

Transmission and Prevention of Mood Disorders Among Children of Affectively Ill Parents: A Review

William R. Beardslee, M.D., Tracy R.G. Gladstone, Ph.D., Erin E. O'Connor, B.A.

Objective: To provide a conceptual review of the literature on children of depressed parents over the past 12 years. **Method:** This selective review focused on published studies that delineate the diagnosis of depression in parents, have large samples, describe children 6 to 17 years old, and are methodologically rigorous. The review emphasized conceptual advances and major progress since 1998. Recent efforts in prevention research were discussed, gaps in the existing literature were noted, and directions for targeted research on children of depressed parents were highlighted. **Results:** Over the past 12 years there has been considerable progress in delineating the gene-by-environment interplay in determining the range of outcomes in children. In addition, progress has been made in identifying risk mechanisms and moderators that underlie the transmission of disorder and in developing effective prevention programs. **Conclusions:** This review highlights directions for further research, including different areas affected by parental depression in parents and children, and in understanding the underlying mechanisms involved in the intergenerational transmission of depression, so that preventive and treatment efforts can be tailored effectively. *J. Am. Acad. Child Adolesc. Psychiatry*, 2011; 50(11):1098–1109. **Key Words:** depression, prevention, children, adolescents

Depression is the most common psychiatric disorder in the United States, with more than 16% of the population reporting a major depressive episode (MDD) during their lifetime.¹ It is one of the leading causes of morbidity and mortality in the world,² places a significant economic burden on society,³ and often becomes a chronic recurrent illness.⁴

Depression is remarkably common among parents.⁵ According to an Institute of Medicine (IOM) report, at least 15 million children are living with a depressed parent. Moreover, the number of children exposed to parental depression is much larger when the entire span of childhood is considered, rather than a single year, and when other forms of parental mood disorders are included. In addition, because many parents who recover from an episode of depression continue to experience subclinical levels of depressive symptomatology, many children are repeatedly ex-

posed to depression and to associated disruptions in parenting.⁶

One of the most potent risk factors for developing depression is having a depressed parent, and children of depressed parents are, in general, at a two- to fourfold risk of developing depressive disorders.⁵ Likewise, these children are at risk for other internalizing and externalizing disorders, cognitive delays, medical difficulties, and academic and social failure.^{7,8} At the same time, there are many children who grow up in homes with depression who do not develop impairments. In fact, it is the balance of risk factors and protective resources that determines outcome.^{9,10}

The literature on the children of depressed parents was reviewed in this *Journal* in 1998.¹¹ Since then, there has been dramatic progress in understanding the multiple domains in which parental depression may affect children and the multiple mechanisms through which depression in parents exerts its effects. There also has been significant progress in the development and evaluation of preventive intervention strategies. Two IOM reports have addressed these issues (the senior author was a coauthor of these reports).^{5,12}



An interview with the author is available by podcast at www.jaacap.org.

In this report, the progress in this area is reviewed with a focus on published studies that delineate the diagnosis of depression in parents, have large samples, describe children 6 to 17 years old, and are methodologically rigorous.

THE MATURING OF LONG-TERM LONGITUDINAL STUDIES

Over the past 12 years, data have accumulated on several longitudinal samples of depressed parents and their offspring.¹³⁻¹⁶ Weissman et al.¹⁴ followed a sample of the offspring of depressed and nondepressed parents ($n = 47$) over the course of 20 years, and all the offspring are now adults and have their own children.¹⁴ At the last assessment, rates of diagnoses of mood disorders and other disorders were threefold in the now adult offspring compared with the comparison group.¹⁷ Among grandchildren (mean age = 12 years, $n = 161$) of depressed grandparents, there was a twofold increased risk of anxiety and other disorders when the grandchildren's parents were depressed compared with grandchildren of nondepressed parents.¹⁴ These findings suggest that anxiety disorders in at-risk children may be an early sign of psychopathology, thus providing a possible focus for prevention efforts.

Espejo et al.,¹⁸ in a sample of depressed parents drawn from a larger representative sample ($n = 816$), found that children who experienced greater adversity in childhood and/or had an anxiety disorder exhibited more depressive symptoms after low levels of episodic stress. The investigators speculated that early anxiety disorders, in the context of adverse life events, may be indicators of a dysfunctional stress response that may help explain the connection between anxiety and depression.¹⁸ Several other studies have similarly found that a history of anxiety increases the risk of depression for offspring of depressed parents.^{13,14,18} Likewise, studies of other longitudinal samples have demonstrated that, when parental depression is comorbid with other disorders, risk to offspring increases.¹⁹

INTEGRATIVE MODEL OF TRANSMISSION OF RISK TO CHILDREN OF DEPRESSED PARENTS

Goodman and Gotlib²⁰ developed an integrative model of areas of interest in the transmission of risk from depressed mother to child that incorporates biological and environmental factors and uses a transactional perspective (Figure 1). Some of these

factors describe mechanisms, some are markers, and some are risk factors for disorder. This model was used to structure the present review.

Bidirectionality of Impact

A major advance in the past 12 years in understanding the transmission of risk from parent to child has been the increasing awareness that this is a bidirectional process across the span of development. That is, although parental behaviors influence child outcome, the child's behavior likewise influences the parent.^{21,22} Similarly, Goodman and Gotlib's integrative model is strengthened by the bidirectionality inherent in its structure, in that the mechanisms for transmission of risk are proposed to overlap and interact with one another.

Risk Moderators

Risk for depression can be grouped into two classes: those specific for depression, such as having a depressed parent; and those nonspecific risk factors that affect a wide range of psychiatric outcomes including depression (e.g., poverty, child abuse). This review focuses on the specific risk factors of parental depression, but it should be noted that nonspecific risk factors convey an increased lifelong risk for depression and other disorders^{5,12} and that comprehensive prevention efforts need to address both domains.^{12,23}

