Childhood and Adolescent Depression: The Role of Primary Care Providers in Diagnosis and Treatment

Laura P. Richardson, MD, MPH, and Rachel Katzenellenbogen, MD

It is estimated that 20% of youth will experience at least one episode of major depression before they reach the age of 18 years.[1] At any given time, up to one in 13 adolescents have major depression making it more common than asthma and most other chronic medical disorders in this age group.[2] This high prevalence of depression, coupled with a limited availability of pediatric and adolescent mental health specialists, has resulted in an increased need for primary care providers to be comfortable with both diagnosing depression and providing initial treatment. Yet, few pediatric residency programs provide training in treatment of affective disorders and most primary care providers report feeling uncomfortable treating these conditions.[3] The goals of this article are to review the epidemiology of depression, criteria for depression diagnosis, evidence regarding effective treatments, and strategies that can be successfully employed by primary care doctors to treat their patients with depression.

Epidemiology of Depression

Over the past six decades, the prevalence of depression has increased and the age at time of diagnosis has decreased.[2,4,5] Among community samples of adolescents, the prevalence of major depressive disorder (Table 1) is estimated to be between 4 and 8%,[2,6] and the prevalence of dysthymia (Table 2) is between 1.6 and 8.0%.[2] The number of children and adolescents who report depressive symptoms is even higher than the number with depressive disorders. At any given time, about 15% of children and adolescents have elevated depressive symptoms.[6] Even though these youth may not meet criteria for major depression, these subsyndromal depressive symptoms may still have long-term implications. Studies suggest that elevated depressive symptoms in adolescence, even in the absence of a depressive disorder, may predispose to later development of major depression.[7,8]

The prevalence of depression increases with age and pubertal development. In early adolescence, girls and boys are equally likely to have a depressive disorder. However, as youth move through puberty, the female-to-male ratio changes to 2:1.[9] The reason for the rise in depressive symptoms in girls during adolescence is not fully understood. Some hypotheses include increased social orientation of girls compared with boys, differences in coping techniques for girls versus boys, higher rates of sexual abuse in females, and neurobiologic differences between the sexes.[2,10] Puberty and accompanying hormonal changes may play an important role in the development of depression, with most studies showing a rise in the prevalence of depression after Tanner Stage III.[11]

Risk Factors for Depression

The main risk factors for the development of depression in childhood and adolescence can be grouped into four categories: genetics, environmental factors, negative life events, and child characteristics. Genetic factors have been some of the most widely studied. It has been found that 20 to 50% of youth who experience depression in early childhood or adolescence have a family history of depression or other mental health disorder.[12-14] Parental depression is a particularly strong predictor for depression; children of depressed parents are more than three times as likely as children of nondepressed parents to experience a depressive disorder.[9,15] Offspring of depressed parents are also at increased risk for other types of psychopa-

Adolescent Medicine Section, Division of General Pediatrics, University of Washington, Seattle, Washington
Curr Probl Pediatr Adolesc Health Care 2005;35:1-24
1538-5442/$ - see front matter
© 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.cppeds.2004.09.001

TABLE 1. DSM-IV criteria for **major depressive disorder**

A major depressive episode must include five or more of the symptoms listed below most days for at least 2 weeks. *One of the symptoms must be either item 1 or 2.* The symptoms should represent a change from previous function.

1. Depressed/irritable mood most of the time.
2. Loss of interest or pleasure in all or almost all activities.
3. Significant weight loss or weight gain, failure to gain weight as expected with growth, or change in appetite.
4. Insomnia or hypersomnia.
5. Observable psychomotor agitation or retardation.
6. Fatigue or loss of energy.
7. Feelings of worthlessness or excessive inappropriate guilt.
8. Diminished ability to think or concentrate or indecisiveness.
9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or suicide attempt or a specific plan for committing suicide.

TABLE 2. DSM-IV criteria for **dysthymia**

1. Chronic depressed mood lasting for at least 1 year (2 years for adults). The depressed mood should be present:
   - for most of the day
   - for more days than not
   - with lapses not lasting more than 2 months
2. The symptoms are not as severe or disabling as a Major Depressive Disorder episode and include two or more of the following features:
   - poor appetite or overeating
   - loss of self-esteem
   - feelings of hopelessness
   - insomnia or hypersomnia
   - low energy or fatigue
   - poor concentration or difficulty making decisions

thology, including anxiety and disruptive behavior disorders.[9]

Environmental factors, such as the family and social context in which the child is living, may also play an important role in the development of depression in youth with both high and low genetic risk. For example, increased family conflict, low socioeconomic status, and early death of a parent have been shown to increase the risk for depression in childhood and adolescence.[2] Sexual abuse, physical abuse, and neglect are also risk factors for the development of childhood and adolescent depression.[16] Since parental depression has a strong influence on the home environment, some of the effect of parental depression on child depression may be due to environment as well as genetics.

Another risk factor related to environment is exposure to negative life events such as parental divorce or separation, loss of friendships, less positive peer relationships, or death of a family member or friend. Children and adolescents with depression are more likely to report having experienced negative life events than those without depression.[2] Some of these events may trigger the onset of depression, but other events, such as loss of a friendship or family conflict, may have been caused by the depression. Individuals at high genetic risk seem to be more sensitive to the effects of adverse environment or negative life events than those who are at low risk.[17]

Finally, characteristics of the child that may contribute to the development of depression include elevated levels of anxiety, low self-esteem, high self-criticism, cognitive distortions, negative attributional style, poor school performance, and social skills deficits.[18] Children with medical and nondepressive mental health disorders (such as anxiety disorders, attention deficit hyperactivity disorder, and conduct disorder) are also at increased risk for the subsequent development of depression.[2] Most studies have shown that children and adolescents with anxiety disorders such as social phobia and panic and separation anxiety disorder are at high risk for the development of subsequent major depressive episodes.[19]

Course and Natural History of Depression

Approximately 90% of major depressive disorder (MDD) episodes remit by 1.5 to 2 years after onset, with only 6 to 10% becoming more persistent.[20-22] In the absence of treatment, the typical duration for an episode of MDD in adolescents is 7 to 9 months.[20,22,23] Although recovery from major depression is the rule, recurrence is very common. Twenty to 40% of depressed adolescents will relapse within 2 years, and 70% will do so within 5 years.[20-24] Predictors of increased risk for MDD recurrence include younger age at onset, increased number of previous episodes, increased severity of index episode, increased psychosocial stressors, psychosis, dysthymia or other comorbid disorders, and failed compliance with treatment.[25,26]

Dysthymia, by definition, has a much longer course than MDD: a mean episode of dysthymia lasts between 3 and 4 years.[27-29] Dysthymia is associated with an increased risk for psychiatric comorbidity including subsequent MDD, bipolar disorder, and substance use disorders.[27-29] If a patient develops MDD, it usually occurs within 2 to 3 years after the onset of dysthymia.[27] Youth with both MDD and dysthymia are often

referred to as having "double depression." Because of the prolonged course of dysthymia, youth with this condition may require a longer treatment period than youth with MDD alone.

The clinical picture of depression varies with age. Younger children may have more symptoms of anxiety, somatic complaints, auditory hallucinations, and behavioral problems including irritability and frustration.[30-32] Similar to younger children, adolescents also have symptoms of irritability. However, adolescents also tend to have symptoms that more closely parallel those of adults including sleep and appetite changes, suicidal ideation, and impairments of functioning.[31,32] There is also evidence that the clinical course of MDD that starts before puberty is different from MDD that begins after puberty. Children with prepubertal onset of depression are at increased risk for the development of other mental health disorders, such as bipolar disorder, in adulthood. In contrast, youth who experience depression in later adolescence are more likely to experience recurrent depression but not other mental health disorders.[23,24,33,34]

Bipolar depression is estimated to occur in 20 to 40% of youth within 5 years of a diagnosis of MDD.[26,35] Bipolar disorder is characterized by episodes of depression that alternate with manic episodes, defined by a decreased need for sleep, increased energy, grandiosity, euphoria, and an increased propensity for risk-taking behavior. Factors that increase the risk for the later development of bipolar disorder include earlier onset of depressive symptoms, the presence of psychomotor retardation (confusion, lack of energy), or psychotic features of depression, family history of bipolar disorder or psychotic depression, multiple family members with mood disorders, and occurrence of pharmacologically induced hypomania.[35]

Psychiatric comorbidity is common in youth with MDD: 40 to 90% of youth with MDD have another psychiatric disorder, with at least 20 to 50% having two or more disorders.[2,9] The most frequent comorbid diagnoses are dysthymia and anxiety disorders, occurring in 30 to 80% of youth with MDD, followed by disruptive disorders in 10 to 80%, and substance use disorders in 20 to 30%.[26,36-38] The frequency and type of psychiatric comorbidity varies with age. Comorbid substance abuse, conduct disorder, social phobia, and general anxiety disorder are more frequent in adolescents, while separation anxiety disorder is more common in children.[2] With the exception of substance use disorders and some conduct disorders, which may occur as a result of a depressive disorder, most of these comorbid disorders usually predate and likely contribute to the development of depression.

