

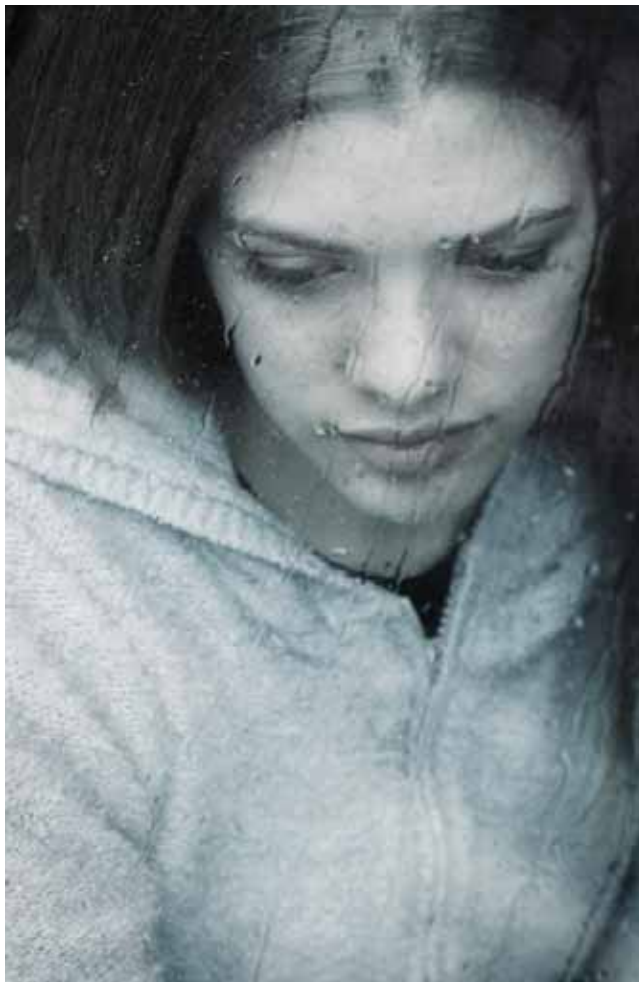
EARN CATEGORY I CME CREDIT by reading this article and the article beginning on page 18 and successfully completing the posttest on page 44. Successful completion is defined as a cumulative score of at least 70% correct. This material has been reviewed and is approved for 1 hour of clinical Category I (Preapproved) CME credit by the AAPA. The term of approval is for 1 year from the publication date of March 2009.

LEARNING OBJECTIVES

- Describe the different classifications of depressive disorder and their symptoms
- Discuss how to recognize the child or adolescent suffering from depression
- Review the pathogenesis of depression
- Explain how to treat depressive disorders in children and adolescents

How to recognize depressive disorders in children and adolescents

Mental health disorders are difficult to diagnose in the nonadult patient. Complications range from limited language and communications skills to a struggle for autonomy.



Punchstock

Brett Reisman Greenberg, PA-C

Depression was once thought to affect only adults. Clinical evidence has revealed that children and adolescents experience both depressive symptoms and depressive disorders.^{1,2}

However, the limited language skills of young children and adolescents' reluctance to cooperate can make it difficult for clinicians to diagnose these disorders in the pediatric population. This article reviews the criteria used to make an accurate diagnosis and initiate the most appropriate treatments.

Depressive disorders are divided into three classifications: major depressive disorder (MDD), dysthymic disorder (DD), and depressive disorder not otherwise specified (NOS). Approximately 2% of children and 4% to 8% of adolescents suffer from MDD.^{3,4} Although only a few studies have reported on the prevalence of DD, it is reported to be 0.6% to 1.7% of children and 1.6% to 8% of adolescents.⁵ Combined, these statistics indicate a collective incidence of MDD during childhood and adolescence of 15% to 20%.⁶ Although the criteria for these classifications differ, treatment is fairly similar.

Major depressive disorder A diagnosis of MDD is made when the patient is in a depressed mood or has a consistent loss of interest in daily activities for at least 2 weeks. The disorder is characterized by one or more major depressive episodes with no manic, hypomanic, or mixed episodes of mood disturbance. An adolescent must exhibit at least five of the symptoms of depression, as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*, in order to meet the criteria for a diagnosis of MDD⁷ (see Table 1, page 40). These symptoms must not be the result of drug abuse, medications, a medical condition, or the loss of a loved one.