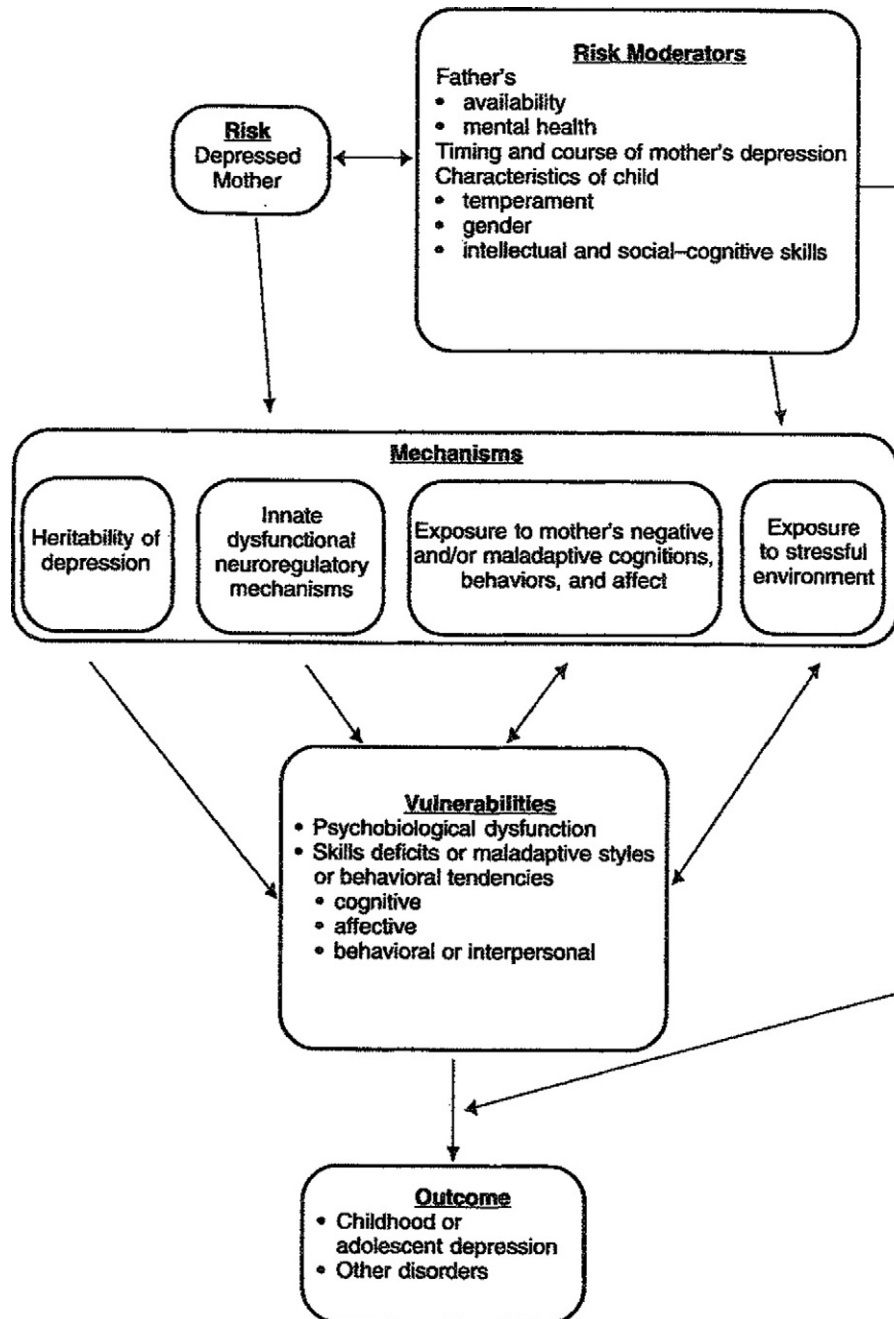
Other Parent's Availability and Mental Health.

In recent years, paternal depression has been found to make unique contributions to offspring outcomes.²⁴ For instance, father-child conflict has been found to mediate the contribution of paternal depression to offspring's internalizing and externalizing symptoms.²⁵ Moreover, having a father and a mother with depression increases the risk of offspring having an emotional disorder, emphasizing the need to examine maternal and paternal depression when considering adolescent outcomes in this high-risk population.^{26,27}

Timing and Course of Parental Depression.

Increased chronicity and severity of parental depression have long been shown to increase the likelihood that children will become ill.^{6,15,28} Recently, Campbell et al.¹⁵ followed mothers and children ($N = 1,357$) from 1 month to 12 years of age with follow-up at age 15, and found that adolescents whose mothers had more severe and chronic depression had more internalizing and externalizing problems and reported engaging in more risky behavior than adolescents whose

FIGURE 1 Goodman and Gotlib's²⁰ integrative model of transmission of risk from depressed mother to offspring. Note: From Goodman SH, Gotlib IH, eds. *Children of Depressed Parents: Mechanisms of Risk and Implications for Treatment*. Washington, DC: American Psychological Association; 2001.²⁰ Reprinted with permission. The use of American Psychological Association information does not imply endorsement by the American Psychological Association.



mothers were never depressed. Similarly, in a sample of 4,953 young children, Brennan et al.²⁸ found that the severity and chronicity of self-reported maternal depressive symptoms were significantly associated with lower vocabulary scores and more behavioral problems.

Characteristics of Child.

Temperament. Some researchers have demonstrated that difficult child temperament is associated with parental depression.^{16,29} Specifically, in Weissman et al.'s 20-year longitudinal study, Bruder-Costello et al.¹⁶ found that offspring of

depressed parents who had a difficult temperament early in life were twice as likely to develop MDD as those who did not have a difficult temperament. Keeping in mind the work of Forbes et al.²¹ and the bidirectionality of the model of Goodman and Gotlib,²⁰ however, it is not clear whether difficult child temperament contributes to parental depression, if difficult child temperament is partially the result of parental depression, or if parental depression and difficult child temperament may be due to an additional underlying factor.

Gender. Compared with their male counterparts, female individuals have been found to be more vulnerable to depressive disorders from adolescence through adulthood.^{5,27} However, many of the studies looking at the effects of maternal depression on offspring outcomes have failed to consider the role of offspring gender.³⁰ The studies that have looked at the role gender plays in offspring outcomes, in the context of parental depression, have yielded inconsistent findings. Some recent studies have found that parental depression signals risk for male and female offspring, but for different disorders.^{31,32} For example, Essex et al.³¹ found that maternal depression and exposure to family conflict were associated with more externalizing problems for male offspring and more internalizing problems for female offspring.

Mechanisms of Transmission

Heritability of Depression and Genetic Effects.

In the past 20 years, there has been rapid progress in examining heritability and the interaction between genes and environment. In a recent review, Bagot and Meaney³³ described findings from animal studies indicating that early environmental influences can have significant effects on later stress responsiveness and that environmental modifications of gene expressions can occur across development. These insights and advances in quantitative genetics and in genomewide association studies form an essential cornerstone to current scientific knowledge.

Twin and adoption studies have established that genetics explain approximately 30% to 40% of the variance of adult MDD. Family studies have found significantly higher risks for depression among first-degree relatives. The highest rates of heritability have been found in the offspring of depressed parents.³⁴

The impact of the environment on the expression of certain genes depends on the degree to which an individual is exposed to a particular environment, the degree to which an individual's behavior influences the environment, and the degree to which an individual's behavior is itself

subject to genetic influences. In an extensive literature review, Kendler and Baker³⁵ noted that, although genes do influence the environment, for example, in the areas of life stress and parenting, the degree of influence is modest, with heritability estimates generally ranging from 15% to 35%.

