Depression and Bipolar Support Alliance Consensus Statement on the Unmet Needs in Diagnosis and Treatment of Mood Disorders in Children and Adolescents

JOSEPH T. COYLE, M.D., DANIEL S. PINE, M.D., DENNIS S. CHARNEY, M.D., LYDIA LEWIS, CHARLES B. NEMEROFF, M.D., GABRIELLE A. CARLSON, M.D., PARAMJIT TOOR JOSH I, M.D., DAVID REISS, M.D., RICHARD D. TODD, M.D., PH.D., MARTHA HELLANDER, J.D., AND THE DEPRESSION AND BIPOLAR SUPPORT ALLIANCE CONSENSUS DEVELOPMENT PANEL

ABSTRACT

Objective: To focus attention on the critical unmet needs of children and adolescents with mood disorders and to make recommendations for future research and allocation of healthcare resources. Method: The 36-member Consensus Development Panel consisted of experts in child/adolescent or adult psychiatry and psychology, pediatrics, and mental health advocacy. Reviews of the literature concerning youth mood disorders were performed on the subjects of risk factors, prevention, diagnosis, treatment, and services delivery, and opinions and experiences of mental health advocates were obtained. Results: The Consensus Development Panel listened to presentations and participated in discussions. Independent workgroups of clinicians, scientists, and mental health advocates considered the evidence and prepared preliminary statements. Workgroup leaders presented drafts for discussion by the Consensus Development Panel. The final document was reviewed by the entire group and edited to incorporate input from all participants. Conclusions: Evidence suggests high rates of unmet needs for children and adolescents with depression or bipolar disorder. Training is largely limited to child mental health specialists; general psychiatrists, pediatricians, and other primary care physicians receive little or no training. As a result, treatment patterns may reflect adult treatment plans that are not validated for youths. Effective treatments have been identified and some preliminary prevention models have been developed, but they are not yet widely applied. Patients experience limited exposure to clinicians adequately trained to address their problems and little information to guide care decisions, particularly concerning bipolar disorder. National efforts are required to restructure healthcare delivery and provider training and to immediately develop more advanced research on pathophysiology, prevention, and services delivery effectiveness. J. Am. Acad. Child Adolesc. Psychiatry, 2003;42(12):1494–1503. Key Words: mood disorders, major depression, bipolar disorder.

Major depression is a common, serious psychiatric disorder in the United States, with prevalence rates of up to 2% for prepubertal children (Bird et al., 1988; Cohen et al., 1993; Costello et al., 1996, 2002; Fleming et al., 1996; McGee et al., 1990; Shaffer et al., 1996). The prevalence of bipolar disorder in children and adolescents is not known with precision because of the lack of large-scale epidemiological studies. The lifetime prevalence of bipolar disorder could be as high as 1% (Lewinsohn et al., 1995) by adolescence, although rates in childhood are likely to be lower (Costello et al., 2002, 1996). Early-onset mood disorders are associated with turbulent, dysfunctional lives, poor school performance, impaired peer and family relationships, alcohol and substance abuse, and other psychiatric comorbidity.
Nearly one out of five high school students seriously considers taking his or her own life (Kann et al., 2000), and suicide is the third leading cause of death in this age group (Brent, 2001; Murphy, 2000; Shaffer and Craft, 1999). Children and adolescents with major depression or bipolar disorder are at greatly increased risk for suicidal behavior and completed suicide (Pfeffer, 2001; Pfeffer et al., 1993). Prepubertal suicidal behavior predicts adolescent suicide attempts, and mood disorders increase the risk of repeated suicide attempts (Pfeffer et al., 1993).

Youngsters with mood disorders often grow up to be adults with mood disorders and other serious psychiatric comorbidity (Lewinsohn et al., 2000; Weissman et al., 1999a). This continuity of mood disorders into adulthood underscores the need for early recognition and intervention. Unfortunately, efforts at early detection and intervention are generally neglected by the legislative, scientific, and medical communities (Mrazek and Haggerty, 1994). Although treatments of early-onset mood disorders remain inadequately studied, recent efforts to examine efficacy in major depression have begun to address the need for more research in this area (Brent et al., 1998; Curry, 2001; Emslie and Mayes, 2001). More significant deficiencies exist in studies of bipolar disorder and in aspects of service delivery for all pediatric mood disorders. More than 70% of children and adolescents with serious mood disorders are either undiagnosed or inadequately treated (Burns et al., 1995; Lewinsohn et al., 2000; NIMH Blueprint Report, 2001). These statistics underscore the crisis in mental health care for children and adolescents with mood disorders in a healthcare system that is currently inadequate to meet their needs.