Dysthymic disorder DD in adolescents is characterized by an overwhelming and chronic state of depressed or irritable mood for at least 1 year. Other symptoms include poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness. The adolescent must experience two or more of the symptoms, with a reduction of symptoms lasting for 2 months or less.⁷ Often, symptoms of DD are missed or overlooked because they are less severe than the symptoms of MDD. DD has an extended course, therefore early recognition is critical to prevent extensive impairment to the patient's ability to function.

Depressive disorder not otherwise specified Persons with depressive disorder NOS present with clinically significant symptoms of depression. However, these patients do not meet the criteria for any specific mood disorder.

RECOGNIZING DEPRESSION IN THE PEDIATRIC PATIENT

Depression does not have specific symptoms in children and adolescents. In fact, depressive disorders may manifest differently in each age-group. For instance, infants and preschoolers have a limited ability to express feelings of sadness through language skills; therefore, psychiatric disorders are often difficult to diagnose at this young age. Depressive symptoms must be inferred from overt behavior such as apathy, withdrawal from caregivers, a delay in or regression of developmental milestones, and failure to thrive that has no organic cause.^{8,9} Clinicians must rely heavily on parental history, evaluation of parent-child interactions, and play interviews conducted by mental health specialists.¹⁰

School-age children are cognitively able to internalize environmental stressors and display low self-esteem and excessive guilt. Many times they may present with somatic complaints (headache, stomachaches), anxiety (school phobia, excessive separation anxiety), and irritability (temper tantrums, other behavioral problems).^{1,11,12} Teachers are a valuable source of information on the behaviors and attitudes of these children.

Common manifestations of depression in a teenager are a sudden drop in grades, a change in friends, participation in fewer social or recreational activities, frequent irritability, a

recent change in eating or sleeping patterns, frequent fatigue, feelings of worthlessness or hopelessness, or suicidal thinking. Adolescents experience many challenges as they strive to establish their own identities. Patients in this age-group can be extremely challenging to treat because they tend to be struggling for autonomy from authoritative figures. A good rapport is absolutely essential to building the trust of an adolescent patient.

PATHOGENESIS OF DEPRESSION

Pathogenic contributors to the risk of depression are supported by substantial clinical evidence; however, the proportion of contribution to the etiology varies from case to case. One of the most significant pathogenic factors is genetics. Depression is both polygenic and multifactorial.¹³ Genetic factors can predispose a person to depression, but additional nongenetic factors are required to produce the disorder. For example, an interaction between an allele of the serotonin transporter (*5-HTT*) gene and stressful life events can increase the risk of depression.^{14,15} Genetic factors may also influence response to treatment.

Many studies have shown that persons with depression have altered brain structure and function. Monoamine neurotransmitters, specifically norepinephrine and serotonin, have been researched; these agents are also used in the therapeutic approach to depressive disorders. Early study models postulated that hypoactivity occurs in the neurotransmitter systems. However, more complex dynamics involving intracellular cascades triggered by the monoamines appear to be involved in depression and a person's response to antidepressant medication.¹⁶ In addition, overproduction of corticotrophin-releasing hormone causes hyperactivity in the hypothalamic-pituitary-adrenal cortex axis in depressed persons,¹⁷ which may, in turn, lead to glucocorticoid-mediated hippocampal atrophy.¹⁸ Functional neuroimaging studies have shown altered brain function occurring in several regions, often including the frontal cortex and striatum.¹⁹ Neuropsychological findings also support the theory that functional abnormalities occur in these brain regions.