Recently, there has been increased interest in epigenetics as a driving force behind the gene/environment influences present in various psychiatric disorders, including depression.³³ The reviews by Hochberg et al.³⁶ and Bagot and Meaney³³ described the way in which epigenetics may account for the role the environment plays in modifying certain genotypes that predispose individuals to certain disorders. These investigators described the process of phenotypic plasticity as potentially resulting from epigenetic remodeling, a process in which the environment interacts with an individual's genome to produce specific individual differences in the expression of certain traits. Applying this model to the heritability of depression, a child who inherits a certain genetic makeup from a depressed parent has the raw materials for developing depressive symptoms, but only when certain environmental effects come into play does the combination of gene and environment create the finished product, namely a depressive disorder.

Molecular genetics has focused on finding specific genes that may affect outcomes. Some identified genes include one or two S alleles in the serotonin transporter promoter region polymorphism (5HTTLPR) in the context of chronic stress (girls),³⁷ the gene brain-derived neurotrophic factor,³⁸ homozygous carriers of the T allele methylenetetrahydrofolate reductase (MTHFR), and carriers of the 9/10 genotype compared with the 10/10 genotype (SLC6A3 allele).³⁹ Genes involving serotonin (5HT) transmission have been extensively studied by Caspi et al.⁴⁰ who found that depressive symptoms in offspring can be predicted by the interaction among environment (maternal criticism), 5HT transmission, and child depressogenic cognitive style and among chronic stress, 5HT transmission, and gender (female offspring).^{37,41} Unfortunately, some recent meta-analyses have failed to replicate these findings.^{42,43} The lack of replication points to an overarching problem plaguing these genetic studies. Often, these studies look at one specific or "candidate" gene and its role in the presentation of various diseases and disorders. However, disorders rarely result from the expression of a single gene. For instance, the meta-analysis performed by Munafò et al.⁴³ found no

support for the effect of stressful life events on the serotonin transporter gene in causing various psychopathologies.⁴³ The investigators concluded that, owing to a lack of statistical power and the logistic regression models used in the studies, the positive results found in the replication of the findings of Caspi *et al.* are no better than chance findings.

Because of the difficulty in finding significant gene-by-environment interactions and effects, research has begun to develop more sensitive ways of studying these important interactions. For instance, cytogenetics, the study of chromosomal variation at high resolution using microarray-based detection, has provided the field with a closer look at how DNA can be structurally and sequentially different in individuals with and without certain disorders.⁴⁴ Likewise, imaging-genetics studies represent an area of research that has immense potential to shed light on various genetic and environmental processes underlying many common mental disorders, such as adolescent depression, and may make it possible to link genes directly to specific neural systems using a noninvasive procedure.⁴⁵ However, Pine *et al.*⁴⁵ pointed out that one of the downsides of using imaging-genetics to look at complex phenotypes, such as mood disorders, is that many of these show only small associations with individual genes. Consequently, until techniques are refined further, looking at a specific gene, such as the 5HT transporter gene, may continue to produce mixed findings.

Clearly, there is tremendous potential in the future for using various genetic strategies in investigating outcomes in children of depressed parents. For example, additional research in genome sequencing among families with parental depression may increase the understanding of the multiple genes involved in the transmission of genetic risk. In the discussions of various phenomena associated with offspring of depressed parents that follow, it should be emphasized that there are undoubtedly important genetic influences that contribute to these phenomena. The more precise the descriptions of manifest behavior, the more likely it will be that behavior can be linked to underlying processes of gene expression.

Dysfunctional Neuroregulatory Mechanisms.

Structural factors. Brain asymmetry. Many researchers have found brain asymmetry and cortical activity to be associated with vulnerability to depression.^{46,47} Rao *et al.*⁴⁸ found that adolescents who were depressed or who had a de-

pressed parent had significantly smaller left and right hippocampal volumes than adolescents who were not at risk for depression. Smaller hippocampal volume partly mediated the effect of early-life adversity on depression.⁴⁸

Right hemisphere thinness. Peterson *et al.*,⁴⁷ in a study spanning multiple generations, found that individuals who were descendants of parents or grandparents with MDD (at high risk) had greater cortical thinness in the right hemisphere compared with individuals who were at low risk. The cortical thinning was found to be associated with current symptom severity, inattention, and visual memory for emotional and social stimuli. The results indicated that cortical thinness mediated the association between familial risk and inattention, visual memory, and clinical symptoms.⁴⁷ It is important to note, however, that many of these brain imaging studies are the first of their kind because the ability to connect behavior to brain anatomy and structure is relatively recent. These findings are intriguing but need confirmation from larger and more diverse samples.

Process-related factors. Reward/loss. Anomalies in the processing of reward and loss also have been linked to vulnerability for depression.⁴⁹ Gotlib *et al.*⁴⁹ examined neural activity in reward and loss in 10- to 14-year-old girls who were at high risk (mother had history of recurrent depression) and low risk. High-risk girls showed less activation in their reward processing areas in the brain when presented with the possibility of a reward compared with girls who were low risk. Girls who were at risk for developing depression exhibited neurologic anomalies in certain areas of the brain even before they developed depressive symptoms, indicating a potential mechanism by which offspring of depressed parents are at increased risk for depression.⁴⁹

Sleep disturbances. Depression and sleep processes are often regulated by similar neural processes, and insomnia has been documented as a risk factor for depression onset and relapse.⁵⁰ In the 20-year longitudinal study by Weissman *et al.*, Ong *et al.*⁵¹ examined eating and sleeping in children of depressed and nondepressed parents. Irregularities in eating and sleeping schedules in childhood were correlated with adolescent-onset major depression and anxiety disorder and childhood-onset anxiety disorder.⁵¹ Unfortunately, the sample of children of nondepressed parents was too small to use as a comparison with children of depressed parents. Therefore, at this point, all one can conclude for this

specific population is that sleep irregularities may be a *marker* for depression in offspring of depressed parents. One cannot claim that sleep disturbance acts as a risk factor for depression until more research has been conducted comparing children of depressed parents with children of nondepressed parents.

Birth weight. In the longitudinal study by Weissman et al., Nomura et al.⁵² examined the effect of birth weight on medical and psychological outcomes in the offspring of depressed and nondepressed parents. They found that the low-birth-weight offspring had significant increases in risk of MDD, anxiety disorders, phobia, suicidal ideation, impaired functioning, hypertension, and allergies compared with the reference group. The association between depression and low-birth-weight offspring was stronger among the offspring of depressed parents. The investigators postulated that parental depression may increase the detrimental effects that low birth weight can have on offspring, especially in terms of risk for depression.⁵²

Early menarche. Hormone regulatory systems also have been identified as possible vulnerability markers for depression in adolescence, especially for girls. Some studies have found that early-maturing girls are at an increased risk for depression.^{53,54} Ellis and Garber⁵⁴ found that a history of maternal depression predicted earlier pubertal timing in daughters, and this association was mediated by dyadic stress, the absence of the biological father, and the presence of a stepfather.⁵⁴ The investigators theorized that father absence and stepfather presence affect pubertal timing because these create a more stressful home environment, which has been found to be associated with earlier pubertal timing.⁵⁴

Parental Behaviors and Cognitions.