**CONSENSUS STATEMENT**

Recognizing the need to address these concerns, the Depression and Bipolar Support Alliance (DBSA, formerly known as the National Depressive and Manic Depressive Association [National DMDA]), the nation's largest patient-directed, illness-specific organization, convened a consensus conference in October 2000. The Consensus Group, which consisted of experts in child and adolescent psychiatry and psychology, pediatrics, epidemiology, and mental health advocacy, was charged with drafting a statement defining the knowledge base for early-onset mood disorders and providing recommendations for remediation. This Consensus Statement was developed in response to the discussion prompted by expert presentations on diagnosis, risk factors, treatment, prevention, and services for children and adolescents with mood disorders.

**Risk Factors**

Risk factors refer to agents, intrinsic characteristics, or environments that precede the onset of illness (Kraemer et al., 1997, 2001). Ideally, risk assessment should consider the entire context of the child’s life rather than focusing on individual factors (Beardslee and Gladstone, 2001; Kessler et al., 1997). One salient risk factor for mood disorders is family history of mood disorder, although parental illness alone is not sufficient to predict, with high confidence, a childhood outcome. Thus, twin (Eaves et al., 1997; Eley and Plomin, 1997; Silberg et al., 2001, 1999; Thapar and McGuffin, 1994), family (Beardslee et al., 1996; Harrington et al., 1997, 1993; Kovacs et al., 1997; Warner et al., 1999; Williamson et al., 1995), and adoption studies (van den Oord et al., 1994) indicate that the etiology of mood disorders includes both genetic and environmental components. In one study, impoverished children with multiple socioeconomic risk factors and healthy mothers fared less well than children with mentally ill mothers but few other risk factors (Sameroff et al., 1987).

Gender-related changes during development represent a second important set of risk factors in early-onset mood disorders. The prevalence of depression, being equal between boys and girls before puberty, doubles in females during adolescence, and this doubling has been linked specifically to hormonal changes occurring during puberty (Angold et al., 1999b; Birmaher et al., 1996a; Garrison et al., 1990; Lewinsohn et al., 1998, 1994; Reinherz et al., 1989). These changes may directly influence brain function, or they may have an impact on social factors that in turn predispose to depression. Similarly, these changes may also influence the manner in which genetic factors affect the risk of depression. Specifically, whereas environmental factors appear to be a primary etiologic influence on depression before adolescence (Silberg et al., 2001, 1999; Thapar and McGuffin, 1994), twin studies demonstrate an increasing genetic influence as girls enter adolescence (Silberg et al., 1999).

Various forms of psychopathology that arise before full-blown affective syndromes represent a third set of major risk factors for major depressive disorder (MDD), as well as possibly bipolar disorder (BPD). Perhaps the most extensive and unequivocal evidence emerges for symptoms of anxiety disorders, which re-
bustly predict risk for MDD and BPD (Johnson et al., 2000; Pine et al., 2001, 1998). In prospective studies, subclinical depressive symptoms also have been found to predict full-blown episodes of MDD (Pine et al., 1999). Finally, the relationship between behavior disorders and mood disorders is more complicated. Attention-deficit/hyperactivity disorder (ADHD) shows a weak association with MDD (Angold et al., 1999a), although it may show a stronger association with BPD, depending on application of particular definitions of BPD. Conduct disorder shows a more consistent longitudinal association with MDD (Angold et al., 1999a; Pine et al., 1998), although these findings are also somewhat controversial (Weissman et al., 1999b). For example, some evidence suggests variation across development in the nature of these associations: namely, mood disorders arising before puberty may show the strongest association with behavior disorders (Weissman et al., 1999b), although some studies have also found associations in older adolescents followed prospectively (Kasen et al., 2001).

Findings from the studies reviewed above clarify some aspects of risk for mood disorders, but other aspects of risk remain less clearly understood. For example, research on familial associations has stimulated studies of molecular genetics. Although linkage and association studies have identified several sites on the human genome of associated heritable risk for mood disorders, specific genes have yet to be unequivocally identified. Therefore, molecular genetics currently plays no role in early identification. This likely reflects the complicated role played by multiple risk factors, including genetic and environmental factors, in pathophysiology. Knowledge is accumulating linking genetic factors to indices of brain function, and indices of brain function to indices of risk for depression. For example, a specific variant of the 5-HT transporter may relate both to a measure of amygdala function and to measures of personality associated with depression (Hariri et al., 2002). These data are consistent with other evidence implicating dysfunction in the amygdala and prefrontal cortex in depression (Drevets, 2001).