Continued on page 40

KEY POINTS

- Depressive disorders may manifest differently in each age-group. For instance, infants and preschoolers have a limited ability to express feelings of sadness through language skills. Clinicians must rely heavily on parental history, evaluation of parent-child interactions, and play interviews conducted by mental health specialists.
- School-age children are cognitively able to internalize environmental stressors and display low self-esteem and excessive guilt. Many times they may present with somatic complaints, anxiety, and irritability.
- A common manifestation of depression in a teenager is a sudden drop in grades, a change in friends, participation in fewer social or recreational activities, frequent irritability, a recent change in eating or sleeping patterns, frequent fatigue, feelings of worthlessness or hopelessness, or suicidal thinking.
- Pathogenic contributors to the risk of depression are supported by substantial clinical evidence; however, the proportion of contribution to the etiology varies from case to case. One of the most significant pathogenic factors is genetics. Depression is both polygenic and multifactorial.
- Referral to a psychiatrist, psychologist, or other mental health care provider is warranted whenever depression is recurrent or chronic, complicated by comorbid conditions, causes a high degree of functional impairment, or if the adolescent's presentation is unclear or guarded.

Social system dynamics such as isolation and negative or critical comments from family members may also contribute to depression onset or perpetuate a depressive episode.^{20,22} Societal and cultural factors strongly influence both the symptomatic expression and a person's willingness or ability to seek care for depression.²³

EFFICACY OF TREATMENT

The typical course of a major depressive episode in adolescence lasts 7 to 9 months. Young persons recover from a depressive episode within 1 to 2 years in 90% of cases;^{24,25} however, relapse is common, and the probability of recur-

rence within 2 years is 40% and within 5 years is 70%.^{1,3} Adolescents with depression are more likely to suffer depressive episodes or have other mental health issues in adulthood than are adolescents who do not have depression.^{26,27} Education can help patients and family members understand depression as an illness and emphasize the importance of adherence to treatment. Developing supportive and understanding relationships with the patient is key to improving treatment outcomes.^{28,29}

Psychotherapy can be a useful initial therapy for children and adolescents with mild to moderate depression; it can also be an adjunct to medications for those patients with more severe depression.³⁰ Psychotherapeutic approaches include play therapy, psychodynamic therapy, supportive therapy, interpersonal therapy, family therapy, group therapy, and cognitive behavior therapy (CBT). The Treatment for Adolescents with Depression Study (TADS) found that a combination of psychosocial and pharmacologic therapies is the most beneficial treatment for adolescents suffering from a depressive disorder.

TADS evaluated the efficacy of short-term (12 weeks) and long-term (36 weeks) treatment with fluoxetine (Prozac), a selective serotonin reuptake inhibitor (SSRI); CBT; fluoxetine plus CBT; and pill placebo in adolescents with MDD.³¹ The typical response rate for psychosocial or pharmacologic monotherapy for MDD is approximately 60%,^{32,33} and the rate of remission is 35% to 40%.³² However, TADS results support combination therapy with fluoxetine and CBT as the most effective treatment during the acute phase (the first 12 weeks).³²

The outcomes were measured using the Children's Depression Rating Scale-Revised (CDRS-R) and a dichotomized Clinical Global Impression-Improvement (CGI-I) score.³² A positive response on the CGI-I was defined as a score of 1 (very much improved) or 2 (much improved). Outcomes based on the CDRS-R indicated that the most significant improvement in depressive symptoms occurred in the fluoxetine combined with CBT treatment group. However, outcomes based on the CGI-I indicated that fluoxetine alone was effective, although not as effective as fluoxetine/CBT combination therapy. After 12 weeks of treatment, 71% of adolescents treated with combination therapy reported a much improved or very much improved mood on the CGI-I compared to 61% treated with fluoxetine monotherapy, 43% treated with CBT monotherapy, and 35% who received placebo.³² In addition, the patients treated with combination therapy or fluoxetine alone recovered earlier than those patients treated with CBT or placebo alone.³⁴ Combination therapy showed favorable results at 12, 18, and 36 weeks; however, all the therapies showed similar results by 36 weeks.³²

SAFETY OF ANTIDEPRESSANT USE IN CHILDREN

Tricyclic antidepressants are not beneficial in pediatric patients, therefore SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) are increasingly being used to treat

TABLE 1. Depression symptoms

Depressed mood or irritable most of the day, nearly every day, as indicated by either subjective report or an observation made by others
Diminished ability to think or concentrate or indecisiveness
Fatigue or loss of energy
Feelings of worthlessness or excessive or inappropriate guilt
Insomnia or hypersomnia
Markedly diminished interest or pleasure in all or almost all activities most of the day, nearly every day
Significant weight loss when not dieting, weight gain, or decrease or increase in appetite
Psychomotor agitation or retardation
Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, a suicide attempt, or a specific plan for committing suicide
Data from American Psychiatric Association. ⁷

