

Childhood and Adolescent Depression

SHASHI K. BHATIA, M.D., and SUBHASH C. BHATIA, M.D., *Creighton University, Department of Psychiatry, Omaha, Nebraska*

Major depression affects 3 to 5 percent of children and adolescents. Depression negatively impacts growth and development, school performance, and peer or family relationships and may lead to suicide. Biomedical and psychosocial risk factors include a family history of depression, female sex, childhood abuse or neglect, stressful life events, and chronic illness. Diagnostic criteria for depression in children and adolescents are essentially the same as those for adults; however, symptom expression may vary with developmental stage, and some children and adolescents may have difficulty identifying and describing internal mood states. Safe and effective treatment requires accurate diagnosis, suicide risk assessment, and use of evidence-based therapies. Current literature supports use of cognitive behavior therapy for mild to moderate childhood depression. If cognitive behavior therapy is unavailable, an antidepressant may be considered. Antidepressants, preferably in conjunction with cognitive behavior therapy, may be considered for severe depression. Tricyclic antidepressants generally are ineffective and may have serious adverse effects. Evidence for the effectiveness of selective serotonin reuptake inhibitors is limited. Fluoxetine is approved for the treatment of depression in children eight to 17 years of age. All antidepressants have a black box warning because of the risk of suicidal behavior. If an antidepressant is warranted, the risk/benefit ratio should be evaluated, the parent or guardian should be educated about the risks, and the patient should be monitored closely (i.e., weekly for the first month and every other week during the second month) for treatment-emergent suicidality. Before an antidepressant is initiated, a safety plan should be in place. This includes an agreement with the patient and the family that the patient will be kept safe and will contact a responsible adult if suicidal urges are too strong, and assurance of the availability of the treating physician or proxy 24 hours a day to manage emergencies. (*Am Fam Physician* 2007;75:73-80, 83-4. Copyright © 2007 American Academy of Family Physicians.)

► **Patient information:** A handout on depression in children and adolescents, written by the authors of this article, is provided on page 83.

At any given time, up to 15 percent of children and adolescents have some symptoms of depression. Five percent of those nine to 17 years of age meet the criteria for major depressive disorder,^{1,2} and 3 percent of adolescents have dysthymic disorder.³ The incidence of depressive disorders markedly increases after puberty. By 14 years of age, depressive disorders are more than twice as common in girls as in boys, possibly because of differences in coping styles or hormonal changes during puberty.⁴ Adolescent depressive disorders often have a chronic, waxing-and-waning course, and there is a two- to fourfold risk of depression persisting into adulthood.^{5,6} Depression impacts growth and development, school performance, and peer or family relationships, and it can be fatal. Major depressive disorder is a leading cause of youth suicidal behavior and suicide.^{7,8}

More than 70 percent of children and adolescents with depressive disorders or other serious mood disorders do not receive appropriate diagnosis and treatment.⁹ Possible

reasons for this may be the stigma attached to these disorders, an atypical presentation, a lack of adequate child mental health training for health care professionals, an inadequate number of child psychiatrists, and inequalities in mental health care insurance.

Underdiagnosis and undertreatment are greater problems in children younger than seven years, in part because of this age group's limited ability to communicate negative emotions and thoughts with language and consequent tendency toward somatization. Thus, young children with depression may present with general aches and pains, headaches, or stomachaches. Additionally, if a parent has major depressive disorder, he or she may minimize the child's depressive symptoms through a lack of awareness or an unwillingness to recognize symptoms that may be similar to his or her own.

Risk Factors

Risk factors for child and adolescent depressive disorders include biomedical and psychosocial factors (*Table 1*).^{1,3,4,6,10-15}

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Tricyclic antidepressants should not be used to treat childhood or adolescent depression.	A	18, 40, 41
Selective serotonin reuptake inhibitors have limited evidence of effectiveness in children and adolescents and should be reserved for treatment of severe major depression.	B	42-44
Cognitive behavior therapy is effective for the treatment of mild to moderate depression.	A	18, 37-39
Children and adolescents taking antidepressants should be monitored closely for suicidal thoughts and behavior.	C	53
Depression should be treated for a minimum of six months.	C	29

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 13 or <http://www.aafp.org/afpsort.xml>.

Approximately two thirds of children and adolescents with major depressive disorder also have another mental disorder.¹⁵ It is essential that physicians recognize and treat associated psychiatric comorbidities; the most common of these are dysthymic disorder, anxiety disorders, attention-deficit/hyperactivity disorder, oppositional defiant disorder, and substance use disorder.