Medically unexplained symptoms such as headache, abdominal pain, and fatigue are also common in children and adolescents with depression. A common initial presentation of depression in the primary care office is a youth who has had recurrent visits for somatic complaints with negative medical evaluation. In some cases a clear pattern of symptoms may appear. For example, symptoms are triggered by a stressful life event, escalate with stressful experiences, or increase with start of the school week. In other instances, no source of stress or pattern of pain symptoms is identifiable. Because many of these patients experience their symptoms as somatic (and not psychiatric) concerns, they present a significant challenge for primary care providers. Many of these patients require multiple visits and the establishment of a treatment relationship before they are willing to accept the diagnosis of depression and initiate treatment.

Adding to the challenge that medical providers face, depression can also co-occur with medical problems, such as diabetes and asthma. In fact, studies suggest depression is more common among youth with chronic medical disorders, particularly when these disorders interfere with normal daily activities.[39] When present as a comorbidity, depression may result in poor adherence to treatment and lack of engagement in follow-up care for the chronic medical condition. In adults, comorbid depression has been shown to be associated with poor outcomes for multiple chronic medical disorders.[40,41]

Potential Consequences of Depression

Depression is one of the leading risk factors for suicide during childhood and adolescence, the third leading cause of death for adolescents in the United States.[42] In 2001, suicide accounted for 7% of deaths in American 10 to 14 year olds and 12% of deaths in 15 to 19 year olds.[43] The rate of adolescent suicide increased from the 1950's to the 1990's, but has decreased in the last decade. A recent study found that the decline in adolescent suicide was greatest in geographical regions with the highest rates of antidepressant use.[44] This finding suggests that part of this decline may be attributable to better treatment of depression.

TABLE 3. Differential diagnosis for major depressive disorder

Medications
Beta-blockers
Corticosteroids
Contraceptives
Neuroleptic medications
Medical disorders
Hypothyroidism/Hyperthyroidism
Anemia
Mononucleosis
Chronic Fatigue Syndrome
Inflammatory Bowel Disease
Lupus or other collagen vascular disease
Stroke, tumor, or other central nervous system disorder
Infectious etiologies: HIV, hepatitis
Psychiatric disorders
Dysthymia
Adjustment disorder with depressive features
Anxiety disorders
Attention-deficit/hyperactivity disorder
Conduct disorder
Substance use disorders (alcohol, barbiturates, heroin)
Anorexia nervosa
Bulimia

Girls are twice as likely as boys to attempt suicide; however, boys are approximately four times as likely to complete a suicide attempt. Among depressed youth, some additional important risk factors for suicide include the presence of firearms or other lethal weapons in the home, exposure to abuse or violence at home, family history of suicide, history of substance abuse or impulsive behaviors, and history of a prior suicide attempt.[45-48]

In addition to suicide, there are many other potential consequences of depression. Depression affects all areas of youth functioning and can result in school failure, substance use behaviors (drugs, nicotine, and alcohol),[49] early pregnancy, obesity,[50-52] and social isolation.[15,26] In the long term, depressed adolescents are at risk for low educational achievement poor physical health, and the development of other mental health disorders including recurrent depression.[15,53-56] While some of these consequences are directly due to depression, others may be due to negative exposures in the environments in which many depressed youth live. Some of these exposures include frequent negative life events, low socioeconomic status, presence of physical illness, poor family functioning, and parental psychiatric disorder.[33,57-59]

Diagnosis of Depressive Disorders

The first step to appropriately treating depression is making the correct diagnosis. All providers who see youth and treat depression should be familiar with the Diagnostic and Statistical Manual IV (DSM-IV) diagnostic criteria for major depressive disorder (MDD) (Table 1). To meet these criteria, symptoms should be present most days for at least 2 weeks and must include five of the nine key symptoms. At least one of the five symptoms must be either depressed mood/irritability or anhedonia. Irritability is an additional criteria for the diagnosis of depression in children and adolescents. Unlike depression in adults, depression in children and adolescents may manifest more frequently as irritability, acting out, boredom and trouble with relationships at home and at school.[60]

The first step in making the diagnosis of MDD is to rule out alternative causes for depressive symptoms and to identify current symptoms of depression. Table 3 provides a broad differential diagnosis for MDD including medications, medical disorders, and other psychiatric disorders, which can mimic MDD. Most of these other potential causes can be ruled out with a thorough history and physical. At least part of the history should be conducted with the child or adolescent alone.

When evaluating for depression, it is not unusual to find variation between parent-reported and youth-reported symptoms. In general, studies have shown that children and adolescents are more likely to report internalizing symptoms, such as suicidality and depressed mood, while parents report more externalizing symptoms, such as irritability.[61]

There may also be differences between parents and children regarding the diagnosis and perceived need for treatment. When a depressed youth is reluctantly brought to the clinic by his or her parents, it can threaten the primary care providers ability to establish rapport. It is important to spend at least part of the visit one-on-one with the youth. This allows a primary care provider to establish the office as a place where the adolescent can safely discuss his or her symptoms and concerns. Because parents may report symptoms that the youth does not notice or is too ashamed to report, it is also helpful to spend some time interviewing parents or guardians. However, when meeting with parents, it is important to emphasize that the child is the primary focus for care.

Although a full review of ethnic and racial differences in depression presentation is beyond the scope of this article, practitioners should be aware of cultural factors that might influence the presentation of depression. One way that culture affects depression is in the

way that patients present their symptoms. In some cultures, depression may be experienced predominantly in somatic terms rather than feelings of sadness or hopelessness. For example, Asian patients may be more likely to report their somatic symptoms, such as dizziness, while not reporting their emotional symptoms. However, when directly queried, the same patients do acknowledge having emotional symptoms.[62]

An additional cultural concern is stigma regarding depression and mental health problems, which may be a particular concern for youth of some cultures. This may affect the types of treatment that are acceptable to youth and families.[63] For example, some youth may prefer to receive counseling from members of their own cultural group or religion or may prefer not to engage in counseling if there are cultural norms that prohibit discussing personal matters outside of the family.

The history component of the evaluation should include assessment of current symptoms, recent or past negative life events, and social support. Social dynamics at home and in school can affect outcome in depression and may need to be addressed to assure recovery.[60] In addition, information about the effect of depression on the patient's daily functioning can be used to guide the selection of an appropriate intensity of treatment. Asking about suicidal ideation, personal suicide attempts, and access to firearms helps define the safety of the patient and the need for emergent intervention.

Because antidepressant treatment can increase risk for the development of mania in susceptible individuals, it is important to assess for any history of atypical symptoms, such as psychosis or hypomania. Comorbid psychiatric disorders, such as substance abuse disorder, should also be assessed as their presence may alter the appropriate initial treatment or may indicate a need for a mental health specialty referral. Family history of psychiatric disorders, especially bipolar disorder, depression, or suicide attempts, should be investigated as they are associated with increased risk for mental health disorders in the youth.

Finally, it is important to review any medications, prescription, over-the-counter, or illicit, that may cause depressive symptoms or mood changes. Some examples of these medications, listed in Table 3, include beta-blockers and corticosteroids. Although the data are controversial, hormonal contraceptives may also cause depressed mood in individuals with a personal or family history of depression.[64] The assessment should include more than prescription medications, and it is important to also assess for the use of marijuana, alcohol, and other drugs such as stimulants, cocaine, and opiates.

The physical examination should be directed at any medical concerns that were raised during the history and at ruling out other medical causes for depressive symptoms (Table 3). Hypothyroidism and hyperthyroidism are high on the differential for depressive disorders but are very unlikely to be present in the absence of other symptoms, such as weight gain, cold intolerance, or constipation. Routine testing of thyroid stimulating hormone is probably not warranted in youth who do not also have other symptoms of hypothyroidism. Youth with anemia and chronic fatigue syndrome may present with fatigue but are unlikely to present the full spectrum of depressive symptoms such as anhedonia or suicidal ideation in the absence of comorbid MDD. Youth with mononucleosis also have fatigue but there is usually a history of a viral syndrome at the onset of symptoms. Rheumatologic disorders would be a rare cause of depression in the absence of other inflammatory changes or systemic symptoms. Similarly, youth with HIV should have other infections or symptoms associated with HIV and youth with hepatitis usually have some elevation of transaminases. Youth with stroke or central nervous system disorders should have other neurological changes on evaluation.

MDD can occur in the presence of chronic medical disorders such as diabetes and lupus. Identifying depression in the presence of a medical disorder can be difficult when the medical disorder causes sleep disturbance, appetite change, somatic symptoms, and loss of energy. However, feelings of guilt, worthlessness, hopelessness, and thoughts of suicide are unlikely to be due to a medical disorder and strongly suggest the presence of MDD.