Depressed parents often exhibit deficits in parenting skills.⁵⁵ In an early article, Rutter⁵⁶ pointed out that the proximal mechanism through which risk is transmitted from depressed parents to offspring is through their interactions with their children, and this remains true.

Parent-child interactions. Attachment. Children of depressed mothers are less likely to exhibit secure attachment relationships than are children of mothers who do not have depression, and the attachment relationship is an important predictor of child outcome.^{57,58} Milan et al.⁵⁷ demonstrated that variability in the course of maternal depression predicted depressive symptoms in 11-year-old offspring, but only if the offspring demonstrated insecure attachment to the mother at age 3. Secure attachment history acted as a protective factor in

predicting better outcomes for children of depressed mothers, but only when the mother had a long-term history of depression.⁵⁷

Parenting style. Some studies have investigated how parenting style, in the context of maternal depression, accounts for various child and adolescent outcomes.^{6,29,32,59} Parental disengagement, responsiveness, unpredictability, expressed emotion, and hostility have been found to affect offspring in the context of parental depression,^{55,60-62} as has parent-child conflict.²⁵ For example, in a classic early study, Schwartz et al.⁶³ demonstrated that high expressed emotion had a substantial impact on poor outcome over and above the chronicity and severity of parental depression. More recently, Tompson et al.⁶⁴ found that high levels of maternal criticism and emotional over involvement were associated with maternal depression history, thereby increasing the chance that offspring will be exposed to critical parenting, potentially increasing their risk for displaying depressive symptoms.

Family System.

Because the family is clearly a dynamic system, it follows that the marital and family subsystems in the face of parental depression will have far-reaching consequences, as mediated by factors such as parental and marital conflict, divorce,^{5,65} family structure, and history of depression and other psychopathology.^{14,66} For instance, higher levels of parental depressive symptoms have been associated with higher levels of interparental conflict and higher levels of internalizing symptoms in offspring.⁶⁷ Moreover, children of depressed mothers have been found to be more reactive to stressful family environments (e.g., marital dissatisfaction, less parental warmth/acceptance) than children of depressed mothers.⁶⁸ Also, depressed women tend to exhibit spouse similarity for depressive disorders and for antisocial and substance-use disorders, creating further opportunity for parental conflict.¹⁰

Exposure to Stressful Environment.

Adverse life events greatly increase the likelihood that offspring of depressed parents will be negatively affected by parental illness.^{5,18,48} Sources of stress include exposure to violence, rejection, abuse, marital and family discord, or chronic stress, such as poverty.^{65,69,70} Individuals with depression may inadvertently select environments of higher stress because of poor choices, individual or marital psychopathology, or downward social mobility due to a depressive disorder.⁵ In the Stress Generation Theory, Ham-

men *et al.*^{68,71} demonstrated that early adverse circumstances might sensitize those with depressed parents, increasing their risk for later depression.

Vulnerabilities

These mechanisms of risk are associated with the emergence of vulnerabilities in children of depressed parents, such as psychobiological dysfunction and skills deficits. These vulnerabilities can then lead to various child outcomes such as depression or other disorders. These vulnerabilities are in some cases in and of themselves outcomes that are worthy of prevention and treatment efforts.

Psychobiological Dysfunction.

Although depressed mood has been found to be a marker of risk for subsequent depressive syndromes,⁷²⁻⁷⁴ to date researchers have not presented data that address the relation between subsyndromal depression and depressive disorder specifically in children of depressed parents. Although depressive symptoms likely are associated with subsequent depression in the offspring of depressed parents, future research is needed to address this issue.

Skills Deficits or Maladaptive Styles or Behaviors. Depressogenic cognitive style. Some studies have demonstrated that how a child interprets the world and the way in which he or she responds to it will affect the likelihood of developing psychopathology or other adverse outcomes in the context of parental depression.^{75,76} For example, Garber and Flynn⁷⁵ found that maternal depression history is positively associated with depressive cognitions in adolescent offspring, specifically hopelessness, self-worth, and attribution style.

Interpersonal functioning. Certain characteristics of a person may lead that person to experience more acute stressors, potentially increasing the risk for depression.^{77,78} Rudolph and Klein⁷⁷ found that depressive personality traits in children were correlated with maternal depressive personality traits and with maternal major depression. These findings highlight the need for effectively treating parental depression as soon as it occurs to avoid adverse long-term effects on offspring.

Affective expression. Forbes *et al.*²¹ examined the relation between maternal childhood-onset depression and offspring (3–9 years old, $n = 74$) affective expression. Results showed that mothers who had childhood-onset depression whose offspring had right frontal EEG asymmetry ex-

hibited increased depressive symptoms over time, and maternal depressive symptoms were associated with high child negative affect. Further analysis indicated that there were bidirectional effects of child affective expression and maternal depressive symptoms.

Reflections on this Model

Goodman and Gotlib's model provides an important structure for a review of new literature on children of depressed parents. However, this model fails to consider protective resources and the interplay between risk and resilience in the transmission of depression from parent to child. Although some studies have examined some aspects of resilience,^{9,79} the area is worthy of much more study.

PREVENTION-INTERVENTION

In the past several decades, research on the prevention of youth depression has blossomed, and as a result, much more is known about ways to maximize the efficacy of prevention efforts.⁸⁰⁻⁸² To date, selective prevention efforts targeting children of depressed parents have been conducted with groups of teens, with families, and within the community setting. Examples of different promising prevention strategies identified in the IOM reports are presented.^{5,12}

Teen Groups

Clarke *et al.*⁸³ developed the Coping With Stress (CWS) course, a manual-based psychoeducational group program targeting at-risk adolescents with depressed parents. They found that over a 15-month follow-up period, compared with teens assigned to the usual-care condition, teens in the CWS program reported fewer depressive symptoms, fewer symptoms of suicide, and better overall functioning.⁸³ A four-site effectiveness study by Garber *et al.*⁸⁴ is being conducted using a variant of the CWS program.⁸⁵ Known as the Prevention of Depression in At-Risk Adolescents study, Garber *et al.* modified the CWS program to include eight weekly and six monthly continuation sessions and recruited 316 teens who were assigned randomly to the Cognitive Behavioral Prevention Program or the usual-care condition.⁸⁴ Results indicate that, through the 8-month follow-up assessment, significantly fewer teens in the Cognitive Behavioral

Prevention Program group had a probable or definite episode of depression compared with adolescents in the usual-care condition. A long-term follow-up of this sample is currently underway.