Screening

It is unclear whether routinely screening all children and adolescents for depression is beneficial in the primary care setting.¹⁶ Physicians who choose to screen may use the Children's Depression Inventory (CDI), a reliable and

valid self-rating scale for boys and girls seven to 17 years of age.¹⁷⁻¹⁹ The CDI scale requires a first-grade reading level; it is available in long (27-item) and short (10-item) forms and in parent and teacher versions. Each item on the scale is scored from 0 to 2 according to the presence or absence of symptoms in the previous two weeks: 0 indicates symptom absence, 1 indicates mild symptoms, and 2 indicates a definite symptom. The raw score is plotted on a scoring grid and converted to a T-score. A raw score greater than 20 on the long form or greater than 7 on the short form and a T-score greater than 65 are clinically significant.

Presentation

Juvenile depression may manifest in different forms. As stated above, children younger than seven years may not be able to describe their internal mood state and may express their distress through vague somatic symptoms or pain. Irritable mood may be the cause of angry, hostile behavior. Impaired attention, poor concentration, and anxiety may resemble attention-deficit/hyperactivity disorder, and substance abuse may be a means of self-medication for depression.

Diagnosis

Diagnosis of primary depressive mood disorders (*Table 2*) requires that physicians rule out depression from medical causes, such as endocrinopathies, malignancies, chronic diseases, infectious mononucleosis, anemia, and vitamin deficiency (especially folic acid),¹⁰ and from medications, such as isotretinoin (Accutane).¹³ If any of these causes are present, the condition is referred to as secondary depressive mood disorder or depressive mood disorder secondary to medical conditions. Lack of improvement following treatment or medication discontinuation warrants further evaluation and treatment.

Major depressive disorder is the most severe of the depressive mood disorders. The *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed., criteria for

TABLE 1

Risk Factors for Child and Adolescent Depressive Disorders

Biomedical factors

- Chronic illness (e.g., diabetes)¹⁰
- Female sex⁴
- Hormonal changes during puberty^{4,11}
- Parental depression or family history of depression^{1,12}
- Presence of specific serotonin-transporter gene variants¹¹
- Use of certain medications (e.g., isotretinoin [Accutane])¹³

Psychosocial factors¹²

- Childhood neglect or abuse (physical, emotional, or sexual)
- General stressors including socioeconomic deprivations
- Loss of a loved one, parent, or romantic relationship

Other factors

- Anxiety disorder^{6,14}
- Attention-deficit/hyperactivity, conduct, or learning disorders^{12,15}
- Cigarette smoking¹²
- History of depression³

Information from references 1, 3, 4, 6, and 10 through 15.

diagnosing major depressive disorder in children and adolescents are similar to those for adults (Table 3).²⁰⁻²⁴

If substance abuse is present, an independent diagnosis of major depression requires the presence of depression before substance abuse or during periods of remission. Concurrent treatment of substance use disorder and depression is needed to improve outcomes for both.²⁵

Adjustment disorder with depressed mood is the most common depressive mood disorder in children and adolescents. Symptoms start within three months of an identifiable stressor (e.g., loss of a relationship), with distress in excess of what would be expected and interference with social, occupational, or school functioning. Symptoms should not meet criteria for another psychiatric disorder, are not caused by bereavement, and do not last longer than six months after the stressor has stopped.

Dysthymic disorder is a chronic, milder form of depression characterized by a depressed or irritable mood (indicated subjectively or described by others) present for more days than not for at least one year (as opposed to two years for adults). Two of the following additional symptoms also are required: changes in appetite, sleep difficulty, fatigue, low self-esteem, poor concentration or difficulty

with making decisions, and feelings of hopelessness.²⁰ About 70 percent of children and adolescents with dysthymic disorder eventually develop major depression.²⁶

Diagnosis of minor depression requires the presence of two out of the nine symptoms for major depression (Table 3), one being depressed mood or decreased interest, and a time course similar to that of major depression. If present between the episodes of major depression, minor depression can be a risk factor for relapse.²⁰

Atypical depression is characterized by hypersomnia, increased appetite with carbohydrate craving, weight gain, interpersonal rejection sensitivity, feeling of heaviness in the arms and legs, and reactivity of mood.²⁰ It is relatively common in children and adolescents.²⁷

Presence of depressed mood, increased sleep, decreased appetite, and social isolation between October and February of two consecutive years suggests seasonal affective disorder.