Since treatment needs to be altered if other mental health conditions are present, it is also important to distinguish other mental health disorders from MDD (Table 3). Some of the most common comorbidities and potential overlaps with MDD are reviewed in the next few paragraphs. Other mood disorders, such as dysthymia and adjustment disorder, have significant symptom overlap and can easily be mistaken for MDD. As mentioned previously, dysthymia is a depressive disorder characterized by fewer symptoms than MDD that have a longer duration (Table 2). It can be comorbid with MDD. When both are present in the

TABLE 4. DSM-IV criteria for adjustment disorder

1. The development of emotional or behavioral symptoms in response to an identifiable stressor(s), which occurs within 3 months of the onset of the stressor(s) (eg, divorce, new home).
2. These symptoms or behaviors are clinically significant as evidenced by either of the following:
   (a) Marked distress that is in excess of what would be expected from exposure to the stressor, or
   (b) Significant impairment in social or academic functioning
3. The stress-related disturbance does not meet the criteria for other mood or mental disorders and is not merely anexacerbation of a preexisting mental disorder or general medical condition.
4. Symptoms do not persist longer than 6 months following the cessation of the stressor.

same individual, it is often referred to as "double depression" and is associated with a poorer outcome than having just MDD alone. Youth with dysthymia should be treated in a similar manner to those with MDD, including counseling and medications when appropriate, but may require a longer course of treatment for depression.

Patients with adjustment disorder develop depressive symptoms and functional impairment within 3 months of an identifiable stressor (Table 4). However, they do not have enough symptoms to meet criteria for MDD, and by definition their disorder is self-limited with no risk for relapse.[2] Youth with adjustment disorder should have close follow-up and, if symptoms are not resolving, alternative diagnoses including MDD should be considered.

Anxiety disorders in childhood put affected youth at increased risk for the subsequent development of depression.[19] Symptoms of anxiety, such as social withdrawal, may also overlap with those of depression, making it difficult to tease apart. Although treatments are similar for depression and anxiety, it is helpful to have a clear picture of the primary disorder that is being targeted.

Attention deficit disorder and conduct disorder can be associated with depression but also can have some features that overlap with depression. School failure and poor functioning may be features of MDD, but they may also be features of attention deficit disorder, learning disabilities, or anxiety disorders. In the case of an underlying learning disability or attention deficit disorder, addressing school failure problems through medication or altering the school program may also help to diminish depressive symptoms. Similarly, substance use can cause symptoms consistent with a mood disorder or can be triggered by a mood disorder. In general, if substances are responsible for the depressed mood, discontinuing them should result in resolution of the depressive symptoms.

Youth with anorexia nervosa or bulimia can present with depressed mood that may resolve with normalization of nutritional status and body mass or may need treatment with combined psychotherapy and antidepressant medications.

Screening Instruments for Depressive Disorders

Evaluating a child for depression can be time consuming in a busy pediatric practice; yet, current standards of care, both Guidelines for Adolescent Preventive Services (GAPS)[65] and Bright Futures,[66] dictate that primary care providers screen for depression annually beginning at 11 years of age.

One approach to screening for depression is to perform a thorough adolescent psychosocial evaluation. There are many acronyms to describe the key features that should be performed during a psychosocial evaluation. One example is the HEADSS (Home, Education, Activities, Drugs, Sex, and Suicide) evaluation.[67] This type of evaluation allows providers to ask less invasive questions first and to gain a glimpse into adolescents' day-to-day lives, not just their depressive symptoms. To speed this process, the GAPS provides a questionnaire that covers the main areas of social functioning for adolescents, including a few brief questions on feeling sad and hopeless or having suicidal thoughts.[65] These forms are available online at http://www.ama-assn.org/ama/pub/category/2280.html and can be reproduced for use in clinics at no charge.

Another approach to screening for depression is to use a written questionnaire that screens either for general behavior problems or more specifically for depressive symptoms. There are many potential benefits to using questionnaires. One benefit is that questionnaires provide a structured format, which can help busy providers remember to review all of the key symptoms. Questionnaires also can be completed before a visit, potentially saving provider time and allowing depression to be addressed earlier in the course of a visit. A final benefit is depression-specific symptom screens can be used to generate severity scores that then can be followed to gauge the effectiveness of treatment.

While screening instruments can be very useful, it is important to know that none of these questionnaires

TABLE 5. Screening instruments

Name	Age range	No. of items	Clinical cutoff score	Source	Cost
			General Mental Health Screening Scales		
Pediatric Symptom Checklist (PSC)	3-16 years	35	≥28 is indicative of significant psychosocial impairment	Pediatric Symptom Checklist, Massachusetts General Hospital Department of Child Psychiatry, Bullfinch 351, 55 Fruit Street, Boston, MA 02114 http://psc.partners.org/	Free
Child Behavior Checklist, Youth Self-Report (CBCL, YSR)	2-18 years	113	Age and gender based norms used to generate *t* scores created to mark the level of risk for depression	Child Behavior Checklist, University Medical Education Associates, 1 South Prospect St., Burlington, VT 05401-3456, 802-656-8313 http://checklist.uvm.edu	$10 for 25 forms
			Depressive Symptom Scales		
Beck Depression Inventory–2nd ed. (BDI-II)	13-18 years	21	20 to 28 for moderate depression, 29 or more for severe depression	The Psychological Corporation, 555 Academic Court, San Antonio, TX 78204-2498 http://www.psychcorp.com	$75 for manual and 25 record forms
Children's Depression Inventory (CDI)	7-17 years	27	*t* scores over 65 clinically significant	The Psychological Corporation, 555 Academic Court, San Antonio, TX 78204-2498 http://www.psychcorp.com	$100 for manual and 25 record forms
Moods and Feelings Questionnaire (MFQ)	8-17 years	32 (long) 11 (brief)	≥12 for adolescents, ≥9 for children	Developmental Epidemiology Program, Duke University Medical Center, Attn: Jane Duncan, DUMC Box 3454, Durham, NC 27710 http://devepi.mc.duke.edu/mfq.html	$10 for printed package or available as a PDF through the website and contacting the authors.
Patient Health Questionnaire — Adolescent Version (PHQ-A)	13-18 years	83	DSM-based diagnostic algorithms to assign likely depression diagnoses	PHQ-A is available through its authors at Columbia University	Free

are designed to diagnose depression. Instead, they are designed to detect youth with elevated symptoms and to characterize these symptoms. They narrow the population a clinician must formally evaluate for a depressive disorder. However, a clinician assessment is still required to make the diagnosis and confirm responses.

In Table 5 and the next few paragraphs there is an overview of general mental health and depression screening instruments. There are many instruments available and this article is not intended to be an exhaustive review of all instruments. Instead, this is an overview of selected instruments that are designed to be brief, self-administered, and easily implemented in primary care settings. Because youth are better reporters of internalizing symptoms than their parents,[68] included instruments are designed for youth self-administration. Information is also provided regarding parent versions of instruments when available.

For ease of presentation, the depression screening instruments have been categorized into two groupings: general mental health screening instruments and depressive symptom scales. The general mental health scales are used to evaluate the presence of behavioral

and psychosocial concerns. They often have internalizing disorder subscales but are not specific for depression or other disorders. In contrast, depressive symptom scales are designed to be more specific to the types of symptoms that individuals with depression experience.

General Mental Health Screening Instruments

This section includes two instruments that are used to screen for a variety of behavioral and psychosocial problems in youth. Both of these instruments have been used in primary care settings.

The **Pediatric Symptom Checklist (PSC)** was developed by researchers at the Massachusetts General Hospital as a brief psychosocial screen for youth in primary care settings. It is a one-page questionnaire with 35 questions and is designed for screening in youth aged 3 to 16 years. All questions have three response options (scored 0, 1, or 2), resulting in a total possible score of 70. For children aged 6 to 16 years, a total score of 28 or higher is taken as an indication of significant psychosocial impairment. The main version of this instrument is a parent questionnaire, but a child self-report questionnaire is also available for older children. The benefits of this instrument are its brief nature and the ability to screen for a variety of behavioral and psychosocial concerns. Although an internalizing scale has been developed for this instrument, it is not designed to identify specific mental health disorders. The PSC is available for free download at http://psc.partners.org/psc_order.htm.

The **Child Behavior Checklist (CBCL)** is one of the most commonly used screens for general mental health problems in children. It is a 113-item instrument that is designed to screen for a variety of behavioral concerns. The CBCL has two versions: one for children aged 2 to 3 years and another for children aged 4 to 18 years. Both versions are designed to be completed by the parents, not the youth. The **Youth Self-Report Scale (YSR)** is a youth-administered version of the CBCL. It is designed for use with adolescents aged 11 to 18 years.

Responses to questions on both the YSR and the CBCL are on a three-point scale. Once completed, responses are added together and used to define a *t* score based on normative responses for youth of the same age and gender. Similar to the PSC, the CBCL and YSR do have internalizing scale subscores, but they do not provide information on specific depressive disorder diagnoses. *t* scores above the 98th percentile for internalizing symptoms are considered to be in the clinical range and warrant further evaluation.[69] The main benefit of these instruments is they provide information regarding multiple areas of behavioral concerns, including externalizing disorders. There are also teacher report forms that can be used to enhance information obtained from parents and youth. One concern is the length of the instrument and the complexity of scoring. However, scoring can be made easier using computerized algorithms to assist with scoring. Scores between parents, patients, caregivers, and teachers can be cross-referenced to check consistency in syndrome areas. All of these scales and scoring computer programs are available for purchase through the University of Vermont at http://checklist.uvm.edu.