Family Based

Some intervention programs for children of depressed parents have incorporated the family system as an integral target of intervention. For example, Compas et al.^{86,87} assessed the efficacy of a family cognitive-behavioral preventive intervention aimed at preventing depression in the offspring of parents with a history of depression.⁸⁶ They found that the intervention compared with the control condition produced significant parent and child benefits, including significantly fewer depressive episodes, up to 24 months after randomization.⁸⁷

Beardslee et al.⁸⁸ also developed family-based, public health interventions for families when parents are depressed: a clinician-based program and a lecture program. Both approaches emphasize a cognitive orientation, focus on building strengths and resilience in youth and their parents, and highlight the importance of treatment for parental depression. Although both intervention approaches were associated with positive family changes^{88,89} compared with the lecture group, the clinician-facilitated condition was associated with greater understanding by children of their parents' depressive illness and improved family communication. This work has been adapted for use with single-parent African-American and Latino families⁹⁰ and has been used widely in countrywide programs for children of the mentally ill in Holland, Finland, Norway, Sweden, and Costa Rica.^{91,92}

Community Based

Although this review generally focuses on school-age children, the period from conception through 5 years of age is crucially important for intellectual and emotional development, and infants and very young children are especially vulnerable to certain types of environmental stressors.⁹³ Thus, intensive efforts are warranted to help depressed parents and their children negotiate this crucial developmental epoch.^{5,12} Comprehensive efforts are needed for multi-risk families and such efforts should cover multiple domains. Nurse home visitation and center-

based care such as Early Head Start provide important models for all high-risk families. Embedding additional outreach and support services for depressed parents, such as enriching nurse home visitation programs with mental health interventions⁹⁴ or training and consultation programs about parental depression for Head Start and Early Head Start teachers,⁹⁵ appear to be useful strategies.

Future prevention efforts should include assessment and treatment for depressed parents. There has been a debate in the literature about whether treatment of parents alone is sufficient to help children.^{96,97} It is the reviewers' view that both treatment of parental depression to significant remission and help with parenting must be essential components of preventive efforts for families with depression. Also, prevention efforts must address nonspecific risk factors that are common in families with parental depression, such as poverty, abuse, and exposure to violence. Given that the genetic effects of depression are expressed in adverse environmental circumstances⁹⁸ and that the effects of multiple risk factors are additive, it follows that prevention programs should target the environmental and the psychological risks to children of depressed parents. In addition, new delivery mechanisms for such prevention interventions are indicated. In recent years, Internet-based prevention programs have been developed that have the potential to reach a large number of people, especially populations that may have difficulty accessing more conventional treatment options.⁹⁹ Although more intensive, clinician-based interventions may yield greater benefits, even lower-intensity group interventions have yielded meaningful positive results,⁸⁸ suggesting that such programs may have an important place in public health approaches to preventing mental illness. Moreover, a recent meta-analysis has shown the value of preventive interventions that decrease depressive symptomatology,¹⁰⁰ and these should be considered for children of depressed parents. Because parental depression is associated with internalizing and externalizing problems in youth, such preventive interventions should target a range of outcomes and may have broad mental health benefits.

DISCUSSION

In emphasizing conceptual advances and major progress since 1998, all studies could not be

exhaustively reviewed and the methodologies used could not be presented in detail. Although depression in parents is a heterogeneous entity, this review did not focus on details about this heterogeneity because it is often not discussed in the studies themselves beyond presenting diagnostic information. This review did not focus primarily on families in which depression is one of a number of risks, because, in the reviewers' opinion, that literature requires a separate review.

Future Research Directions

Remarkable progress has been made in understanding the effects of parental depression on children's biology and functioning, including brain asymmetry, right hemisphere thinness, dysregulation of sleep, early menarche, and low birth weight, and in understanding the range and kind of impairments associated with these effects. Clearly, there is a connection in the progress between these two areas. For example, sleep dysregulation or right hemisphere thinning affects functioning, which is then manifested in behavior. In the future, it would be useful to study multiple domains simultaneously to better understand their overlap. Also, one limitation of research to date is that the underlying mechanisms involved in the intergenerational transmission of depression have not always been identified. Although certain mechanisms, such as dysfunctional neuroregulatory factors, are known to be involved in the cross-generational transmission of depression, the active ingredients in these mechanisms (e.g., genes, traits, adverse events) are not known. Future studies should emphasize testing alternative hypotheses about underlying mechanisms causing disorder, including gene-environment interactions, and understanding gene expression and epigenesis related specifically to children of depressed parents. Depression is a heterogeneous condition. Better ways of understanding that heterogeneity of parental depression could lead to better matching of preventions to offspring in much the same way that psychogenomics allows better matching of particular treatments to an individual's particular genetic makeup.

Need for Prevention

Currently, the problem of youth depression is significant, the costs of treatment are high, and

most children do not receive treatment, highlighting the need for expanded treatment and prevention efforts targeting youth depression. Parental depression must be recognized as a major public health problem. Much greater emphasis on developing large-scale effective preventive interventions for families with parental depression is needed, with specific examination of how to take promising practices to a broader scale while continuing rigorous research on those they help and on those they do not.¹² Developing the appropriate infrastructure, funding streams, and training for personnel are needed.⁵ Moreover, prevention efforts should be integrated into primary care and school systems. Broadly speaking, prevention offers one of the best ways of addressing health disparities, another key public health concern.

Be Bold in a Vision for the Future

In the IOM volume on prevention, the committee tried to envision a future in which the promise of preventive interventions was fully realized.¹² Such a system would involve: ready access to health care for all; a strong emphasis on mental health and physical health prevention; partnerships with families in prevention and treatment; and the ongoing development of new services.¹² As a part of that larger vision, as we think about the next 10 years, we hope there will be continued scientific advances, and that programs will be developed so that all families with parental depression will receive the care they need. &

Accepted July 25, 2011.

Drs. Beardslee and Gladstone are with Children's Hospital, Boston. Drs. Beardslee and Gladstone and Ms. O'Connor are with the Judge Baker Children's Center. Dr. Gladstone is also with the Wellesley Centers for Women, Wellesley College.

This work was supported by a grant from the Sidney R. Baer, Jr. Foundation to Dr. Beardslee.

Disclosure: Drs. Beardslee and Gladstone and Ms. O'Connor report no biomedical financial interests or potential conflicts of interest.