Nevertheless, considerably more research is needed on the pathophysiology of mood disorders in children and adolescents. Such research should focus on the manner in which brain function relates to both social and environmental risk factors for depression as well as genes and clinical predictors of outcome. As our understanding of relationships among genes, brain function, and mood disorders increases, this may assist us in redefining the classification of mood disorders and identifying neural systems for neurobiological studies or specific targets for pharmacological interventions, thereby guiding optimal treatment approaches.

Considerable questions also remain with respect to the risk factors for BPD. In preliminary work, a number of factors have been proposed to increase risk specifically for an early-onset variety of the condition, with a family history of mania or BPD being particularly important (Geller and Luby, 1997; Geller et al., 2001; Todd et al., 1996). A history of early-onset depression or rapid-onset depression with psychosis or mixed-mood states also may be a predictor of an incipient BPD. Finally, children with a heritable predisposition for BPD may be vulnerable to drug-induced hypomania, mania, or rapid cycling with antidepressants (Geller and Luby, 1997; Geller et al., 2000). Although anecdotal evidence suggests that stimulants may be associated with treatment-emergent mania in children at risk for BPD, findings from controlled studies do not support a causal relationship (Carlson and Kelly, 2001, 1998; Carlson et al., 2000, 1992). Nevertheless, each of these findings remains relatively less well replicated than findings on risk factors for major depression. As a result, considerable further study is needed in this area.

**Diagnosis**

The diagnostic criteria for major depression in school-aged children and adolescents are the same as those for adults and are explicit in the *DSM-IV* (American Psychiatric Association, 1994). However, the methods used to elicit information concerning these criteria vary among adults, adolescents, and children, with children being less able to precisely describe temporal details of fluctuations in internal mood states (Angold et al., 1996). For a diagnosis to be properly made, children must be able to understand questions and provide information both on their current mood state as well as their mood state during the previous few weeks. Because not all children are capable of providing such information accurately, interviews with both the child and the parent are necessary at least until the age of 14. The presence of comorbid conditions (e.g., ADHD, conduct disorders, anxiety disorders) in children with depression complicates diagnosis because symptoms of mood disorders are common in children with these conditions, even among children who do not meet the criteria for major depression or BPD (Angold et al., 1999a).
Although the *DSM-IV* provides explicit diagnostic criteria for BPD in adults, these criteria may not be broadly applicable to children and adolescents. A pattern of discrete episodes of mania is the hallmark feature of BPD in adults. In contrast, juvenile-onset BPD may manifest as chronic, nonepisodic, rapid-cycling, mixed episodes, although considerable controversy on this point remains (Geller and Luby, 1997; Wozniak et al., 1995). The presentation of early-onset BPD varies widely, and these symptoms can overlap with other disorders (e.g., distractibility observed in ADHD) (Spencer et al., 2001), thus confounding the diagnosis. Moreover, studies using various external validators, such as longitudinal course or familial aggregation, generate somewhat inconsistent findings, leaving open questions on the most appropriate criteria to apply in children. There was consensus that standard diagnostic criteria for early-onset BPD that are developmentally appropriate and that exhibit high interrater reliability and validity should be developed (Geller and Luby, 1997; Giedd, 2000; Papulos and Papolos, 2000).

A number of structured diagnostic instruments for mood disorders have been developed, and their use has increased the reliability of diagnoses in research settings (McClellan and Werry, 2000). In general, there is an ongoing need for better training in diagnostic procedures, as well as a specific need for refinements in the diagnosis of BPD. For advancements in the field to continue, research efforts must move diagnostic processes beyond semantic descriptions of disorders and base them on epidemiological characteristics and biological processes (McClellan and Werry, 2000).

**Treatment**

The early part of the 1990s witnessed a pronounced increase in the prescription of antidepressants to children and adolescents, before (Emslie et al., 1999; Hughes et al., 1999; Rushton and Whitmire, 2001; Zito and Safer, 2001; Zito et al., 2000) well-controlled studies of the efficacy and effectiveness of treatments for childhood and adolescent mood disorders had been implemented. This highlights the fact that treatment practice in pediatric mood disorders has been insufficiently guided by available data from randomized controlled trials.

