depression Inventory; CT-Cognitive Therapy; HRSD-Hamilton Rating Scale-Depression; RDC-Research Diagnostic Criteria; MDD Major Depressive Disorder; MBCT-Mindfulness-Based Cognitive Therapy; TAU-Treatment as usual.

follow-up; there was no statistical difference between the MBCT and TAU groups for individuals with less than three prior episodes of depression (Ma & Teasdale, 2004; Teasdale et al., 2000).

Protective interventions: Preventing recurrence

To our knowledge, no randomized controlled clinical trials have been conducted that specifically address protective interventions that are clearly targeting recurrence as opposed to relapse. Three studies, however, suggest intriguing possibilities in the effects found beyond one year of follow-up. Given the standard two-month threshold for operational definitions of recovery (Frank et al., 1991b; Rush et al., 2006), proposed thresholds of four months (Rush et al., 2006), and an empirical study using a six-month threshold (Riso et al., 1997), individuals who have remained episode free beyond one year of follow-up have presumably entered a period of recovery. The first MBCT study had stratified participants by the recency of recovery (0–12 months versus 13–24 months), and found no difference between the treatment groups as a function of recency suggesting that MBCT may have protective effects against both relapse and recurrence; some caution is warranted however, given that recurrence rates are combined with relapse rates in this report (Teasdale et al., 2000). In their naturalistic follow-up of CT, Hollon and colleagues found that CT still demonstrated protective effects 13 to 24 months after the end of treatment; 82.7% of CT individuals remained well compared to 46.4% of individuals who had been maintained on medication for a year; however this study may also have been subject to the differential sieve effect, so the protective effect of CT may be confounded with selection effects due to response to treatment (Hollon et al., 2006). Finally, even though recurrence wasn't specifically studied in the Fava studies reviewed above, their results also are suggestive of a protective effect against recurrence, given the demonstrated superiority of CT over clinical management at both two- and six-year follow-up periods; this conclusion is strengthened by their randomization procedure which reduces the potential impact of the differential sieve effect (Fava et al., 1998, 2004).

Summary

Preliminary evidence suggests that psychosocial interventions may function as protective interventions against relapse and perhaps even against recurrence. While the evidence for protective effects are encouraging, additional research is required to extend these effects further, particularly for the prevention of recurrence. Additionally, to truly impact the public health burden of depression, such preventative efforts should be scalable to beyond the individual level. MBCT provides one example of an intervention that is designed to address this need, as it is delivered in a group treatment format, so that several individuals may benefit at one time from the preventative intervention. Scaling such efforts to even wider levels using distance technologies such as the Internet may be an ambitious, but not unreasonable goal for future research.

Future directions

In 2002, NIMH released an initiative (Hollon et al., 2002) that called upon researchers to improve psychosocial interventions for unipolar and bipolar depression. The workgroup charged with this task recommended that researchers consider three priorities when designing and implementing psychosocial interventions for depression: '1) development of new and more effective interventions that address both symptom change and functional capacity, 2) development of interventions that prevent onset and recurrence of clinical episodes in at-risk populations, and 3) development of user-friendly interventions and nontraditional delivery methods to increase access to evidence-based interventions' (Hollon et al., 2002, p. 610). In keeping with the general recommendations charged by the workgroup, we recommend that researchers target their prevention of depression efforts in the following areas.

We propose that targeted intervention studies include more diverse samples in their investigations so that group comparisons on the effectiveness of prevention interventions can be examined. By doing so, researchers will hopefully gain a deeper understanding of the generalizability of research findings, as well as uncover areas within specific interventions that may need tailoring to fit the needs of a wider range of individuals worldwide. Few researchers have adapted prevention interventions to reflect the needs of individuals from diverse backgrounds. This presents a problem for scientists and clinicians as we seek to provide mental health services to more and more diverse groups across the world. To address this conflict, Castro et al. (2004) suggest using a community-based participatory research approach so that researchers and community health providers collaborate in the planning, evaluation, and empirical testing of prevention interventions. A goal of this approach is to reduce the likelihood of programme-community mismatch (e.g., characteristics of target group, staff delivering the intervention and setting) and, consequently decreased efficacy of the adapted intervention. Reppucci, Woolard, and Fried (1999) argue that within the field of psychology, there is an interrelationship between the needs of our communities and the problems tackled by prevention