Correspondence to William R. Beardslee, M.D., Director, Baer Prevention Initiatives and Chairman Emeritus, Department of Psychiatry, Children's Hospital Boston, Gardner/Monks Professor of Child Psychiatry, Harvard Medical School, 21 Autumn Street, Suite 130.2, Boston, MA 02215; e-mail: william.beardslee@childrens.harvard.edu

0890-8567/\$36.00/©2011 American Academy of Child and Adolescent Psychiatry

DOI: 10.1016/j.jaac.2011.07.020

REFERENCES

1. Kessler RC, Berglund P, Demler O *et al.* The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289:3095-3105.
2. World Health Organization. *The Global Burden of Disease*. Geneva: World Health Organization; 1996.
3. Greenberg PE, Kessler RC, Birnbaum HG *et al.* The economic burden of depression in the United States: how did it change between 1990 and 2000? *J Clin Psychiatry*. 2003;64:1465-1475.
4. Mueller TI, Leon AC, Keller MB *et al.* Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. *Am J Psychiatry*. 1999;156:1000-1006.
5. England MJ, Sim LJ. *Depression in Parents, Parenting, and Children: Opportunities to Improve Identification, Treatment, and Prevention*. Washington, DC: National Academies Press; 2009.
6. Brennan PA, Le Brocque R, Hammen C. Maternal depression, parent-child relationships, and resilient outcomes in adolescence. *J Am Acad Child Adolesc Psychiatry*. 2003;42:1469-1477.
7. Lewinsohn PM, Petit JW, Joiner TE Jr, Seeley JR. The symptomatic expression of major depressive disorder in adolescents and young adults. *J Abnorm Psychol*. 2003;112:244-252.
8. Weissman MM, Wolk S, Goldstein RB *et al.* Depressed adolescents grown up. *JAMA*. 1999;281:1707-1713.
9. Beardslee WR. *Out of the Darkened Room: When a Parent is Depressed; Protecting the Children and Strengthening the Family*. 1st ed. Boston: Little, Brown and Company; 2002.
10. Hammen C. *Depression Runs in Families: The Social Context of Risk and Resilience in Children of Depressed Mothers*. New York: Springer-Verlag; 1991.
11. Beardslee WR, Versage EM, Gladstone TRG. Children of affectively ill parents: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry*. 1998;37:1134-1141.
12. Committee NRCAOMP. *Preventing Mental, Emotional, and Behavioral Disorders among Young People: Progress and Possibilities*. Washington, DC: National Academies Press; 2009.
13. Warner V, Weissman MM, Mufson L, Wickramaratne PJ. Grandparents, parents, and grandchildren at high risk for depression: a three-generation study. *J Am Acad Child Adolesc Psychiatry*. 1999;38:289-296.
14. Weissman MM, Wickramaratne P, Nomura Y *et al.* Families at high and low risk for depression: a 3-generation study. *Arch Gen Psychiatry*. 2005;62:29-36.
15. Campbell SB, Morgan-Lopez AA, Cox MJ, McLoyd VC. A latent class analysis of maternal depressive symptoms over 12 years and offspring adjustment in adolescence. *J Abnorm Psychol*. 2009;118:479-493.
16. Bruder-Costello B, Warner V, Talati A, Nomura Y, Bruder G, Weissman M. Temperament among offspring at high and low risk for depression. *Psychiatry Res*. 2007;153:145-151.
17. Weissman MM, Wickramaratne P, Nomura Y, Warner V, Pilowsky D, Verdelli H. Offspring of depressed parents: 20 years later. *Am J Psychiatry*. 2006;163:1001-1008.
18. Espejo EP, Hammen CL, Connolly NP, Brennan PA, Najman JM, Bor W. Stress sensitization and adolescent depressive severity as a function of childhood adversity: a link to anxiety disorders. *J Abnorm Child Psychol*. 2007;35:287-299.
19. Pilowsky DJ, Wickramaratne PJ, Rush AJ *et al.* Children of currently depressed mothers: a STAR*D ancillary study. *J Clin Psychiatry*. 2006;67:126-136.
20. Goodman SH, Gotlib IH. Transmission of risk to children of depressed parents: Integration and conclusions. In: Goodman SH, Gotlib IH, eds. *Children of Depressed Parents: Mechanisms of Risk and Implications for Treatment*. Washington, DC: American Psychological Association; 2002:307-326.
21. Forbes EE, Shaw DS, Silk JS *et al.* Children's affect expression and frontal EEG asymmetry: transactional associations with mothers' depressive symptoms. *J Abnorm Child Psychol*. 2008;36:207-221.
22. Gross HE, Shaw DS, Moilanen KL. Reciprocal associations between boys' externalizing problems and mothers' depressive symptoms. *J Abnorm Child Psychol*. 2008;36:693-709.
23. Beardslee WR. Prevention and the clinical encounter. *Am J Orthopsychiatry*. 1998;68:521-533.
24. Wilson S, Durbin CE. Effects of paternal depression on fathers' parenting behaviors: A meta-analytic review. *Clin Psychol Rev*. 2010;30:167-180.
25. Kane P, Garber J. Parental depression and child externalizing and internalizing symptoms: unique effects of fathers' symptoms and perceived conflict as a mediator. *J Child Fam Stud*. 2009;18:465-472.
26. Landman-Peeters KMC, Ormel J, Van Sonderen ELP, Den Boer JA, Minderaa RB, Hartman CA. Risk of emotional disorder in offspring of depressed parents: Gender differences in the effect of a second emotionally affected parent. *Depress Anxiety*. 2008;25:653-660.
27. Reeb BT, Conger KJ, Wu EY. Paternal depressive symptoms and adolescent functioning: the moderating effect of gender and father hostility. *Fathering*. 2010;8:131-142.
28. Brennan PA, Hammen C, Andersen MJ, Bor W, Najman JM, Williams GM. Chronicity, severity, and timing of maternal depressive symptoms: relationships with child outcomes at age 5. *Dev Psychol*. 2000;36:759-766.
29. Chazan-Cohen R, Ayoub C, Pan BA *et al.* It takes time: Impacts on Early Head Start that lead to reductions in maternal depression two years later. *Infant Ment Health J*. 2007;28:151-170.
30. Sheeber L, Davis B, Hops H. Gender-specific vulnerability to depression in children of depressed mothers. In: Goodman SH, Gotlib IH, eds. *Children of Depressed Parents: Mechanisms of Risk and Implications for Treatment*. Washington, DC: American Psychological Association; 2002:253-274.
31. Essex MJ, Klein MH, Cho E, Kraemer HC. Exposure to maternal depression and marital conflict: Gender differences in children's later mental health symptoms. *J Am Acad Child Adolesc Psychiatry*. 2003;42:728-737.
32. Foster CE, Webster MC, Weissman MM *et al.* Course and severity of maternal depression: associations with family functioning and child adjustment. *J Youth Adolesc*. 2008;37:906-916.
33. Bagot RC, Meaney MJ. Epigenetics and the biological basis of gene \times environment interactions. *J Am Acad Child Adolesc Psychiatry*. 2010;49:752-771.
34. Rice F, Harold G, Thaper A. The genetic aetiology of childhood depression: a review. *J Child Psychol Psychiatry*. 2002;43:65-79.
35. Kendler KS, Baker JH. Genetic influences on measures of the environment: a systematic review. *Psychol Med*. 2007;37:615-626.
36. Hochberg Z, Feil R, Constancia M *et al.* Child health, developmental plasticity, and epigenetic programming. *Endocr Rev*. 2011;32:159-224.
37. Hammen C, Brennan PA, Keenan-Miller D, Hazel NA, Najman JM. Chronic and acute stress, gender, and serotonin transporter gene environment interactions predicting depression symptoms in youth. *J Child Psychol Psychiatry*. 2010;51:180-187.
38. Schumacher J, Jamra RA, Becker T *et al.* Evidence for a relationship between genetic variants at the brain-derived neurotrophic factor (BDNF) locus and major depression. *Biol Psychiatry*. 2005;58:307-314.
39. López-León S, Janssens ACJW, Ladd AMG-Z *et al.* Meta-analyses of genetic studies on major depressive disorder. *Mol Psychiatry*. 2008;13:772-785.
40. Caspi A, Sugden K, Moffitt TE *et al.* Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science*. 2003;301:386-389.
41. Gibb BE, Uhrlass DJ, Grassia M, Benas JS, McGeary J. Children's inferential styles, 5-HTTLPR genotype, and maternal expressed emotion-criticism: an integrated model for the intergenerational transmission of depression. *J Abnorm Psychol*. 2009;118:734-745.
42. Risch N, Herrell R, Lehner T *et al.* Interaction between the serotonin transporter gene (5-HTTLPR), stressful life events, and risk of depression: a meta-analysis. *JAMA*. 2009;301:2462-2471.
43. Munafò MR, Durrant C, Lewis G, Flint J. Gene \times environment interactions at the serotonin transporter locus. *Biol Psychiatry*. 2009;65:211-219.
44. Hoffman EJ, State MW. Progress in cytogenetics: implications for child psychopathology. *J Am Acad Child Adolesc Psychiatry*. 2010;49:736-751.