Advances in therapeutics research create an opportunity for practice to be more comprehensively informed by available data. Recent studies (Brent et al., 1997; Clarke et al., 1999; Jayson et al., 1998; Kazdin, 2000), both of cognitive-behavioral therapy and interpersonal psychotherapy (Curry, 2001), as well as of selective serotonin reuptake inhibitors (SSRIs) (Emslie and Mayes, 2001; Emslie et al., 1997; Keller et al., 2001; Nixon et al., 2001; Wagner et al., 2001), document the utility of these treatments for major depression in youngsters. In particular, at least five large randomized controlled trials document superiority of an SSRI over placebo (Donnelly and Wohlberg, 2001; Emslie and Mayes, 2001; Wagner et al., 2001), with one of these studies also demonstrating superiority over a tricyclic antidepressant (Keller et al., 2001). Moreover, more than 10 studies document the efficacy of cognitive-behavioral therapy for MDD, with a few studies suggesting a possible role for cognitive-behavioral therapy in prevention (Beardslee and Gladstone, 2001; Clarke et al., 2001; Curry, 2001). Finally, two studies document the efficacy of interpersonal psychotherapy, with one being conducted in a minority sample (Rossello and Bernal, 1999). A large-scale NIMH-funded head-to-head trial, the Treatment of Adolescent Depression study, is also under way and will weigh the advantages and disadvantages of SSRIs and cognitive-behavioral therapy.

These data on treatment of acute major depression stand in contrast to those on treatment of other pediatric mood disorders. Although there is an emerging literature on the treatment of juvenile-onset BPD, it consists almost entirely of case reports, open-label studies, and studies using nonstandardized criteria. Double-blind, placebo-controlled studies are lacking, and the evidence base for treatment of early-onset BPD remains inadequate (Biederman et al., 1998; Geller and Luby, 1997; Giedd, 2000). Similar limitations apply to other areas of therapeutics. These include studies of treatment-resistant depression and dysthymia in children and adolescents.

The widespread use of SSRIs before positive results were reported in clinical trials, coupled with the lack of controlled trials in BPD, led some to question the ethics of using psychopharmacological treatments in children and adolescents. Further, the ambiguity of diagnosis, age-related safety issues in young children, and evidence of age-related differences in efficacy of the tricyclic antidepressants underscore concern about relying on adult data. Clearly, more research is needed on each of these issues. Nevertheless, such questions should not detract from the overall conclusions that significant treatment gains have been documented in recent randomized, controlled trials for pediatric...
MDD. These findings should stimulate research designed to refine such effective treatments. For example, some suggest that different doses of SSRIs may be needed across diagnoses or age groups. Others suggest that SSRIs may be associated with unique side effects. Given that the risks associated with mood disorders in youngsters are serious and the evidence of efficacy in MDD is strong, there was consensus that it is ethically acceptable to withhold treatment until definitive evidence becomes available.

Although the identification, reporting, and monitoring of adverse drug events have not been carried out systematically in children and adolescents, some cautions are applicable, given potential interactions between pharmacological effects and development. For example, the tricyclic antidepressants, which are associated with adverse cardiac events and lethality when taken in overdose, may have unique cardiac effects in children (Emslie et al., 1999; Ryan and Varma, 1998). Given their lack of efficacy in placebo-controlled trials of major depression (Birmaher et al., 1996b), tricyclic antidepressants should be avoided in this population. Similarly, there is concern that the use of valproic acid in developing girls may be associated with polycystic ovaries (Geller and Luby, 1997; Ryan et al., 1999). Antipsychotic drug therapy in children and adolescents is often associated with marked weight gain and extrapyramidal side effects. Moreover, limited evidence documents efficacy in any pediatric mood disorder. Children may develop akathisia on antipsychotics and SSRIs, which can be misconstrued as ADHD (Hamilton and Opler, 1992; King et al., 1991). The long-term effects of lithium on renal and thyroid function, particularly in children, are also a concern (Geller and Luby, 1997; Hagino et al., 1995; Ryan et al., 1999). Systematic monitoring of drug therapy, particularly when multiple medications are involved, should include patients, parents, and clinicians as collaborators to increase the likelihood of recognizing adverse drug reactions.