Depressive Symptom Scales

Depressive symptom scales are designed to screen individuals for specific symptoms that occur with depression. Some scales include a broad range of symptoms, while others are based more closely on the DSM-IV diagnostic criteria for depression. Most depressive symptom scales have an identified cut-off above which a youth is felt to be at higher risk for having a depressive disorder. These scales can be interpreted for the purpose of identifying youth at risk for depression or as an overall score. Four depressive screening instruments are listed in Table 5 and are reviewed in detail here: the Beck Depression Inventory, the Child Depression Inventory, the Mood and Feelings Questionnaire, and the Patient Health Questionnaire.

Originally published in 1961, the **Beck Depression Inventory (BDI)** is one of the most commonly used scales in clinical practice. Its most up-to-date form is the BDI-II, which more closely parallels DSM-IV symptoms of depression than prior versions of the instrument. It contains 21 questions: 19 use a three-point scoring scale, and 2 ask to indicate an increase or decrease in behaviors. The questionnaire is designed to be completed by the adolescent (ages 13 and older) and takes about 10 minutes to fill out and score. The BDI-II has been shown to accurately differentiate youth who are likely to have depression versus those who are unlikely to have depression within outpatient populations.[70] A score of above 20 suggests moderate depression and of 29 or more suggests severe depression.[71] In addition, BDI scores have been shown to decrease as depression wanes. Therefore, once a patient begins treatment, the scale can be used to follow symptoms with treatment.[70]

A nine-item version of the BDI designed for quick implementation in clinical settings, the Beck Depression Inventory for Primary Care (BDI-PC), is also available and has been validated in adolescents in primary care.[70]

All of the Beck Depression Inventories are copyrighted and require purchase for use; details regarding these instruments can be obtained at http://www.psychcorp.com.

The **Children's Depression Inventory (CDI)** is a depressive symptom scale that is derived from the Beck Depression Inventory and is specifically designed to assess depression in children ages 7 to 17 years. The CDI replaces some questions from the BDI, such as questions about sexual activity, with more age-appropriate questions. It contains 27 questions and uses a three-point scale for each question. The CDI is completed by the youth and takes less than 20 minutes to complete, including scoring. There is also a brief form of the instrument (the CDI-S): a 10-question form which takes just 5 minutes to complete. The scoring system for the 27-item instrument is based on standards for age and gender. The total responses are summed and then used to generate a *t* score comparing responses to other respondents of the same age and gender. *t* scores above 65 are considered indicative of a probable depressive disorder.[72] Similar to the BDI, the CDI is useful for tracking depressive symptoms with therapy.[70] One benefit of the CDI over the BDI is that the language is more appropriate when being administered with younger pediatric populations, although some studies have found that the wording and the three-point response scale can still be difficult for children to understand.[70] The CDI is available for purchase through the Psychological Corporation at http://www.psychcorp.com.

The **Moods and Feelings Questionnaire (MFQ)** was developed specifically for use in youth aged 8 to 17 years. A strength of the MFQ is that it closely follows the DSM criteria for depression, making it based on a tangible construct and increasing its reliability.[73] The MFQ includes 32 items with three response options ("true," "sometimes true," and "not true"). There is also a brief version of the scale that contains the 11 items that were found to have the best discriminatory power when tested against clinical diagnoses of depression.[73] For the full instrument, the recommended cut point for distinguishing youth who are likely to have a depressive disorder from those who are not differs with age: the cut point is ≥12 for adolescents and ≥9 for younger children.[73] The MFQ has a parent version that also can be used to evaluate symptoms based on parent report. This scale can be obtained through the website http://devepi.mc.duke.edu/mfq.html.

The **Patient Health Questionnaire (PHQ)** was developed as part of the PRIME-MD study to diagnose and monitor depression and other mental health disorders among adults in primary care settings.[74] The depression section of this instrument is nine items and can be administered separately as a depression screen. This instrument has been used extensively in the treatment of depression in primary care settings among adults. It is currently recommended as the tool of choice by many depression in primary care initiatives, including the MacArthur Foundation Depression in Primary Care Initiative (website: http://www.depression-primarycare.org). The **Patient Health Questionnaire Adolescent Version (PHQ-A)** is a version of the PHQ that was specifically developed for use with adolescents in primary care settings. It includes 83 questions about the major mental health disorders that are typically seen in adolescents (aged 13 to 18 years) including depression, generalized anxiety disorder, panic attacks, illicit drug use, and eating disorders. The PHQ-A was found to have high specificity and sensitivity in the diagnosis of MDD.[75]

PHQ instruments are designed to be self-administered. The adolescent version provides three response options ("not at all," "several days," and "nearly every day"). Survey responses can be used to generate a symptom score. Although data are not yet available for the adolescent version, these scores have been shown to be sensitive to changes with treatment in adults. The PHQ questionnaires are closely based on DSM-IV diagnostic criteria for depression and, rather than using a cut-point score, there are easy-to-use algorithms to determine if a patient meets diagnostic criteria for MDD or dysthymia. As with all screening instruments, the diagnosis should still be confirmed by a clinical evaluation. The nine-item depression component and the adult PHQ is free through Pfizer and the MacArthur Foundation at http://www.depression-primarycare.org/clinicians/toolkits/. The PHQ-A can be obtained by contacting the developers of the instrument.[75]

One important criterion that many providers use to diagnose depression is the effect of symptoms on regular functioning. Most clinicians would not diagnose depression in the absence of impairment or

TABLE 6. Seven key challenges in managing depression

1. Make a diagnosis.
2. Educate and recruit the patient as a partner in treatment.
3. Start with the best possible treatment. Avoid minor tranquilizers. Use antidepressants and/or psychotherapy.
4. Use an adequate dose of treatment. This includes an adequate frequency of psychotherapy.
5. Treat long enough. Patients often take 6 to 10 weeks to respond.
6. Follow outcomes and adjust treatment as needed. Consider specialty consultation if a patient is not improving.
7. Prevent relapse. 20-40% of children and adolescents will relapse within 2 years of a first episode, and 70% will do so by adulthood.

significant change in functioning. Understanding the level of functional impairment is also important for determining the appropriate intensity of treatment. Although in general children with more depressive symptoms might be expected to have higher functional impairment, this is not always the case. This is one reason that a physician or mental health professional assessment is required to confirm the diagnosis of depression. Of the instruments listed above, only the PHQ has a question asking about the effect of symptoms on daily functioning that can be used as additional information in confirming the diagnosis.

Treatment of Depression

Screening and diagnosis is only the first step in treating depression for youth. To improve outcomes for depressed youth, it is essential that screening and diagnosis be linked to appropriate treatment. This treatment section will detail the subsequent steps shown to be essential in primary care for improving depression outcomes for adults: educating and activating patients, selecting an appropriate initial treatment, closely monitoring symptoms, adjusting treatment if symptoms are not improving, and making plans to prevent relapses once symptoms have remitted (Table 6).

Patient Education and Activation

Regardless of where a patient is treated, education should begin at the time of diagnosis. This helps patients and parents to overcome concerns about stigma and depression treatments and to engage in treatment. This means that depression education should begin in the primary care office. Although education can be time consuming, recent changes in reimbursement have made it possible for primary care providers to charge for the time spent providing counseling. Providers can bill for the time spent with the patient as long as more than 50% of the visit is spent providing this counseling.

One main area of counseling is education regarding the diagnosis and addressing concerns about stigma that may prevent patients from seeking care or following through with a treatment plan. In discussing depression with adolescents and their families, it can be helpful to mention that depression is common during adolescence and that it is a medical illness, not a character defect or weakness. Patients and families can be encouraged that recovery from depression is the rule, not the exception, but that treatment will require commitment and there is a risk for future recurrence. It is important to address any hopelessness regarding depression and its treatment, as hopelessness has been shown to predict withdrawal from treatment and suicidal behavior.[76]

A video that shows other adolescents with depression and discusses the benefit of treatment may be very helpful in decreasing stigma and promoting hopefulness regarding treatment. When selecting a video or other educational material, it is important to choose materials that appeal to adolescents and children and that do not focus too heavily on suicide, as epidemics of suicide have been shown to occur among adolescents. One example of a good video for adolescents with depression is "Day for Night: Recognizing Teenage Depression," which is available at http://www.drada.org.

Since many patients present with somatic complaints, it can also be helpful to specifically discuss that depression is not just in the mind: it affects the body, behavior, and thinking. When children and adolescents have difficulty in relating their physical symptoms to depression, it may help to discuss other situations in which there are clear links between the mind and the body. For example, feeling anxious about performing in front of people can cause "butterflies in the stomach," or a stressful test can result in "headaches." Whenever possible, it is helpful to directly discuss the symptoms that the patient is having in the context of depression.

When educating patients, primary care providers can begin some basic counseling about interventions that have been shown to improve depressive symptoms. This may be particularly important if there is a long delay before the patient can be seen by a mental health specialist. A first step is encouraging patients to discontinue substances or prescriptions that might make depres-

sion worse, such as drugs, alcohol, and certain prescription medications (eg, narcotics or benzodiazepines). The next step is encouraging patients to engage in activities that might help lessen depressive symptoms. Patients with depression often withdraw from activities that they used to enjoy and instead spend more time ruminating about their symptoms or sleeping. Providers can explain how behaviors and thoughts contribute to a negative spiral that worsens depression, and reversing these thoughts and behaviors are the first steps to feeling better.