Although less common, bipolar disorder is an important differential diagnosis. In 40 percent of children and adolescents with bipolar disorder, the illness begins with a major depressive episode.² Risk factors for bipolar disorder are acute and early onset of depression, presence of psychotic symptoms (e.g., hallucinations), significant psychomotor slowing, family history of bipolar disorder, any mood disorder in three consecutive generations of family members, and antidepressant-induced mania.²⁸ Physicians should maintain a higher level of surveillance in patients at greater risk of bipolar disorder.

In severe major depression with psychosis, auditory hallucinations (often criticizing the patient) rather than delusions (as occur in adults) are present. This age-related variability in psychotic symptoms may be a result of differences in cognitive maturation. Treatment of major depressive disorder with psychosis requires the combination of an antidepressant and an antipsychotic medication.²⁹ Patients with this disorder are at a greater risk of suicide and often require inpatient psychiatric admission.

Suicide Risk Assessment

During the first visit, physicians should assess the suicide risk of patients with depression and decide on the most appropriate treatment venue. Depressive disorders are the most common diagnoses present in all suicides. Twenty percent of teenagers

TABLE 2
Key Clinical Decision Points for Depressive Disorders

Question	Action
Is this depression caused by a general medical condition, a medication, or both?	Rule out other causes of depressive mood disorders.
Is this depression related to drug or alcohol abuse?	Determine whether secondary to or complicated by substance abuse.
Is this depression related to a reaction to a stressful life event?	Consider a diagnosis of adjustment disorder.
Is this a chronic, mild depression?	Consider dysthymic disorder.
Is this another type of depressive disorder?	Consider minor depression, bipolar depression, depression caused by seasonal affective disorder, or atypical depression.
Is this major depression?	Apply DSM-IV criteria (see Table 3). Assess for severity and psychotic features.
Is there a coexisting mental illness?	Dysthymic disorder, anxiety disorders, attention-deficit/hyperactivity disorder, oppositional defiant disorder, and substance use disorder are common comorbidities.
Is this a dangerous depression?	Perform suicide risk assessment.

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th ed.

TABLE 3

Criteria for Major Depressive Episode in Adults, Children, and Adolescents

<i>Adults</i>	<i>Children and adolescents</i>
A. Five (or more) of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is (1) depressed mood or (2) loss of interest or pleasure.	
(1) Depressed mood most of the day, nearly every day, as indicated by subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)	Mood can be depressed or irritable. Children with immature cognitive-linguistic development may not be able to describe inner mood states and therefore may present with vague physical complaints, sad facial expression, or poor eye contact. Irritable mood may appear as "acting out"; reckless behavior; or hostile, angry interactions. Adult-like mood disturbance may occur in older adolescents.
(2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by subjective account or observation made by others)	Loss of interest can be in peer play or school activities.
(3) Significant weight loss when not dieting, or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day	Children may fail to make expected weight gain rather than losing weight.
(4) Insomnia or hypersomnia nearly every day	Similar to adults
(5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feeling of restlessness or being slowed down)	Concomitant with mood change, hyperactive behavior may be observed.
(6) Fatigue or loss of energy nearly every day	Disengagement from peer play, school refusal, or frequent school absences may be symptoms of fatigue.
(7) Feeling of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)	Child may present with self-depreciation (e.g., "I'm stupid," "I'm a retard"). Delusional guilt usually is not present.
(8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (by subjective account or as observed by others)	Problems with attention and concentration may be apparent as behavioral difficulties or poor performance in school.
(9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide	There may be additional nonverbal cues for potentially suicidal behavior, such as giving away a favorite collection of music or stamps.
B. Symptoms do not meet the criteria for mixed bipolar disorder.	Same as adults
C. Symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.	Clinically significant impairment of social or school functioning is present. Adolescents also may have occupational dysfunction.
D. Symptoms are not caused by the direct physiologic effects of a substance (e.g., drug of abuse, medication) or a general medical condition (e.g., hypothyroidism).	Similar to adults
E. Symptoms are not caused by bereavement—i.e., after the loss of a loved one, the symptoms persist for longer than two months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.	Psychotic symptoms in severe major depression, if present, are more often auditory hallucinations (usually criticizing the patient) than delusions.