In the context of the need for more well-controlled research on the treatment of mood disorders in children and adolescents, concerns about the ethics of placebo-controlled trials have been raised. Questions on the ethics as well as on the need for further placebo-controlled trials are likely to persist in light of recent data suggesting efficacy for SSRIs or cognitive-behavioral therapy. However, there was consensus that when carried out with proper informed consent and precise safety monitoring procedures, placebos can be an integral and ethically acceptable component of valid clinical studies. Rigorously designed studies of early-onset mood disorders, which include randomization of patients to placebo, are urgently needed. When the clinical trial evidence base evolves to the point at which effective treatments are consistently identified, the use of alternate non-placebo study designs should be considered (Charney et al., 2002; Fost, 2001). However, even in this situation, use of placebo may still be justified.

Controlled studies of the expanding number of antidepressants, mood stabilizers, psychotherapeutic interventions, and combined pharmacotherapy/psychotherapy need to be carried out in the pediatric and adolescent age groups. There is a particular need for studies in young children. These findings then need to be translated into effectiveness research in real-world clinical settings. The management of youngsters with mood disorders can be difficult at best, and attention to family dynamics, peer relationships, and coping skills is needed for favorable, long-term outcomes. Long-term safety and neurobiological consequences of the use of these interventions in the developing nervous system must be explored in subhuman primates and documented in clinical trials. The determination of the optimal duration of treatment, markers for relapse, and methods for relapse prevention also need to be determined.

As noted above, the findings of some but not all intervention studies have suggested that certain features of depression may be prevented. In contrast, research on prevention is silent with regard to early-onset BPD. Two studies that assessed the outcome of brief group sessions in at-risk adolescents demonstrated a significant reduction in depressive symptoms (Clarke et al., 1995; Jaycox et al., 1994). In other studies, a clinician-facilitated or lecture-based intervention program involved families in which one or both parents had a mood disorder. This intervention resulted in parents reporting significant sustained changes in focus on their children, communication, and understanding of the illness. Adolescents whose parents experienced improvement in their mood disorders reported better communication and improved overall functioning (Beardslee et al., 1996, 1997a,b). In contrast, one study of a home-based, family intervention program in depressed and nondepressed children and adolescents who had attempted suicide found that psychosocial intervention failed to reduce suicidal ideation in sub-
Services

Currently available services are inadequate to meet the needs of at-risk youngsters and those with mood disorders. More than 75% of children with mental health needs do not receive any services, and the unmet need is highest among minority youth (Mrazek and Haggerty, 1994). There are many barriers to the availability and delivery of care, including a scarcity of child psychiatrists and insufficient funding. In addition, the services infrastructure inadequately addresses the needs that span primary care, schools, mental health settings, foster care, social services, and the juvenile justice system. There is a marked lack of insurance parity, especially among minority populations, who often have difficulty obtaining healthcare, and poor private benefits for mental health care compared with general medical care. In addition, there are no national data on children or adolescents with mood disorders, which limits the research and service planning capabilities (Wells et al., 2001).

Child and adolescent psychiatrists are scarce, and care is often unavailable even for patients with insurance. The mean number of child psychiatrists per 100,000 youngsters is 6.7 nationwide. However, the national distribution is markedly inequitable, ranging from 0.8 per 100,000 in Mississippi to 18.9 per 100,000 in Massachusetts (Thomas and Holzer, 1999). The National Center for Health Workforce Information and Analysis estimates that the current number of child psychiatrists (approximately 6,300) will increase to approximately 8,300 by 2020, which falls far short of the nearly 30,000 needed to meet demand (AACAP Workforce Group, written communication, May 2003). Pediatricians and other primary care physicians are in a unique position to fill this void by recognizing and treating mood disorders in youth. However, time constraints, lack of reimbursement for case management, and poor training in diagnosis hinder the delivery of care (U.S. Public Health Service, 2000). Primary care physicians should work with local mental healthcare providers (e.g., psychiatrists, psychologists) to consult about interventions for youngsters with or at risk for mood disorders.

Given adequate training and time for assessment and follow-up, there was consensus that primary care physicians can diagnose and treat mood disorders in uncomplicated patients who are not seriously ill. Most primary care physicians are not adequately trained in the diagnosis and treatment of severe and/or complex mood disorders, particularly BPD, and often do not have sufficient time to provide adequate assessment and follow-up. In these instances, consultation with or referral to a child and adolescent psychiatrist is recommended, particularly for bipolar or suicidal patients. As such, there is a desperate need to establish an infrastructure to support closer alliances by way of primary care and mental health practitioners working with children.