For children and adolescents, returning to school and having activities with friends can be very important first steps to feeling better. Studies have also shown that physical activity can decrease depressive symptoms, independent of other treatments for depression.[77] Encouraging patients to begin walking each day or joining a noncompetitive sport can be very helpful toward changing negative thoughts and improving depression. Families can support younger children with increasing activities by planning family outings, such as walks, bicycle rides, or trips to the pool. Since sleep dysfunction is common with depression, providers can also counsel youth on good sleep hygiene and setting regular sleeping hours, including discontinuing daytime naps.

Finally, since decisions regarding initial treatment are often made before referral, providers should also be comfortable in talking about potential treatments for depression and helping the youth and parents select an appropriate treatment. Patients and parents often have strong feelings about what type of treatment is acceptable. Some adolescents and parents have fears about medications and "altering the way they think." Other families have concerns about the stigma and time associated with seeing a psychotherapist. Although the evidence is mixed, studies in adults suggest that incorporating patient preference into treatment decisions may improve treatment adherence, satisfaction, and outcomes for depression.[78,79]

Treatments: Medications and Therapy

There are two main options for the treatment of major depression and dysthymia in youth: medications and psychotherapy. Available studies of comparable subjects show similar rates of clinical response to either psychotherapy or medication. Treatment guidelines from the American Academy of Child and Adolescent Psychiatry recommend that all youth receive some form of psychotherapy, even if they take antidepressant medications.[2] This is based on the clinical experience and expert opinion that many depressed youth have significant psychosocial difficulties. Studies that provide for the direct comparison of antidepressants and psychotherapy are currently underway. A recent multi-center study found that combination treatment was superior to either medication or psychotherapy alone in the short-term treatment of adolescent depression.[80] In the absence of evidence to support one type of treatment over another, either or both approaches may be empirically justified. The final selection of treatment type should take into account patient and provider preferences, availability of treatments based on geographic location and insurance coverage, and depression severity. Medications and psychotherapy are reviewed in further detail below.

Medications

Although many medications have been shown to be effective in treating depression in adults, not all antidepressant medicines work as well for youth. Selective serotonin reuptake inhibitors (SSRIs) are one of the few classes of antidepressants that have demonstrated efficacy in the treatment of child and adolescent depression. Despite multiple trials, tricyclic antidepressants have not been shown to be effective for treating MDD in adolescents[81]; therefore, this article focuses specifically on SSRIs and a few of the newer antidepressants that are frequently used in primary care settings. Antidepressants to be reviewed in this article are listed in Table 7.

To date, there have been five trials demonstrating effectiveness of SSRI medications over placebo treatment in children and adolescents. The first two trials of SSRI medications in youth used fluoxetine (Prozac) and showed it to be effective over placebo in the treatment of depression in the outpatient setting.[82,83] A recent randomized, double-blind, placebo-controlled study found that sertraline (Zoloft) was significantly effective over placebo in treating MDD in children ages 6 to 17 years old.[84] Paroxetine (Paxil) was also shown to be effective over placebo or tricyclic antidepressant in treating adolescent depression.[85] Finally, in a recent study, citalopram (Celexa) was shown to result in significantly decreased depressive symptoms when compared with placebo.[86] No randomized controlled trials have been conducted using escitalopram (Lexapro) in children or adolescents.

Recently, SSRI medications have received much negative press regarding the potential for increasing

TABLE 7. Medications for treatment of depression

Drug name (Brand name) Category	Available dosages (mg)	Starting dose for adolescents >45 kg (mg)	Target dose by week 2–4 (mg)	Sample dose adjustment for partial or nonresponders (mg)	Therapeutic dose range (mg)
Fluoxetine (Prozac) SSRI	10, 20, 40, 20/5 ml	10 daily	10 to 20 daily	Increase to 20 after 1 week, 30 after 4 weeks, 40 after 8 weeks	10 to 40 daily
Sertraline (Zoloft) SSRI	25, 50, 100, 20/ml	25 daily	50 to 100 daily	Increase to 50 after 1 week, 100 after 3 weeks, 150 after 6 weeks	25 to 200 daily
Citalopram (Celexa) SSRI	10, 20, 40, 10/5 ml	10 daily	10 to 20 daily	Increase to 20 after 1 week, 30 after 3 weeks, 40 after 6 weeks	10 to 40 daily
Escitalopram (Lexapro) SSRI	10, 20	10 daily	10 daily	No proven increase in efficacy over 10 mg	10 daily
Paroxetine (Paxil, Paxil CR) SSRI	10, 20, 30, 40, 10/5 ml	10 daily	10 to 20 daily	Increase to 20 after 1 week, 30 after 4 weeks, 40 after 6 weeks	10 to 40 daily
Buproprion (Wellbutrin) NE/DRI	75, 100	75 qam	75 to 150 bid	Increase to 75 BID after 4 days, 100 BID after 2 weeks, 150 bid after 4 weeks, 150 TID after 6 weeks	75 to 150 bid to tid
Buproprion (Wellbutrin SR) NE/DRI	100 SR 150 SR	100 SR qam	100 to 150 SR bid	Increase to 100 after 1 week, 150 BID after 3 weeks, 150 TID after 6 weeks	100 to 150 SR bid
Venlafaxine (Effexor) SNRI	25, 37.5, 50, 75, 100	25 qam	25 to 150 bid	Increase to 25 bid after 4 days, 50 bid after 2 weeks, 75 bid after 3 weeks, 100 bid after 5 weeks, 150 qam/100 qhs after 6 weeks	12.5 to 150 bid
Venlafaxine (Effexor XR) SNRI	37.5 XR, 75 XR, 150 XR	37.5 qam	75 to 300 daily	Increase to 75 after 1 week, 150 after 3 weeks, 225 after 6 weeks	37.5 to 225 daily

SSRI, selective serotonin reuptake inhibitor; NE/DRI, norepinephrine and dopamine reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor.

suicidal ideation in youth and adults. Initial attention was focused specifically on paroxetine, although all antidepressants, including buproprion and venlafaxine, are currently being evaluated regarding their risks for increasing suicidal ideation. The United States Food and Drug Administration has found insufficient evidence to conclude that reports of increased risk of suicidal thoughts and actions can be directly attributed to SSRIs. However, the FDA continues to investigate available data. At this point, it has made the following recommendations regarding the use of antidepressants. First, health care providers should closely monitor patients who are receiving antidepressants for signs of worsening depression or suicidality, especially in the first few months of therapy or with a change in dose. Second, providers are encouraged to discuss this potential risk with patients and to encourage patients and parents to monitor for agitation, irritability, worsening of symptoms, or increase in suicidality (*FDA Public Health Advisory*, October 15, 2004). Finally, manufacturers are asked to place warnings of the “black box” potential risks of suicide on labels for medications.

Despite the negative press SSRIs have received in the recent past, they are still the only antidepressants with any evidence for effectiveness in children and

adolescents and they are still the first line of treatment for depression when medications are indicated. The main SSRI medications are fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa), and escitalopram (Lexapro). Currently, fluoxetine is the only SSRI with Food and Drug Administration approval for the treatment of major depressive disorder in youth. When selecting a specific SSRI, it is appropriate to try to choose the medication that is the best fit for the patient. Some factors that should be taken into account include prior response to the medication, response of family members to the medication, presence of comorbidities (eg, anxiety, ADHD), and patient depressive symptoms.

The usage and side effects of SSRI medications are quite similar with only minor differences among SSRIs.

The main side effects are gastrointestinal symptoms, jitteriness, restlessness, and headache. Some SSRI antidepressants, like fluoxetine, tend to cause more restlessness, while others, like paroxetine, are more sedating. Other potential side effects include nausea, appetite changes, dizziness, sedation, diaphoresis, vivid dreams, headaches, bruising, sleep disturbance, and decreased sexual functioning (ie, anorgasmia or, less frequently, decreased libido).[2] Before starting antidepressants, youth should be warned of potential side effects and encouraged to call if they are having any difficulties with the medication. The side effects of antidepressants are dose dependent and may subside with time, usually within the first 1 to 2 weeks of starting or changing the dose. Thus, if side effects are minor, patients should be reassured and encouraged to continue. If side effects are bothersome but not severe, the patient can be instructed to decrease the dose until the symptoms resolve and then try increasing again. Because youth may be more sensitive to the side effects of antidepressants than adults, antidepressants should be started at a lower dose than would be given initially to adults.[2] Examples of initial starting doses and the therapeutic dose range for antidepressants are provided in Table 7.

Antidepressants may trigger manic-type episodes in susceptible youth. Therefore, before starting antidepressants it is important to screen all youth for prior manic behaviors or strong family history for mania. Examples of questions to assess for mania in adolescents include the following: "Do you ever have, even for a few days, feelings of being high, increased energy, not needing to sleep with racing thoughts?" and "Do you ever have poor judgment during these "highs" such that you spend too much money or get involved with people you wouldn't normally be involved with?" For younger children and adolescents, the parents can be asked if the child has periods of inappropriate giddiness or silliness, intense outbursts of anger, inflated self-esteem, decreased need for sleep, pressured speech, inappropriate sexual activity, or times of excessive thrill-seeking behaviors with potentially dangerous consequences. If mania occurs secondary to an SSRI medication, the medication should be stopped, and the patient should be referred for psychiatric evaluation.