Adapted with permission from American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR*. 4th ed. rev. Washington, D.C.: American Psychiatric Association, 2000:356, with additional information from references 21 through 24.

seriously contemplate suicide,³⁰ and 8 percent attempt it.³¹ In 2001, there were 1,833 suicides in children and adolescents 10 to 18 years of age; and in 2000, suicide was the third leading cause of death among those 10 to 19 years of age.³¹

Suicidal communication in any form must be

taken seriously. Documentation of suicide risk should include high-risk and protective factors for suicide (Table 4).^{1,30-36} Patients with multiple high-risk factors should be referred to a child and adolescent psychiatrist. However, patients with low-risk and protective factors (e.g., a close, warm, supportive family; religious beliefs

TABLE 4

Risk Factors and Protective Factors for Suicide in Children and Adolescents

<i>High-risk factors</i>	<i>Protective or low-risk factors</i>
Biodemographics	
Age: late teens through early 20s ³² ; 20 percent of teenagers contemplate suicide, ³⁰ and 8 percent attempt it. ³¹	Black female child
Sex: ideation and attempts more common in females ³² ; completed suicides five times more common in males. ³²	
Ethnicity: teenage suicides are more common in whites and Hispanics than in blacks; rates are highest in Native American teens and lowest in Asian teens and those from the Pacific islands.	
History	
Major depression: increases the risk of suicide 12-fold for both sexes, ¹ especially if hopelessness is a symptom	No current depression
Substance abuse: increases the risk of suicide ¹ about twofold	No current alcohol or substance abuse
Conduct disorder: linked to one third of suicides in adolescent boys ¹ and increases overall risk twofold ¹	Good problem-solving and coping skills
Current stressors or losses (e.g., trouble in school or with the law, loss of romantic relationship, unwanted pregnancy, intense humiliation) ³³	No current stressors or losses
Physical or sexual abuse ³²	No history of physical or sexual abuse
Minimal communication with parents ³⁴	Close supportive family relationships and good communications with parents
	Availability of parental support and close supervision during stressful life event
	Strong religious belief or faith
	Positive, hopeful outlook about future with specific positive and concrete plans and goals
	Ability to articulate reasons to live
	Ambivalence about suicide
History of suicidal behavior	
Suicidal thoughts with plan: specific plans for suicide and the means to carry it out, including nonverbal suicidal behaviors (e.g., giving away valued possessions or collections)	No active suicidal thoughts or intent; no nonverbal suicidal behaviors
Previous suicide attempt: one of the strongest predictors of completed suicide ¹	No history of suicide attempt
Family history of suicide and depression ^{35,36}	No family history of suicide
Availability of firearms or toxic substances	No access to firearms or toxic substances
Contagion effect	
Media coverage of suicide: imitation plays a part in suicidal behavior, often following intense media coverage of a celebrity suicide or a string of suicides in school. ³²	No extensive media coverage of suicide

Information from references 1 and 30 through 36.

against suicide; a positive future outlook) are less likely to harm themselves³² and may be treated as outpatients.

Parents or guardians should be asked to remove firearms and toxic substances, including nonprescription medications, from the patient's environment and to provide appropriate supervision, especially during crises in the child's life. They should be made aware of the suicide risk that exists during the early phases of antidepressant treatment and the need for additional supervision.

Treatment

Treatment options depend on the clinical situation and include cognitive behavior therapy alone or with anti-

depressants. The risk/benefit ratio of antidepressant use should be considered. Physicians choosing to prescribe antidepressants must obtain fully informed consent and closely monitor clinical progress, behavioral activation (e.g., impulsivity, daring, silliness, agitation), and suicidality, especially in the initial stages of treatment.²⁹ Follow-up should take place each week during the first month and every other week during the second month; subsequent frequency of follow-up visits should be determined by the clinical care needs of the patient. The choice of an antidepressant also may be guided by patient or family history of antidepressant response; side-effect profile; and drug-drug, drug-disease, and drug-food interactions.

Childhood Depression

COGNITIVE BEHAVIOR THERAPY AND COUNSELING

Cognitive behavior therapy is effective for mild to moderate childhood depression.^{18,37-39} It entails reality-based challenges to pervasive, automatic, negative, distorted thoughts, with the goal of helping patients steer out of a negative view of themselves, the past, and the future.

Children taking antidepressants should be monitored closely for suicidality.