Schools provide an underused setting where children at risk for mood disorders can be identified and referred for treatment. However, the scarcity of mental health programs and the lack of awareness among teachers and school administrators about mood disorders, in conjunction with large class size, limit opportunities for identifying children in need of care. There is a growing trend toward the use of school-based general health services, which provide an opportunity for clinicians to screen and educate students and, in some cases, to provide treatment for depression. However, such services are unlikely to be adequately used unless methods for identifying cases in need are implemented in a school-based setting. For example, parents might take advantage of screening instruments that could be accessed privately via the Internet. Alternatively, a closer alliance with mental health practitioners and school professionals might address the need for implementing better case-finding methods.

Clearly, public health education is needed for teachers, students, and families to address stigma and to increase their awareness of mood disorders and the opportunities for treatment. Discussion of mood disorders should be included in the health curricula with the same emphasis as is currently given to substance abuse, and teachers should be made aware of the cognitive effects of mood disorders, the risk of suicide, and the associated academic and interpersonal dysfunction that can help identify children at high risk.

Overcoming the barriers to care requires changes in practice and policy that include increasing personnel capacity, training front-line providers to be capable of recognizing mental health problems in children, and improving insurance coverage for uninsured and underinsured children. Some barriers may be removed once the costs of not preventing and not treating childhood mood disorders are identified. Enhance-
ment of clinical services will require relocating them into schools, homes, and other community settings, ensuring that they are evidence-based, developing policies to provide adequate reimbursement for clinical case management, ensuring that services are age-appropriate and culturally responsive to the diverse needs of all children and families, and developing strategies for long-term maintenance in community treatment settings.

In this era of limited resources, funding and personnel must be directed where they will be most useful and cost-effective for the greatest number of youths in need. Clearly, children at risk represent the largest number, which argues for a significant allocation of resources for evaluating prevention strategies and providing prevention services. Research needs to be carried out on promising interventions, such as prevention-oriented cognitive-behavioral therapy and integration of prevention research into research on other childhood psychiatric disorders. Mood disorders have an early age at onset and high rates of chronicity, recurrence, and suicide, all of which underlie concerns about the readiness of the current healthcare system to improve the morbidity of future adults and the next generation of children and adolescents. The next group of children deserving of resource allocation are those with mood dysregulation. The effect of early treatment on the course of illness. Research to identify factors leading to relapse and other negative sequelae needs to be carried out.

CONCLUSIONS

The public health crisis in the delivery of mental healthcare for children and adolescents with depression or BPD stems from multiple sources. Of these, stigma, lack of insurance parity, scarcity of child and adolescent psychiatrists, inadequate psychiatric training for pediatricians and other primary care providers, ill-equipped school systems, and insufficient funding to increase public awareness about mood disorders in youth are key factors that severely limit the capacity of the existing healthcare system to provide for children in need. In addition, insufficient funding for research on risk factors, diagnosis, treatment, and prevention impedes the advancement of the field. Addressing these issues requires immediate and sustained action from parents, schools, clinicians, the media, the research community, consumer advocates, and the government.

DBSA CONSENSUS DEVELOPMENT PANEL

DBSA Consensus Development Panel Co-Chairs
Dennis S. Charney, M.D.; Joseph T. Coyle, M.D.

Speakers

Workgroups

Workgroup 1. Risk Factors:

Workgroup 2. Diagnosis:
Paramjit Toor Jothi, M.D. (Workgroup Leader); Barbara Huff; Cynthia R. Pfeffer, M.D.; Uma Rao, M.D.; Neal D. Ryan, M.D.; Thomas J. Spencer, M.D.; Elizabeth B. Weller, M.D.

Workgroup 3. Treatment:
Gabrielle A. Carlson, M.D. (Workgroup Leader); John F. Curry, Ph.D.; Graham J. Emslie, M.D.; Martha Hellander, J.D.; Michael Strober, Ph.D.; Ordean L. Torstenson, M.D.; Karen Dineen Wagner, M.D., Ph.D.

Workgroup 4. Services and Prevention:
David Reiss, M.D. (Workgroup Leader); William R. Beardslee, M.D.; Sherry A. Glied, Ph.D.; Kimberly Hoagwood, Ph.D.; Beverly Benson Long, M.S., M.P.H.; Kenneth B. Wells, M.D., M.P.H.; Julie M. Zito, Ph.D.

Conference Sponsor
Depression and Bipolar Support Alliance; Lydia Lewis, Executive Director

Writer
Sally K. Laden, M.S.

DBSA Consensus Development Panel Affiliations
Harvard University, Boston (Drs. Beardslee, Coyle, Kagan, Kesler, and Spencer); SUNY Stony Brook (Dr. Carlson); NIMH, Bethesda


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