Two non-SSRI medications are commonly used by primary care providers for the treatment of depression: venlafaxine (Effexor) and buproprion (Wellbutrin); therefore, these drugs have also been included in Table 7. Venlafaxine is a norepinephrine and dopamine re-uptake inhibitor and comes in both twice a day dosing and daily dosing (XR) formulations. It is used for both depression and anxiety as an alternative to SSRI medications. One rare side effect specific to venlafaxine is hypertension, which can occur when doses reach $\geq$300 mg/day and requires monitoring by practitioners. There is currently no evidence for efficacy of this medication in youth, and recently the manufacturer of venlafaxine released a statement indicating it is not recommended for youth. This is based on its lack of efficacy for depression or generalized anxiety disorder and on increased symptoms of hostility and suicidality in this age group in unpublished trials (*Health Provider Communication*, Wyeth, August 22, 2003**).

Buproprion (Wellbutrin) is also used in adolescents for depression. It is often used as a second-line agent, but it is sometimes used as a first-line treatment in patients with excessive weight or who also smoke and would like to quit smoking. There are no published randomized-controlled trials on its efficacy in treating depression for children and adolescents. Buproprion has fewer sexual side effects and weight gain than SSRI medications. The potential side effects of buproprion include insomnia, agitation, and risk of seizures, particularly in patients who purge through vomiting or with high doses of medication. Its use is contraindicated in patients with an eating disorder whose seizure threshold can be lowered through purging behaviors. The SR formulation is prescribed twice per day and is preferable to the standard formulation due to lower side effects and decreased dosing frequency.

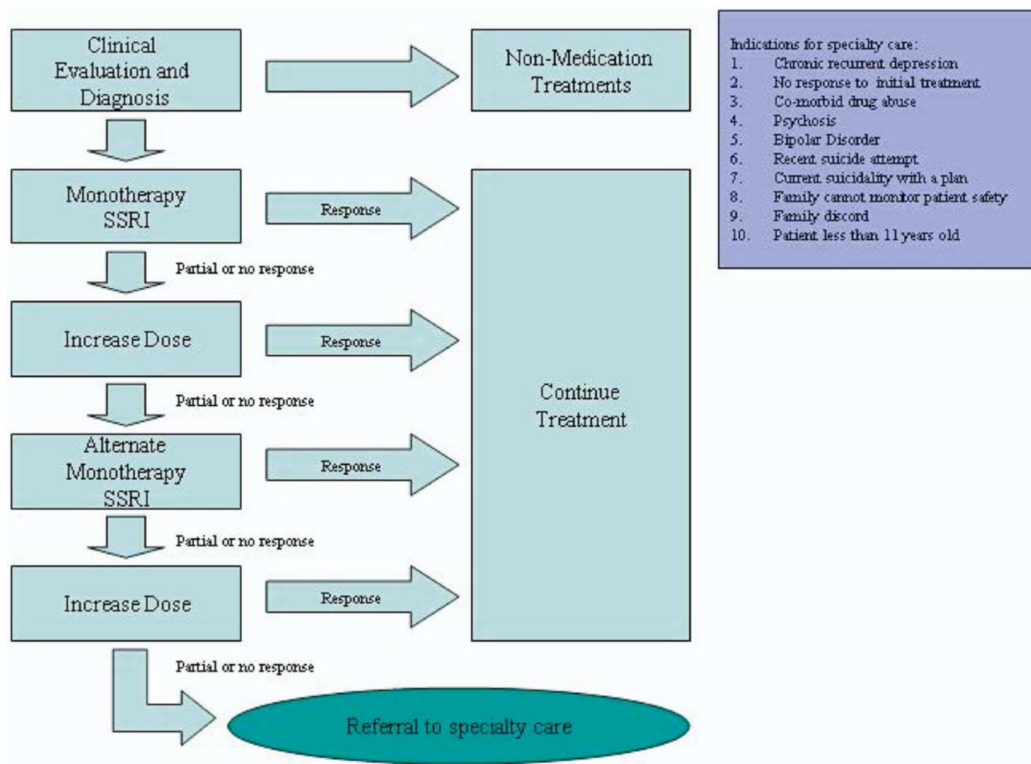

FIG 1. Algorithm for antidepressant treatment of major depressive disorder in adolescents (based on Children's Medication Algorithm Project). (Color version of figure is available online.)

Figure 1 provides an algorithm adapted from the Children's Medication Algorithm Project for the medication treatment of child and adolescent depression.[87] After confirming the diagnosis and deciding that it warrants treatment, the primary care provider should evaluate the severity of the depression and consider whether or not treatment in the primary care setting is appropriate. Some examples of youth who may be safely treated in primary care settings are youth with a first diagnosis of depression, recent onset of depression, and an absence of coexisting conditions. A list of criteria for youth who are more appropriate for immediate mental health referral is provided in Fig 1. Inpatient care is required for youth who are actively suicidal and cannot contract for safety and may be indicated for youth with significant substance abuse, and those with psychosis, mania, or severe impairment.

As mentioned previously, if the provider has decided to start an antidepressant, SSRI medications are still the first-line medication treatment as they have the most evidence for effectiveness in youth. Antidepressants should be started at a low dose, usually half the recommended adult dose, with close monitoring for side effects. After 1 week, if the patient is tolerating the medication well, it can be increased to the lowest effective therapeutic dose. Due to side-effect patterns, the first few weeks of treatment are a critical time period during which many patients discontinue therapy. Therefore, when starting a patient on antidepressants, symptoms should be monitored every 1 to 2 weeks until they begin to remit and the patient is on a stable treatment dose.

The dose of antidepressants can be increased every 4 weeks if a patient has no or only a partial response. The maximal symptom response should be achieved at 4 to 6 weeks of a consistent dose. Patients can get frustrated and stop medications before seeing their full effect; therefore, when antidepressants are started, they should be educated about the anticipated delay in seeing the full benefits of medications. Recommendations for therapeutic doses are provided in Table 7. Because children and adolescents metabolize SSRI medications more rapidly than adults, they may require doses above the minimum therapeutic dose to reach a clinical response.[88]

Although specific data are not available for children or adolescents, 50% of adults who do not respond to the first SSRI tried will respond to the second.[89] Therefore, as seen in Figure 1, if the initial choice of medication is ineffective at its maximal dose, the provider could consider switching to another medication within the SSRI family or changing approach and recommending psychotherapy.

Once an effective medication and dose are found, a patient should take the medication for 6 to 9 months to avoid a relapse of depression and should be monitored at least every 1 to 2 months. During treatment, practitioners need to be aware that SSRIs can affect the liver metabolism of some other medications. Also, care should be taken to avoid anything that enhances the level of serotonin while on SSRIs to decrease the serious risk of serotonin syndrome. Some examples of medications where particular care should be taken are the weight loss medication sibutramine (Meredia) and migraine medications like sumitriptan (Imitrex).

Before concluding that a patient has had no response to an SSRI, the provider should ensure that the patient is receiving and taking an adequate dose. When discontinuing medications, providers need to be aware of the potential for withdrawal and the need to taper. Withdrawal symptoms include depressed mood or behavioral changes. With the exception of fluoxetine, which has a 4-week half-life, all medications should be tapered over a period of weeks to allow for the gradual decrease of medication levels. This is particularly important for medications with a short half-life like paroxetine, which may cause withdrawal symptoms after missing just a few doses.

It is worth pointing out that one of the major challenges in demonstrating the efficacy of antidepressants in youth is the high placebo response rate seen in many trials: between 50 and 60% of adolescents improved in the placebo arm of recent SSRI treatment trials.[82,84,85] Thus, the rate of response to medication must be quite high to demonstrate differences between placebo and treatment in a trial. The reasons for this high placebo response rate are not clear. One potential explanation is some adolescents are likely to improve on their own regardless of treatment and we need better measures of severity to identify youth who are most likely to benefit from treatment. An alternative explanation is that youth in the placebo arm are responding to other components of the intervention. For example, most clinical trials studying antidepressant effects on MDD include weekly provider contacts in both the treatment and the placebo arm. It is possible that youth improve because of this close monitoring, mobilizing home with the therapeutic relationship, and close follow-up of their symptoms. If this is the case, it has important implications for health care providers. Perhaps regular contact with providers is therapeutic to patients even in the absence of medication. Thus, close follow-up is not only prudent in the face of recent warnings, it may also be essential in ensuring patient recovery.

Psychotherapy

Given the psychosocial context of child and adolescent depression, child depression experts recommend that psychotherapy should always be included as a component of depression treatment.[2] This recommendation is further supported by the recent multi-center study showing that the combination of psychotherapy and medication performed better than either treatment alone for depressed adolescents.[80] In the last few decades progress has been made in developing and testing psychotherapeutic techniques for the treatment of mental health disorders. Cognitive Behavioral Therapy (CBT) is one of the most widely tested psychotherapeutic techniques. Eight to 16 sessions of CBT over a period of 3 to 4 months have been shown to be more efficacious than alternative psychotherapies.[90-92] CBT techniques focus on changing negative self-defeating thought patterns, increasing positive behaviors and activities, and improving interpersonal effectiveness. In addition to depression treatment, CBT techniques have also been successfully used for the prevention of depression in high-risk youth in primary care settings.[93]

CBT is a manualized treatment approach, meaning that CBT treatment programs generally have a specific curriculum that allows for the standardized administration by different providers. An example of one curricula shown to be effective for the treatment of depression in adolescents is the *Coping with Depression Course*.[94] This course is developed for group administration with affected adolescents and is geared toward helping depressed adolescents develop the skills they need to overcome their depression. Specific topics covered in this program include relaxation, scheduling pleasant events, addressing irrational and negative thoughts, developing social skills, improving communication, and problem solving. Manuals that further describe this therapy program are available on the internet at http://www.kpchr.org/public/acwd/acwd.html.