researchers and that both are often guided by social policies. Thus, in relation to the adaptation of prevention interventions, the authors suggest that future prevention trials should incorporate multilevel cultural settings and societal norms when designing prevention interventions. Cardemil and Barber (2001) provide initial guidelines for clinicians interested in incorporating prevention programmes into clinical community settings. Although important for the current and future development of depression prevention interventions, specific details regarding the translation of such interventions are beyond the scope of this review. We encourage prevention researchers to consider adapting evidenced-based prevention interventions that incorporate input from community settings and that reflect the needs of individuals from diverse populations.

The Internet is a new powerful tool for healthcare providers and offers numerous opportunities for empirical investigations. A major advantage of conducting empirical research on the Internet is that it expands the reach of research studies, both within local communities and worldwide. Researchers suggest that the Internet is a viable modality to deliver targeted CBT prevention interventions (Christensen & Griffiths, 2002). Our team is currently working on developing Web-based interventions to prevent depression onset and recurrence. Once developed, these interventions will be tested and adapted for the needs of public sector hospital patients and, therefore provide a much-needed service to traditionally underserved populations. Given that the Internet can be used to carry out RCTs with thousands of participants worldwide (e.g., Muñoz et al., 2006), it may allow trials with adequate power even with relatively low incidence rates.

A conceptual issue that should be specifically highlighted in terms of depression prevention is that genetic risk factors do not imply that cognitive and behavioural interventions are not relevant. Indeed, one could argue that individuals with high genetic risk factors are most likely to benefit from behavioural life changes to reduce risk. For example, individuals with phenylketenuria are at risk for severe brain problems, including mental retardation and seizures because of the body's inability to utilize the amino acid phenylalanine. An effective preventive intervention is the systematic reduction of phenylalanine by dietary restrictions, a behavioural intervention. Similarly, at least one study has reported that individuals with one or two copies of the short allele of the serotonin transporter gene (5-HTT) exhibited more depressive symptoms, diagnosable depression, and suicidality in response to stressful life events than individuals homozygous for the long allele (Caspi et al., 2003). We propose that targeted prevention studies be carried out in which individuals with one

or two short alleles are randomly assigned to cognitive-behavioural mood management training or no intervention and followed for a long enough period of time to determine incidence of major depressive episodes, controlling for stressful life events. Genetic high-risk markers, cognitive-behavioural interventions, and community-focused interventions (to reduce stressful life events, such as severe poverty or gang-related violence) could be seamlessly combined to study methods to reduce the incidence of major depression at the population level.

Conclusion

There is little doubt that the negative consequences of depression have a widespread impact on the lives of thousands of individuals around the world. Researchers and clinicians agree that in addition to providing efficacious treatments, efficacious prevention interventions are needed. As of this writing, prevention interventions that use CBT and IPT concepts have been found to be effective in reducing the incidence of major depression. Secondly, interventions that target specific risk populations are more likely to document effectiveness in reducing MDE incidence than the widespread, universal prevention interventions, perhaps because incidence in universal interventions is too low to have adequate statistical power, unless very large samples are studied. Studies using the Internet may help make such studies feasible (e.g., Muñoz et al., 2006).

As of the beginning of the 21st century, depression prevention research has developed methods to consistently identify individuals at high risk for depression within one year and to reduce the risk by one half or better. The few published preventive trials available have repeatedly reported one-year incidence rates of approximately 25% in the control group (e.g., Clarke et al., 1995, 2001; Muñoz et al., 2007). These same trials have reported one-year incidence rates of approximately 14% in the experimental condition (Clarke et al, 1995; Muñoz et al., 2007), and one of them a rate as low as 8% (Clarke et al., 2001). These early attempts at preventing clinical episodes of major depression yield similar results to those attempting to prevent recurrence: it appears that we can currently reduce incidence by about 50%. The impact of such a reduction in depressive episodes at a worldwide scale would be dramatic (Muñoz, 2001).

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