Interpersonal psychotherapy is directed at resolving grief, coming to terms with interpersonal role transitions or role disputes, and correcting interpersonal skill deficits.¹⁸

Office-based counseling may involve: (1) educating patients about healthy coping skills, problem solving, conflict resolution, social and assertiveness skills, and relaxation techniques; (2) educating parents about realistic, age-appropriate expectations and nonjudgmental, noncritical patterns of communication; and (3) supporting healthy behaviors, healthy psychological defenses, and healthy relationships.

ANTIDEPRESSANTS

The effectiveness and safety of various medications for depression in children and adolescents have been systematically studied and reviewed.^{18,37-51} Tricyclic antidepressants are ineffective in children and have limited effectiveness in adolescents, with safety concerns in both groups.^{18,40,41} There also is limited evidence for the effectiveness of selective serotonin reuptake inhibitors (SSRIs). In a systematic review of published and unpublished trials of SSRIs, published reports suggested favorable risk/benefit profiles for some SSRIs, but the addition of unpublished data shifted the risk/benefit ratio toward unfavorable, with the exception of fluoxetine (Prozac).⁴² In children and adolescents, there is limited or no evidence evaluating the use of lithium, monoamine oxidase inhibitors, St. John's wort, and venlafaxine (Effexor).¹⁸

Most trials assessing the use of SSRIs in children and adolescents are of short duration, have small numbers of participants, and are industry-sponsored, thus limiting their ability to detect or report major adverse events. Furthermore, there are high placebo response rates and methodologic flaws in studies supporting SSRI use.^{43,52} For example, although one study indicated that fluoxetine plus cognitive behavior therapy was the best choice, the success of fluoxetine was found only in the unblinded arms of the study: the blinded arms showed no better response than with placebo.³⁹ Finally, most studies are underpowered to address the outcome of suicide.

Concerns about the effectiveness, adverse effects

(Table 5),¹⁸ and safety of antidepressant use have led to important regulatory changes in several countries. Of particular concern is the association of the drugs with increased suicidal behavior.⁵³ For example, the U.S. Food and Drug Administration (FDA) counsels against using paroxetine (Paxil) in children and adolescents because of effectiveness and safety concerns.⁵⁴ The Committee on Safety of Medicines in the United Kingdom analyzed SSRIs and considers the risk/benefit ratio to be favorable only for fluoxetine.⁴⁴ Additionally, fluoxetine is the only SSRI approved by the FDA for the treatment of depression in children eight to 17 years of age. Fluoxetine therefore may be considered for the treatment of moderate to severe depression in children. However, current evidence is inadequate to determine whether safety and effectiveness concerns represent a class effect or individual drug properties; thus, all antidepressants have a black box warning for increased risk of suicidal thoughts and behavior in children and adolescents being treated for depression.⁵⁵

Before initiating an antidepressant, physicians should ensure that a safety plan is in place. This includes an agreement with the patient and the family that the patient will be kept safe and will contact a responsible adult if suicidal urges are too strong, and assurance of the availability of the treating physician or proxy 24 hours a day to manage emergencies.

DURATION AND MAINTENANCE OF TREATMENT

Evidence suggests that early intervention for depression in children can improve long-term outcomes.⁵⁶ Duration of treatment depends on the number of previous episodes of depression. A minimum of six months of

TABLE 5
Common Adverse Effects of SSRIs

With SSRI use	With decrease or discontinuation of SSRI
Akathisia or motor restlessness	Dizziness
Dizziness	Drowsiness
Drowsiness	Fatigue
Gastrointestinal symptoms	Headache
Headache	Impaired concentration
Treatment-emergent agitation or hostility	Lightheadedness
Tremor	Nausea

SSRI = selective serotonin reuptake inhibitor.
Information from reference 18.

treatment is recommended in first episodes, with the drug tapered slowly over six to eight weeks to minimize the risk of withdrawal syndrome. For second episodes of depression, at least one year of treatment should be given. Patients with two or three previous episodes should be treated for at least one to three years, and patients with more than three previous episodes of depression should be treated indefinitely, especially if the episodes are severe or have psychotic features or suicidality.²⁹ The dosage at which symptom relief is achieved often is the dosage for maintenance. Adjunctive psychotherapy and family therapy can help consolidate the gains.²⁹ No optimal treatment duration for therapy has been determined.