45. Pine DS, Ernst M, Leibenluft E. Imaging-genetics applications in child psychiatry. *J Am Acad Child Adolesc Psychiatry.* 2010;49:772-782.
46. Bruder GE, Tenke CE, Warner V, Weissman MM. Grandchildren at high and low risk for depression differ in EEG measures of regional brain asymmetry. *Biol Psychiatry.* 2007;62:1317-1323.
47. Peterson BS, Warner V, Bansal R *et al.* Cortical thinning in persons at increased familial risk for major depression. *Proc Natl Acad Sci U S A.* 2009;106:6273-6278.
48. Rao U, Chen L-A, Bidesi AS, Shad MU, Thomas MA, Hammen CL. Hippocampal changes associated with early-life adversity and vulnerability to depression. *Biol Psychiatry.* 2010;67:357-364.
49. Gotlib IH, Hamilton JP, Cooney RE, Singh MK, Henry ML, Joormann J. Neural processing of reward and loss in girls at risk for major depression. *Arch Gen Psychiatry.* 2010;67:380-387.
50. Szklo-Coxe M, Young T, Peppard PE, Finn LA, Benca RM. Prospective associations of insomnia markers and symptoms with depression. *Am J Epidemiol.* 2010;171:709-720.
51. Ong SH, Wickramaratne P, Tang M, Weissman MM. Early childhood sleep and eating problems as predictors of adolescent and adult mood and anxiety disorders. *J Affect Disord.* 2006;96:1-8.
52. Nomura Y, Wickramaratne PJ, Pilowsky DJ *et al.* Low birth weight and risk of affective disorders and selected medical illness in offspring at high and low risk for depression. *Compr Psychiatry.* 2007;48:470-478.
53. Ge X, Conger RD, Elder GH Jr. Pubertal transition, stressful life events, and the emergence of gender differences in adolescent depressive symptoms. *Dev Psychol.* 2001;37:404-417.
54. Ellis BJ, Garber J. Psychosocial antecedents of variation in girls' pubertal timing: maternal depression, stepfather presence, and marital and family stress. *Child Dev.* 2000;71:485-501.
55. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: a meta-analytic review. *Clin Psychol Rev.* 2000;20:561-592.
56. Rutter M. Resilience in the face of adversity: protective factors and resistance to psychiatric disorder. *Br J Psychiatry.* 1985;147:598-611.
57. Milan S, Snow S, Belay S. Depressive symptoms in mothers and children: preschool attachment as a moderator of risk. *Dev Psychol.* 2009;45:1019-1033.
58. Abela JRZ, Hankin BL, Haigh EAP, Adams P, Vinokuroff T, Trayhern L. Interpersonal vulnerability to depression in high-risk children: the role of insecure attachment and reassurance seeking. *J Clin Child Adolesc Psychol.* 2005;34:182-192.
59. Middleton M, Scott SL, Renk K. Parental depression, parenting behaviours, and behaviour problems in young children. *Infant Child Dev.* 2009;18:323-336.
60. Feng X, Shaw DS, Skuban EM, Lane T. Emotional exchange in mother-child dyads: Stability, mutual influence, and associations with maternal depression and child problem behavior. *J Fam Psychol.* 2007;21:714-725.
61. Dietz LJ, Birmaher B, Williamson DE *et al.* Mother-child interactions in depressed children and children at high risk and low risk for future depression. *J Am Acad Child Adolesc Psychiatry.* 2008;47:574-582.
62. Frye AA, Garber J. The relations among maternal depression, maternal criticism, and adolescents' externalizing and internalizing symptoms. *J Abnorm Child Psychol.* 2005;33:1-11.
63. Schwartz CE, Dorer DJ, Beardslee WR, Lavori PW. Maternal expressed emotion and parental affective disorder: risk for childhood depressive disorder, substance abuse, or conduct disorder. *J Psychiatr Res.* 1990;24:231-250.
64. Tompson MC, Pierre CB, Boger KD, McKowen JW, Chan PT, Freed RD. Maternal depression, maternal expressed emotion, and youth psychopathology. *J Abnorm Child Psychol.* 2010;38:105-117.
65. Avenevoli S, Merikangas KR. Implications of high-risk family studies for prevention of depression. *Am J Prev Med.* 2006;31(suppl 1):S126-S135.
66. Pettit JW, Olino TM, Roberts RE, Seeley JR, Lewinsohn PM. Intergenerational transmission of internalizing problems: effects of parental and grandparental major depressive disorder on child behavior. *J Clin Child Adolesc Psychol.* 2008;37:640-650.
67. Fear JM, Champion JE, Reeslund KL *et al.* Parental depression and interparental conflict: children and adolescents' self-blame and coping responses. *J Fam Psychol.* 2009;23:762-766.
68. Hammen C, Brennan PA, Shih JH. Family discord and stress predictors of depression and other disorders in adolescent children of depressed and nondepressed women. *J Am Acad Child Adolesc Psychiatry.* 2004;43:994-1002.
69. Briggs-Gowan MJ, Carter AS, Clark R, Augustyn M, McCarthy KJ, Ford JD. Exposure to potentially traumatic events in early childhood: differential links to emergent psychopathology. *J Child Psychol Psychiatry.* 2010;51:1132-1140.
70. Morris MC, Ciesla JA, Garber J. A prospective study of stress autonomy versus stress sensitization in adolescents at varied risk for depression. *J Abnorm Psychol.* 2010;119:341-354.
71. Hammen C, Henry R, Daley SE. Depression and sensitization to stressors among young women as a function of childhood adversity. *J Consult Clin Psychol.* 2000;68:782-787.
72. Compas BE, Orosan PG, Grant KE. Adolescent stress and coping: Implications for psychopathology during adolescence. *J Adolesc.* 1993;16:331-349.
73. Pine DS, Cohen E, Cohen P, Brook J. Adolescent depressive symptoms as predictors of adult depression: moodiness or mood disorder? *Am J Psychiatry.* 1999;156:133-135.
74. Brent DA, Birmaher B, Kolko D, Baugher M, Bridge J. Subsyndromal depression in adolescents after a brief psychotherapy trial: course and outcome. *J Affect Disord.* 2001;63(1-3):51-58.
75. Garber J, Flynn C. Predictors of depressive cognitions in young adolescents. *Cogn Ther Res.* 2001;25:353-376.
76. Abela JRZ, Skitch SA, Adams P, Hankin BL. The timing of parent and child depression: a hopelessness theory perspective. *J Clin Child Adolesc Psychol.* 2006;35:253-263.
77. Rudolph KD, Klein DN. Exploring depressive personality traits in youth: origins, correlates, and developmental consequences. *Dev Psychopathol.* 2009;21:1155-1180.
78. Hammen C, Brennan PA, Keenan-Miller D. Patterns of adolescent depression to age 20: the role of maternal depression and youth interpersonal dysfunction. *J Abnorm Child Psychol.* 2008;36:1189-1198.
79. Horowitz JL, Garber J. Relation of intelligence and religiosity to depressive disorders in offspring of depressed and nondepressed mothers. *J Am Acad Child Adolesc Psychiatry.* 2003;42:578-586.
80. Gladstone TRG, Beardslee WR. The prevention of depression in children and adolescents: a review. *Can J Psychiatry.* 2009;54:212-221.
81. Gladstone TRG, Beardslee WR, O'Connor EE. The prevention of adolescent depression. *Psychiatr Clin North Am.* 2011;34:35-52.
82. Muñoz RF, Cuijpers P, Smit F, Barrera AZ, Leykin Y. Prevention of major depression. *Annu Rev Clin Psychol.* 2010;6:181-212.
83. Clarke GN, Hornbrook M, Lynch F *et al.* A randomized trial of a group cognitive intervention for preventing depression in adolescent offspring of depressed parents. *Arch Gen Psychiatry.* 2001;58:1127-1134.
84. Garber J, Clarke GN, Brent D. Preventing depression in at-risk adolescents: design and sample characteristics. Paper presented at: American Academy of Child and Adolescent Psychiatry; Boston, MA; October 2007.
85. Clarke GN, Hawkins W, Murphy M, Sheeber LB. Targeted prevention of unipolar depressive disorder in an at-risk sample of high school adolescents: a randomized trial of group cognitive intervention. *J Am Acad Child Adolesc Psychiatry.* 1995;34:312-321.
86. Compas BE, Forehand R, Keller G *et al.* Randomized controlled trial of a family cognitive-behavioral preventive intervention for children of depressed parents. *J Consult Clin Psychol.* 2009;77:1007-1020.
87. Compas B, Forehand R, Thigpen JC *et al.* Family group cognitive-behavioral preventive intervention for families of depressed parents: 18- and 24-month outcomes [published online ahead of print June 27, 2011]. *J Consult Clin Psychol.* doi:10.1037/a0024254.
88. Beardslee WR, Gladstone TRG, Wright EJ. A family-based approach to the prevention of depressive symptoms in children at risk: evidence of parental and child change. *Pediatrics.* 2003;112:E99-111.