TABLE 2. Online information resources

American Psychiatric Association www.psych.org
American Psychological Association www.apa.org
Antidepressant medications for children and adolescents: Information for parents and caregivers National Institute of Mental Health www.nimh.nih.gov/healthinformation/antidepressant_child.cfm
Antidepressant use in children, adolescents, and adults US Food and Drug Administration www.fda.gov/cder/drug/antidepressants
Mental Health America www.nmha.org
National Alliance for Mentally Ill www.nami.org

depression in this patient population.³⁵ Research on the efficacy and safety of antidepressants in children has increased dramatically over the last 10 years. Only 250 children and adolescents with depression were included in double-blind, randomized controlled trials (RCTs) of antidepressants before 1995, whereas more than 2,800 children and adolescents have been included in more recent RCTs of these medications.

Of the SSRIs and SNRIs that are used to treat depression, fluoxetine is the only drug with FDA approval for use in children and adolescents. However, the other SSRIs and SNRIs are used to treat depression in these patients. Although the

“Children and adolescents must be closely monitored, particularly during the early stages of treatment or after dose titrations.”

outcomes of many of the antidepressant trials have been widely scrutinized, the Medicines and Healthcare Products Regulatory Agency and the FDA considered only the results of the fluoxetine trials, including the TADS study, as positive.

Interpretation of suicidal behavior in depression studies can be difficult because suicide attempts and suicidal ideation are common symptoms of depression. Determining if a suicide attempt made during treatment indicates a lack of improvement, a worsening of depressive symptoms, or a reaction to the medication is difficult. All children and adolescents with depression must be closely monitored during drug therapy, particularly in the early stages of treatment or after dose titrations. FDA recommendations state that patients should be monitored weekly for the first 4 weeks of antidepressant therapy and after any subsequent dose adjustments. In addition, patients and their families need to be fully informed about the risk of suicidal behaviors. Table 2 lists online resources for information about depression. Families must watch closely for signs of worsening depression, worsening or new suicidal ideation or behaviors, and other adverse behaviors.³⁶

Referral to a psychiatrist, psychologist, or other mental health care provider is warranted whenever depression is recurrent or chronic, complicated by comorbid conditions, causes a high degree of functional impairment, or if the adolescent's presentation is unclear or guarded. If the need for psychopharmacologic medications is suspected, a referral to a psychiatrist is indicated.

CONCLUSION

Adolescents with depression typically present in primary care. Unfortunately, the disorder is underdiagnosed and undertreated;³⁷ an estimated 70% of teenagers with depression do not receive any form of treatment.^{4,38} In the United

States, suicide rates doubled among adolescents aged 15 to 19 years and tripled among those aged 10 to 14 years from the 1960s to the 1990s.³⁹ Suicide is the fourth leading cause of death among all children and the third leading cause of death among children aged 10 to 19 years.⁴⁰ From 2003 to 2004, suicide rates among females aged 10 to 14 years increased by 76%; among those aged 15 to 19 years, suicide rates increased by 32% in females and by 9% in males.⁴¹ Furthermore, approximately two-thirds of children and adolescents with MDD also suffer from another mental health disorder. Health care practitioners also need to recognize the associated psychiatric comorbidities, including DD, anxiety disorders, attention-deficit/hyperactivity disorder, oppositional defiant disorder, and substance use disorder.⁴²

Studies have shown that only one-third of parents who had concerns that their child may have a psychosocial disorder planned to discuss it with their child's pediatrician. In cases where parents initiated this discussion, only 40% of pediatricians responded; the response rate was even lower if the parents were less educated.^{43,44} This finding indicates that a majority of psychosocial disorders in children are being missed.

With appropriate evaluation, diagnosis, and treatment, primary care practitioners can do much to prevent the subsequent morbidity and mortality associated with depressive disorders. Prompt recognition ensures effective treatment of depressive disorders in children and adolescents; therefore, PAs must educate themselves, their patients, and their patients' families about the signs and symptoms of these disorders. **JAAPA**

Brett Reisman Greenberg works at the Cleveland Clinic of Florida, Weston, Florida. She has indicated no relationships to disclose relating to the content of this article.