A child psychiatric consultation is helpful for children with severe recurrent depression or treatment-resistant depression. A diagnosis of treatment-resistant depression requires failure of treatment with two antidepressants administered in adequate dosage for an adequate duration (at least six weeks). Patients with treatment-resistant depression may require additional medication augmentation (e.g., lithium). Adjunctive cognitive behavior therapy also improves outcomes. Physicians uncomfortable with prescribing complex therapies should consider referral to a child psychiatrist, especially for patients with multiple comorbidities.

The authors thank Christopher Kratochvil, M.D., Daniel R. Wilson, M.D., Ph.D., and Frederick Petty, M.D., Ph.D., for their review of and suggestions for the manuscript.

The Authors

SHASHI K. BHATIA, M.D., is a professor of psychiatry, child and adolescent psychiatry, and pediatrics, and director of the Division of Child and Adolescent Psychiatry at Creighton University School of Medicine, Omaha, Neb. She also is medical director of the Child and Adolescent Residential Treatment Center at Alegent Health Midlands Hospital, Papillon, Neb. Dr. Bhatia received her medical degree from Panjab University, Chandigarh, India. She completed a residency in obstetrics and gynecology at the Postgraduate Institute of Medical Education and Research, Chandigarh, and a residency in psychiatry and a fellowship in child and adolescent psychiatry at Creighton University.

SUBHASH C. BHATIA, M.D., is professor and vice chair of the Department of Psychiatry, Creighton University, and associate professor at the University of Nebraska College of Medicine, Omaha. He also is chief of the Mental Health and Behavioral Sciences Department at the Department of Veterans Affairs, Nebraska–Western Iowa Health Care System, Omaha. Dr. Bhatia received his medical degree from Panjab University and a graduate degree from the Postgraduate Institute of Medical Education and Research, Chandigarh. He completed a residency in psychiatry at Creighton University.

Address correspondence to Subhash C. Bhatia, M.D., Chief, Mental Health and Behavioral Sciences Dept., VA Nebraska Western Iowa Health Care System, 4101 Woolworth Ave., Omaha, NE 68105 (e-mail: subhash.bhatia@med.va.gov). Reprints are not available from the authors.

Author disclosure: Nothing to disclose.

REFERENCES

- Shaffer D, Gould MS, Fisher P, Trautman P, Moreau D, Kleinman M, et al. Psychiatric diagnosis in child and adolescent suicide. *Arch Gen Psychiatry* 1996;53:339-48.
- Birmaher B, Ryan ND, Williamson DE, Brent DA, Kaufman J, Dahl RE, et al. Childhood and adolescent depression: a review of the past 10 years. Part I. *J Am Acad Child Adolesc Psychiatry* 1996;35:1427-39.
- Garrison CZ, Waller JL, Cuffe SP, McKeown RE, Addy CL, Jackson KL. Incidence of major depressive disorder and dysthymia in young adolescents. *J Am Acad Child Adolesc Psychiatry* 1997;36:458-65.
- Angold A, Costello EJ, Erkanli A, Worthman CM. Pubertal changes in hormone levels and depression in girls. *Psychol Med* 1999;29:1043-53.
- Pine DS, Cohen E, Cohen P, Brook J. Adolescent depressive symptoms as predictors of adult depression: moodiness or mood disorder? *Am J Psychiatry* 1999;156:133-5.
- Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Arch Gen Psychiatry* 1998;55:56-64.
- Kann L, Kinchen SA, Williams BI, Ross JG, Lowry R, Grunbaum JA, et al. Youth Risk Behavior Surveillance—United States, 1999. State and local YRBSS Coordinators. *J Sch Health* 2000;70:271-85.
- Brent DA. Assessment and treatment of the youthful suicidal patient. *Ann N Y Acad Sci* 2001;932:106-28.
- National Institute of Mental Health. Blueprint for change: research on child and adolescent mental health. Bethesda, Md.: National Advisory Mental Health Council's Workgroup on Child and Adolescent Mental Health Intervention, Prevention, and Deployment, 2001. Accessed September 21, 2006, at: <http://www.nimh.nih.gov/publicat/nimhblueprint.pdf>.
- National Institute of Mental Health. Depression in children and adolescents: a fact sheet for physicians. Bethesda, Md.: National Institute of Mental Health. Accessed September 21, 2006, at: <http://www.mental-health-matters.com/articles/article.php?artID=320>.
- Hariri AR, Mattay VS, Tessitore A, Kolachana B, Fera F, Goldman D, et al. Serotonin transporter genetic variation and the response of the human amygdala. *Science* 2002;297:400-3.
- 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;38:289-96.
- Wysowski DK, Pitts M, Beitz J. An analysis of reports of depression and suicide in patients treated with isotretinoin. *J Am Acad Dermatol* 2001;45:515-9.
- Pine DS, Cohen P, Brook J. Adolescent fears as predictors of depression. *Biol Psychiatry* 2001;50:721-4.
- Angold A, Costello EJ, Erkanli A. Comorbidity. *J Child Psychol Psychiatry* 1999;40:57-87.
- U.S. Preventive Services Task Force. Screening for depression: recommendations and rationale. *Ann Intern Med* 2002;136:760-4.
- Kovacs M. The Children's Depression Inventory. North Tonawanda, N.Y.: Multi-Health Systems, 1992.
- Hazell P. Depression in children and adolescents. *Clin Evid* 2004;12:427-42.
- Timbremont B, Braet C, Dreesen L. Assessing depression in youth: relation between the Children's Depression Inventory and a structured interview. *J Clin Child Adolesc Psychol* 2004;33:149-57.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR. 4th ed. rev. Washington, D.C.: American Psychiatric Association, 2000.
- Birmaher B, Williamson DE, Dahl RE, Axelson DA, Kaufman J, Dorn LD, et al. Clinical presentation and course of depression in youth: does onset in childhood differ from onset in adolescence? *J Am Acad Child Adolesc Psychiatry* 2004;43:63-70.