Other psychotherapeutic techniques that have been used in the treatment of depression are psychodynamic psychotherapy, interpersonal psychotherapy (IPT), and family therapy.[2] All have some evidence supporting their use in depressed adolescents, but less than what is currently available for CBT.

IPT, a brief form of psychotherapy, has also been shown to be efficacious for adolescent depression in two clinical trials.[95-97] In IPT, patients learn to cope with interpersonal difficulties, such as loss of relationships, discord, and role transitions that are often associated with depression.

If a patient has no response to CBT or IPT after 6 to 8 weeks of treatment, accepted guidelines recommend adding an SSRI antidepressant to the treatment regimen.[2] Conversely, if a patient has no response to an SSRI, then adding CBT or IPT is also supported in the literature based on empirical therapy in adults.[98] Based on research in adults, patients with chronic depression (lasting more than 1 year) may benefit from both medication and psychotherapy.[99] Regardless of the type of psychotherapy, it may need to be continued on a monthly basis for up to 6 months following the initial course to decrease the risk of relapse.[100]

Psychotherapeutic programs should be administered by individuals with training and experience in using the method. As availability of psychotherapy may vary from community to community, physicians should be aware of the resources in their own community. Providers should have regular follow-up with patients who are engaged in psychotherapy to be sure that they continue to be engaged and that depressive symptoms are improving as anticipated.

Suicide Education and Prevention

The presence of suicidality in a depressed adolescent requires immediate assessment and action. When children and adolescents reveal thoughts of suicide, a thorough assessment is warranted. Questions to be asked by a primary care provider include the following: Do they ever have thoughts of hurting themselves? Do they ever feel that they would be better off dead? Do they have a plan? Have they ever tried before? In the case where youth have suicidal thoughts but no plans, providers should ask them if they feel like they can keep themselves safe. A plan for what to do if these thoughts became more severe must be created and youth should consider who they would tell. All depressed youth and their families should be provided with phone numbers and a plan for crisis services in their community.

Families and youth with depression should be warned of the risk of suicide and the importance of taking all suicidal thoughts seriously. Any guns in the home should be either removed or secured in a locked location to which the adolescent does not have access. Youth who are suicidal should not have access to toxic medications, such as tricyclic antidepressants, for either themselves or other family members. If it is necessary to continue these medications, parents should secure them and take charge of assuring their child receives his or her daily dose.

Children and adolescents who are actively suicidal should be evaluated by a mental health professional emergently, particularly if they are prone to impulsive behaviors, use drugs, have a family history of suicide, or have a specific suicide plan with means to execute it. Each community has different systems for accessing emergency mental health services, but the two common pathways are local crisis lines and emergency departments.

Further Depression Resources

The American Academy of Child and Adolescent Psychiatry has guidelines for the treatment of depression and suicidal behavior in children and adolescents and educational pamphlets for families and patients (available at http://aacap.org). The National Institute for Mental Health (http://www.nimh.nih.gov) also has informational pamphlets regarding adolescent depression for patients, providers, and families. The Depression and Bipolar Support Alliance (http://www.dbsalliance.org/) has information for providers, patients, and families about depression and its treatment as well as information about support groups and treatment resources.

The MacArthur foundation has guidelines and a toolkit available for the treatment of depression in primary care. Although these guidelines were developed for use in adults, many of the tools can also be applied to adolescents with depression (available at: http://www.depression-primarycare.org). Teaching handouts and further treatment algorithms including algorithms for the treatment of comorbid depression and Attention Deficit Hyperactivity Disorder can be found at http://www.mhmr.state.tx.us/centraloffice/medicaldirector/cmap.html.

References

1. Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. J Abnorm Psychol 1993;102(1):133-44.
2. Practice parameters for the assessment and treatment of children and adolescents with depressive disorders. AACAP. J Am Acad Child Adolesc Psychiatry Oct 1998;37(10 Suppl.):63S-83S.
3. Rushton JL, Clark SJ, Freed GL. Primary care role in the management of childhood depression: a comparison of pediatricians and family physicians. Pediatrics 2000;105(4 Pt. 2):957-62.
4. Kovacs M, Gatsonis C. Secular trends in age at onset of major depressive disorder in a clinical sample of children. J Psychiatr Res May-Jun 1994;28(3):319-29.
5. Ryan ND, Williamson DE, Iyengar S, et al. A secular increase in child and adolescent onset affective disorder. J Am Acad Child Adolesc Psychiatry Jul 1992;31(4):600-5.
6. U.S. Department of Health and Human Services. Mental Health: A Report of the Surgeon General. Rockville, MD; 1999.
7. 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(1):133-5.
8. Lewinsohn PM, Solomon A, Seeley JR, Zeiss A. Clinical implications of "subthreshold" depressive symptoms. J Abnorm Psychol 2000;109(2):345-51.
9. 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 Nov 1996; 35(11):1427-39.
10. Schraedley PK, Gotlib IH, Hayward C. Gender differences in correlates of depressive symptoms in adolescents. J Adolesc Health 1999;25(2):98-108.
11. Angold A, Costello EJ, Worthman CM. Puberty and depression: the roles of age, pubertal status and pubertal timing. Psychol Med 1998;28(1):51-61.
12. Kovacs M, Devlin B, Pollock M, Richards C, Mukerji P. A controlled family history study of childhood-onset depressive disorder. Arch Gen Psychiatry Jul 1997;54(7):613-23.
13. Puig-Antich J, Goetz D, Davies M, et al. A controlled family history study of prepubertal major depressive disorder. Arch Gen Psychiatry May 1989;46(5):406-18.
14. Williamson DE, Ryan ND, Birmaher B, et al. A case-control family history study of depression in adolescents. J Am Acad Child Adolesc Psychiatry Dec 1995;34(12):1596-607.
15. Birmaher B, Ryan ND, Williamson DE, Brent DA, Kaufman J. Childhood and adolescent depression: a review of the past 10 years. Part II. J Am Acad Child Adolesc Psychiatry 1996;35(12):1575-83.
16. Kaufman J. Depressive disorders in maltreated children. J Am Acad Child Adolesc Psychiatry Mar 1991;30(2): 257-65.
17. Kendler KS. Genetic epidemiology in psychiatry. Taking both genes and environment seriously. Arch Gen Psychiatry Nov 1995;52(11):895-9.
18. Beasley PJ, Beardslee WR. Depression in the adolescent patient. Adolesc Med 1998;9(2):351-62, vii.
19. Merikangas KR, Zhang H, Avenevoli S, Acharyya S, Neuenschwander M, Angst J. Longitudinal trajectories of depression and anxiety in a prospective community study: the Zurich Cohort Study. Arch Gen Psychiatry Oct 2003; 60(10):993-1000.
20. McCauley E, Myers K, Mitchell J, Calderon R, Schloredt K, Treder R. Depression in young people: initial presentation and clinical course. J Am Acad Child Adolesc Psychiatry Jul 1993;32(4):714-22.
21. Kovacs M, Feinberg TL, Crouse-Novak M, Paulauskas SL, Pollock M, Finkelstein R. Depressive disorders in childhood. II. A longitudinal study of the risk for a subsequent major depression. Arch Gen Psychiatry Jul 1984;41(7):643-9.
22. Kovacs M, Feinberg TL, Crouse-Novak MA, Paulauskas SL, Finkelstein R. Depressive disorders in childhood. I. A longitudinal prospective study of characteristics and recovery. Arch Gen Psychiatry Mar 1984;41(3):229-37.
23. 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):809-18.
24. Rao U, Ryan ND, Birmaher B, et al. Unipolar depression in adolescents: clinical outcome in adulthood. J Am Acad Child Adolesc Psychiatry May 1995;34(5):566-78.
25. Emslie GJ, Rush AJ, Weinberg WA, Gullion CM, Rintelmann J, Hughes CW. Recurrence of major depressive disorder in hospitalized children and adolescents. J Am Acad Child Adolesc Psychiatry Jun 1997;36(6):785-92.
26. Kovacs M. Presentation and course of major depressive disorder during childhood and later years of the life span. J Am Acad Child Adolesc Psychiatry 1996;35(6):705-15.
27. Kovacs M, Akiskal HS, Gatsonis C, Parrone PL. Childhood-onset dysthymic disorder. Clinical features and prospective naturalistic outcome. Arch Gen Psychiatry May 1994; 51(5):365-74.
28. Lewinsohn PM, Rohde P, Seeley JR, Hops H. Comorbidity of unipolar depression: I. Major depression with dysthymia. J Abnorm Psychol May 1991;100(2):205-13.
29. Keller MB, Beardslee W, Lavori PW, Wunder J, Drs DL, Samuelson H. Course of major depression in non-referred adolescents: a retrospective study. J Affect Disord Nov-Dec 1988;15(3):235-43.
30. Chambers WJ, Puig-Antich J, Tabrizi MA, Davies M. Psychotic symptoms in prepubertal major depressive disorder. Arch Gen Psychiatry Aug 1982;39(8):921-7.
31. 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.
32. Ryan ND, Puig-Antich J, Ambrosini P, et al. The clinical picture of major depression in children and adolescents. Arch Gen Psychiatry Oct 1987;44(10):854-61.
33. Lewinsohn PM, Roberts RE, Seeley JR, Rohde P, Gotlib IH, Hops H. Adolescent psychopathology: II. Psychosocial risk factors for depression. J Abnorm Psychol 1994; 103(2):302-15.
34. Harrington R, Fudge H, Rutter M, Pickles A, Hill J. Adult outcomes of childhood and adolescent depression. I. Psychiatric status. Arch Gen Psychiatry May 1990;47(5):465-73.
35. Geller B, Luby J. Child and adolescent bipolar disorder: a