REFERENCES

1. Birmaher B, Ryan ND, Williamson DE et al. Childhood and adolescent depression: a review of the past 10 years. Part I. *J Am Acad Child Adolesc Psychiatry*. 1996;35(11):1427-1439.
2. Saluja G, Iachan R, Scheidt PC, et al. Prevalence of and risk factors for depressive symptoms among young adolescents. *Arch Pediatr Adolesc Med*. 2004;158(8):760-765.
3. Fleming JE, Offord DR. Epidemiology of childhood depressive disorders: a critical review. *J Am Acad Child Adolesc Psychiatry*. 1990;29(4):571-580.
4. Lewinsohn PM, Clarke GN, Seeley JR, Rohde P. Major depression in community adolescents: age at onset, episode duration, and time to recurrence. *J Am Acad Child Adolesc Psychiatry*. 1994; 33(6):809-818.
5. Lewinsohn PM, Hops H, Roberts RE, et al. Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *J Abnorm Psychol*. 1993;102(1):133-144.
6. Carlson GA, Cantwell DP. Unmasking masked depression in children and adolescents. *Am J Psychiatry*. 1980;137(4):445-449.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*. Washington, DC: American Psychiatric Assoc; 2000.
8. Jellinek MS, Snyder JB. Depression and suicide in children and adolescents. *Pediatr Rev*. 1998;19(8):255-264.
9. Wolraich M, Felice ME, Drotar D. *The Classification of Child and Adolescent Mental Diagnoses in Primary Care: Diagnostic and Statistical Manual for Primary Care (DSM-PC) Child and Adolescent Version*. Elk Grove Village, IL: American Academy of Pediatrics; 1996.
10. Lewis M. Psychiatric assessment of infants, children, and adolescents. In: Lewis M, ed. *Child and Adolescent Psychiatry: A Comprehensive Textbook*. Baltimore, MD: Williams & Wilkins; 1991:447-463.
11. Ryan ND, Puig-Antich J, Ambrosini P, et al. The clinical picture of major depression in children and adolescents. *Arch Gen Psychiatry*. 1987;44(10):854-861.
12. Mitchell J, McCauley E, Burke PM, Moss SJ. Phenomenology of depression in children and adolescents. *J Am Acad Child Adolesc Psychiatry*. 1988;27(1):12-20.