Childhood Depression

22. Weller EB, Weller RA, Danielyan AK. Mood disorders in prepubertal children. In: Wiener JM, Dulcan MK, eds. *Textbook of Child and Adolescent Psychiatry*. 3rd ed. Washington, D.C.: American Psychiatric Publishing, 2004:411-35.
23. Weller EB, Weller RA, Danielyan AK. Mood disorders in adolescents. In: Wiener JM, Dulcan MK, eds. *Textbook of Child and Adolescent Psychiatry*. 3rd ed. Washington, D.C.: American Psychiatric Publishing, 2004:437-81.
24. Chambers WJ, Puig-Antich J, Tabrizi MA, Davies M. Psychotic symptoms in prepubertal major depressive disorder. *Arch Gen Psychiatry* 1982;39:921-7.
25. Riggs PD, Davies RD. A clinical approach to integrating treatment for adolescent depression and substance abuse. *J Am Acad Child Adolesc Psychiatry* 2002;41:1253-5.
26. Kovacs M, Akiskal HS, Gatsonis C, Parrone PL. Childhood-onset dysthymic disorder. Clinical features and prospective naturalistic outcome. *Arch Gen Psychiatry* 1994;51:365-74.
27. Williamson DE, Birmaher B, Brent DA, Balach L, Dahl RE, Ryan ND. Atypical symptoms of depression in a sample of depressed child and adolescent outpatients. *J Am Acad Child Adolesc Psychiatry* 2000;39:1253-9.
28. Akiskal HS. Developmental pathways to bipolarity: are juvenile-onset depressions pre-bipolar? *J Am Acad Child Adolesc Psychiatry* 1995;34:754-63.
29. Birmaher B, Brent DA, Benson RS, for the American Academy of Child and Adolescent Psychiatry. Summary of the practice parameters for the assessment and treatment of children and adolescents with depressive disorders. *J Am Acad Child Adolesc Psychiatry* 1998;37:1234-8.
30. Grunbaum JA, Kann L, Kinchen SA, Williams B, Ross JG, Lowry R, et al. Youth risk behavior surveillance—United States, 2001. *MMWR Surveill Summ* 2002;51:1-62.
31. Anderson RN. Deaths: leading causes for 2000. *Natl Vital Stat Rep* 2002;50:1-85.
32. Gould MS, Greenberg T, Velting DM, Shaffer D. Youth suicide risk and preventive interventions: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry* 2003;42:386-405.
33. Johnson JG, Cohen P, Gould MS, Kasen S, Brown J, Brook JS. Childhood adversities, interpersonal difficulties, and risk for suicide attempts during late adolescence and early adulthood. *Arch Gen Psychiatry* 2002;59:741-9.
34. Gould MS, Fisher P, Parides M, Flory M, Shaffer D. Psychosocial risk factors of child and adolescent completed suicide. *Arch Gen Psychiatry* 1996;53:1155-62.
35. Agerbo E, Nordentoft M, Mortensen PB. Familial, psychiatric, and socioeconomic risk factors for suicide in young people: nested case-control study. *BMJ* 2002;325:74.
36. McGuffin P, Marusic A, Farmer A. What can psychiatric genetics offer suicidology? *Crisis* 2001;22:61-5.
37. Harrington R, Whittaker J, Shoebridge P. Psychological treatment of depression in children and adolescents. A review of treatment research. *Br J Psychiatry* 1998;173:291-8.
38. Reinecke MA, Ryan NE, DuBoise DL. Cognitive-behavioral therapy of depression and depressive symptoms during adolescence: a review and meta-analysis. *J Am Acad Child Adolesc Psychiatry* 1998;37:26-34.
39. March J, Silva S, Petrycky S, Curry J, Wells K, Fairbank J, et al., for the Treatment for Adolescents with Depression Study (TADS) Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *JAMA* 2004;292:807-20.
40. Hazell P, O'Connell D, Heathcote D, Robertson J, Henry D. Efficacy of tricyclic drugs in treating child and adolescent depression: a meta-analysis. *BMJ* 1995;310:897-901.