89. Beardslee WR, Wright EJ, Gladstone TRG, Forbes P. Long-term effects from a randomized trial of two public health preventive interventions for parental depression. *J Fam Psychol.* 2007;21:703-713.
90. D'Angelo EJ, Llerena-Quinn R, Shapiro R *et al.* Adaptation of the Preventive Intervention Program for Depression for use with predominantly low-income Latino families. *Fam Process.* 2009;48:269-291.
91. Solantaus T, Toikka S, Alasuutari M, Beardslee WR, Paavonen EJ. Safety, feasibility and family experiences of preventive interventions for children and families with parental depression. *Int J Ment Health Promot.* 2009;11:15-24.
92. Beardslee W, Paez-Soto A, Herrera-Amighetti L *et al.* Adaptation of a preventive intervention approach to strengthen families facing adversities, especially depression. *Int J Ment Health Promot.* 2011;13:5-13.
93. Chu AT, Lieberman AF. Clinical implications of traumatic stress from birth to age five. *Annu Rev Clin Psychol.* 2010;6:469-494.
94. Ammerman RT, Putnam FW, Stevens J *et al.* An open trial of in-home CBT for depressed mothers in home visitation [published online ahead of print October 9, 2010]. *Matern Child Health J.* doi:10.1007/s10995-010-0691-7.
95. Beardslee WR, Ayoub C, Avery MW, Watts CL, O'Carroll KL. Family connections: an approach for strengthening early care systems in facing depression and adversity. *Am J Orthopsychiatry.* 2010;80:482-495.
96. Gunlicks ML, Weissman MM. Change in child psychopathology with improvement in parental depression: A asystematic review. *J Am Acad Child Adolesc Psychiatry.* 2008;47:379-389.
97. Riley AW, Valdez CR, Barrueco S *et al.* Development of a family-based program to reduce risk and promote resilience among families affected by maternal depression: theoretical basis and program description. *Clin Child Fam Psychol Rev.* 2008;11:12-29.
98. Lau JYF, Eley TC. The genetics of adolescent depression. In: Nolen-Hoeksema S, Hilt LM, eds. *Handbook of Depression in Adolescents.* New York: Routledge/Taylor and Francis Group; 2009:259-278.
99. Voorhees BWV, Mahoney N, Mazo R *et al.* Internet-based depression prevention over the life course: a call for behavioral vaccines. *Psychiatr Clin North Am.* 2011;34:167-183.
100. Horowitz JL, Garber J. The prevention of depressive symptoms in children and adolescents: a meta-analytic review. *J Consult Clin Psychol.* 2006;74:401-415.