References continue on page 42

13. Kendler KS, Gatz M, Gardner CO, Pedersen NL. A Swedish national twin study of lifetime major depression. *Am J Psychiatry*. 2006;163(1):109-114.
14. Kendler KS, Kuhn JW, Vittum J, et al. The interaction of stressful life events and a serotonin transporter polymorphism in the prediction of episodes of major depression: a replication. *Arch Gen Psychiatry*. 2005;62(5):529-535.
15. 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(5631):386-389.
16. Nutt DJ, Baldwin DS, Clayton AH, et al. Consensus statement and research needs: the role of dopamine and norepinephrine in depression and antidepressant treatment. *J Clin Psychiatry*. 2006;67(suppl 6):46-49.
17. Gillespie CF, Nemeroff CB. Hypercortisolemia and depression. *Psychosom Med*. 2005;67(suppl 1):S26-S28.
18. Sapolsky RM. Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. *Arch Gen Psychiatry*. 2000;57(10):925-935.
19. Drevets WC. Functional neuroimaging studies of depression: the anatomy of melancholia. *Annu Rev Med*. 1998;49:341-361.
20. Sheline YI, Gado MH, Kraemer HC. Untreated depression and hippocampal volume loss. *Am J Psychiatry*. 2003;160(8):1516-1518.
21. Paykel ES. Life events and affective disorders. *Acta Psychiatr Scand Suppl*. 2003;(418):61-66.
22. Hayhurst H, Cooper Z, Paykel ES, et al. Expressed emotion and depression. A longitudinal study. *Br J Psychiatry*. 1997;171:439-443.
23. Simon GE, VonKorff M, Piccinelli M, et al. An international study of the relation between somatic symptoms and depression. *N Engl J Med*. 1999;341(18):1329-1335.
24. Kovacs M, Feinberg TL, Crouse-Novak MA, et al. Depressive disorders in childhood: I. A longitudinal prospective study of characteristics and recovery. *Arch Gen Psychiatry*. 1984;41(3):229-237.
25. McCauley E, Myers K, Mitchell J, et al. Depression in young people: initial presentation and clinical course. *J Am Acad Child Adolesc Psychiatry*. 1993;32(4):714-722.
26. Harrington R, Fudge H, Rutter M, et al. Adult outcomes of childhood and adolescent depression. I. Psychiatric status. *Arch Gen Psychiatry*. 1990;47(5):465-473.
27. Weissman MM, Wolk S, Goldstein RB, et al. Depressed adolescents grown up. *JAMA*. 1999;281(18):1707-1713.
28. Asarnow JR, Goldstein MJ, Tompson M, Guthrie D. One-year outcomes of depressive disorders in child psychiatric in-patients: evaluation of the prognostic power of a brief measure of expressed emotion. *J Child Psychol Psychiatry*. 1993;34(2):129-137.
29. Asarnow JR, Tompson M, Hamilton EB, et al. Family-expressed emotion, childhood-onset depression, and childhood-onset schizophrenia spectrum disorders: is expressed emotion a nonspecific correlate of child psychopathology or a specific risk factor for depression? *J Abnorm Child Psychol*. 1994;22(2):129-146.
30. Practice parameters for the assessment and treatment of children and adolescents with depressive disorders. AACAP. *J Am Acad Child Adolesc Psychiatry*. 1998;37(10 suppl):63S-82S.
31. Treatment for Adolescents With Depression Study Team. Treatment for Adolescents With Depression Study (TADS): rationale, design, and methods. *J Am Acad Child Adolesc Psychiatry*. 2003;42(5):531-542.
32. March J, Silva S, Vitiello B; TADS Team. The Treatment for Adolescents with Depression Study (TADS): methods and message at 12 weeks. *J Am Acad Child Adolesc Psychiatry*. 2006;45(12):1393-1403.
33. Goodyer I, Dubicka B, Wilkinson P, et al. Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behaviour therapy in adolescents with major depression: randomised controlled trial. *BMJ*. 2007;335(7611):142.
34. Blackburn IM, Moore RG. Controlled acute and follow-up trial of cognitive therapy and pharmacotherapy in out-patients with recurrent depression. *Br J Psychiatry*. 1997;171:328-334.
35. Hazell P, O'Connell D, Heathcote D, Henry D. Tricyclic drugs for depression in children and adolescents. *Cochrane Database Syst Rev*. 2002;(2):CD002317.
36. US Food and Drug Administration Web site. <http://www.fda.gov>. Accessed February 2, 2009.
37. Adolescent medicine: teen depression: overlooked and undertreated. *Patient Care*. 2002;12:37-47.
38. Flament MF, Cohen D, Choquet M, et al. Phenomenology, psychosocial correlates, and treatment seeking in major depression and dysthymia of adolescence. *J Am Acad Child Adolesc Psychiatry*. 2001;40(9):1070-1078.
39. Efforts to reduce the toll of injuries in childhood require expanded research. American Academy of Pediatrics. Committee on Injury and Poison Prevention. *Pediatrics*. 1996;97(5):765-768.
40. Hamilton BE, Minino AM, Martin JA, et al. Annual summary of vital statistics: 2005. *Pediatrics*. 2007;119(2):345-360.
41. Center for Disease Control and Prevention (CDC). Suicide trends among youths and young adults aged 10-24 years—United States, 1990-2004. *MMWR Morb Mortal Wkly Rep*. 2007;56(35):905-908.
42. Angold A, Costello E, Erkanli A. Comorbidity. *J Child Psychol Psychiatry*. 1999;40(1):57-87.
43. Cassidy LJ, Jellinek MS. Approaches to recognition and management of childhood psychiatric disorders in pediatric primary care. *Pediatr Clin North Am*. 1998;45(5):1037-1052.
44. Jellinek M, Little M, Murphy JM, Pagano M. The Pediatric Symptom Checklist. Support for a role in a managed care environment. *Arch Pediatr Adolesc Med*. 1995;149(7):740-746.