41. Maneeton N, Srisurapanont M. Tricyclic antidepressants for depressive disorders in children and adolescents: a meta-analysis of randomized-controlled trials. *J Med Assoc Thai* 2000;83:1367-74.
42. Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. *Lancet* 2004;363:1341-5.
43. Courtney DB. Selective serotonin reuptake inhibitor and venlafaxine use in children and adolescents with major depressive disorder: a systematic review of published randomized controlled trials. *Can J Psychiatry* 2004;49:557-63.
44. Medicines and Healthcare Products Regulatory Agency. Selective serotonin re-uptake inhibitors (SSRIs). London, U.K.: Commission on Human Medicines, 2006. Accessed September 21, 2006, at: http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=242.
45. Hazell P, O'Connell D, Heathcote D, Henry D. Tricyclic drugs for depression in children and adolescents. *Cochrane Database Syst Rev* 2002;(2): CD002317.
46. Emslie GJ, Heiligenstein JH, Wagner KD, Hoog SL, Ernest DE, Brown E, et al. Fluoxetine for acute treatment of depression in children and adolescents: a placebo-controlled, randomized clinical trial. *J Am Acad Child Adolesc Psychiatry* 2002;41:1205-15.
47. Wagner KD, Ambrosini P, Rynn M, Wohlberg C, Yang R, Greenbaum MS, et al., for the Sertraline Pediatric Depression Study Group. Efficacy of sertraline in the treatment of children and adolescents with major depressive disorder: two randomized controlled trials. *JAMA* 2003;290:1033-41.
48. Keller MB, Ryan ND, Strober M, Klein RG, Kutcher SP, Birmaher B, et al. Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial. *J Am Acad Child Adolesc Psychiatry* 2001;40:762-72.
49. Wagner KD, Robb AS, Findling RL, Jin J, Gutierrez MM, Heydorn WE. A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents. *Am J Psychiatry* 2004;161:1079-83.
50. Mulrow CD, Williams JW Jr, Trivedi M, Chiquette E, Aguilar C, Cornelli JE, et al. Treatment of depression—newer pharmacotherapies. *Evid Rep Technol Assess (Summ)* 1999;7:1-4.
51. Gunnell D, Ashby D. Antidepressants and suicide: what is the balance of benefit and harm. *BMJ* 2004;329:34-8.
52. Garland EJ. Facing the evidence: antidepressant treatment in children and adolescents. *CMAJ* 2004;170:489-91.
53. Fergusson D, Doucette S, Glass KC, Shapiro S, Healy D, Hebert P, et al. Association between suicide attempts and selective serotonin reuptake inhibitors: systematic review of randomised controlled trials [Published correction appears in *BMJ* 2005;330:653]. *BMJ* 2005;330:396-402.
54. U.S. Food and Drug Administration (FDA). FDA issues public health advisory entitled: Reports of suicidality in pediatric patients being treated with antidepressant medications for major depressive disorder (MDD) [FDA Talk Paper]. Washington, D.C.: FDA, October 27, 2003. Accessed September 22, 2006, at: <http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01256.html>.
55. "Black Box" warning for antidepressants [transcript]. Washington, D.C.: U.S. Food and Drug Administration, December 2004. Accessed September 21, 2006, at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/prnter.cfm?id=275>.
56. Duffy A. Toward effective early intervention and prevention strategies for major affective disorders: a review of antecedents and risk factors. *Can J Psychiatry* 2000;45:340-8.