review of the past 10 years. J Am Acad Child Adolesc Psychiatry Sep 1997;36(9):1168-76.
36. Goodyer IM, Herbert J, Secher SM, Pearson J. Short-term outcome of major depression: I. Comorbidity and severity at presentation as predictors of persistent disorder. J Am Acad Child Adolesc Psychiatry 1997;36(2):179-87.
37. Lewinsohn PM, Rohde P, Seeley JR, Klein DN. Axis II psychopathology as a function of Axis I disorders in childhood and adolescence. J Am Acad Child Adolesc Psychiatry Dec 1997;36(12):1752-9.
38. Lewinsohn PM, Zinbarg R, Seeley JR, Lewinsohn M, Sack WH. Lifetime comorbidity among anxiety disorders and between anxiety disorders and other mental disorders in adolescents. J Anxiety Disord Jul-Aug 1997;11(4):377-94.
39. Lewinsohn PM, Seeley JR, Hibbard J, Rohde P, Sack WH. Cross-sectional and prospective relationships between physical morbidity and depression in older adolescents. J Am Acad Child Adolesc Psychiatry Sep 1996;35(9):1120-9.
40. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. Arch Intern Med 2000;160(21):3278-85.
41. Lin EH, Katon W, Von Korff M, et al. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. JAMA Nov 12 2003;290(18):2428-9.
42. Shaffer D, Gould MS, Fisher P, et al. Psychiatric diagnosis in child and adolescent suicide. Arch Gen Psychiatry 1996;53(4):339-48.
43. Anderson RN, Smith BL. Deaths: Leading Causes for 2001. Hyattsville, MD: National Center for Health Statistics; 2003.
44. Olfson M, Shaffer D, Marcus SC, Greenberg T. Relationship between antidepressant medication treatment and suicide in adolescents. Arch Gen Psychiatry Oct 2003;60(10):978-82.
45. Brent DA. Risk factors for adolescent suicide and suicidal behavior: mental and substance abuse disorders, family environmental factors, and life stress. Suicide Life Threat Behav 1995;25(Suppl.):52-63.
46. Brent DA, Perper JA, Allman CJ. Alcohol, firearms, and suicide among youth. Temporal trends in Allegheny County, Pennsylvania, 1960 to 1983. JAMA Jun 26 1987; 257(24):3369-72.
47. Fergusson DM, Lynskey MT, Horwood LJ. Childhood sexual abuse and psychiatric disorder in young adulthood: I. Prevalence of sexual abuse and factors associated with sexual abuse. J Am Acad Child Adolesc Psychiatry Oct 1996;35(10):1355-64.
48. Lewinsohn PM, Rohde P, Seeley JR. Psychosocial characteristics of adolescents with a history of suicide attempt. J Am Acad Child Adolesc Psychiatry 1993;32(1):60-8.
49. Brown RA, Lewinsohn PM, Seeley JR, Wagner EF. Cigarette smoking, major depression, and other psychiatric disorders among adolescents. J Am Acad Child Adolesc Psychiatry 1996;35(12):1602-10.
50. Richardson, LP, Davis, R, Poulton, R, et al. A longitudinal evaluation of adolescent depression and adult obesity. Arch Pediatr Adolesc Med Aug 2003;157(8):739-45.
51. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity [see comments]. N Engl J Med 1997; 337(13):869-73.
52. Pine DS, Goldstein RB, Wolk S, Weissman M. The association between childhood depression and adulthood body mass index. Pediatrics 2001(107):1049-56.
53. Bardone AM, Moffitt T, Caspi A, Dickson N. Adult mental health and social outcomes of adolescent girls with depression and conduct disorder. Dev Psychopathol 1996; 8(4):811-29.
54. Lewinsohn PM, Rohde P, Seeley JR, Klein DN, Gotlib IH. Natural course of adolescent major depressive disorder in a community sample: predictors of recurrence in young adults. Am J Psychiatry 2000;157(10):1584-91.
55. Weissman MM, Wolk S, Goldstein RB, et al. Depressed adolescents grown up. JAMA 1999;281(18):1707-13.
56. Fergusson DM, Woodward LJ. Mental health, educational, and social role outcomes of adolescents with depression. Arch Gen Psychiatry 2002;59(3):225-31.
57. Warner V, Mufson L, Weissman MM. Offspring at high and low risk for depression and anxiety: mechanisms of psychiatric disorder. J Am Acad Child Adolesc Psychiatry Jun 1995;34(6):786-97.
58. 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 Feb 1993;34(2):129-37.
59. Asarnow JR, Tompson M, Hamilton EB, Goldstein MJ, Guthrie D. 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 Apr 1994;22(2):129-46.
60. Brent DA, Birmaher B. Clinical practice. Adolescent depression. N Engl J Med 2002;347(9):667-71.
61. Costello EJ, Edelbrock CS, Costello AJ. Validity of the NIMH Diagnostic Interview Schedule for Children: a comparison between psychiatric and pediatric referrals. J Abnorm Child Psychol 1985;13(4):579-95.
62. Lin KM, Cheung F. Mental health issues for Asian Americans. Psychiatr Serv Jun 1999;50(6):774-80.
63. U.S. Department of Health and Human Services. Mental Health: Culture, Race and Ethnicity. A Supplement to Mental Health: A Report of the Surgeon General. Rockville, MD; 2001.
64. Oinonen KA, Mazmanian D. To what extent do oral contraceptives influence mood and affect? J Affect Disord Aug 2002;70(3):229-40.
65. Guidelines for Adolescent Preventive Services. American Medical Association. http://www.ama-assn.org/ama/upload/mm/39/gapsmono.pdf.
66. Bright Futures. The Maternal and Child Health Bureau. http://www.brightfutures.org/.
67. Goldenring JM, Cohen E. Getting into adolescent heads. Contemp Pediatr 1988;5:75-90.
68. Herjanic B, Reich W. Development of a structured psychiatric interview for children: agreement between child and parent on individual symptoms. J Abnorm Child Psychol Feb 1997;25(1):21-31.
69. Achenbach TM, Ruffle TM. The Child Behavior Checklist

and related forms for assessing behavioral/emotional problems and competencies. Pediatr Rev 2000;21(8):265-71.
70. Myers K, Winters NC. Ten-year review of rating scales. II: scales for internalizing disorders. J Am Acad Child Adolesc Psychiatry Jun 2002;41(6):634-59.
71. Beck AT, Steer RA, Brown GK. Beck Depression Inventory—Second Edition Manual. San Antonio, TX: The Psychological Corporation; 1996.
72. Kovacs M. Children's Depression Inventory Manual. Leading Causes for 2001. North Tonawanda, NY: Multi-Health Systems; 1992.
73. Costello EJ, Angold A. Scales to assess child and adolescent depression: checklists, screens, and nets. J Am Acad Child Adolesc Psychiatry 1988;27(6):726-37.
74. Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. Am J Obstet Gynecol 2000; 183(3):759-69.
75. Johnson JG, Harris ES, Spitzer RL, Williams JB. The patient health questionnaire for adolescents: validation of an instrument for the assessment of mental disorders among adolescent primary care patients. J Adolesc Health 2002:30(3):196-204.
76. Brent DA, Kolko DJ, Birmaher B, et al. Predictors of treatment efficacy in a clinical trial of three psychosocial treatments for adolescent depression. J Am Acad Child Adolesc Psychiatry Sep 1998:37(9):906-14.
77. Paluska SA, Schwenk TL. Physical activity and mental health: current concepts. Sports Med 2000;29(3):167-80.
78. Dwight-Johnson M, Unutzer J, Sherbourne C, Tang L, Wells KB. Can quality improvement programs for depression in primary care address patient preferences for treatment? Med Care Sep 2001:39(9):934-44.
79. Bedi N, Chilvers C, Churchill R, et al. Assessing effectiveness of treatment of depression in primary care. Partially randomised preference trial. Br J Psychiatry Oct 2000:177:312-8.
80. March J, Silva S, Petrycki S, Curry J, Wells K, Fairbank J. 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 Aug 18;292(7):807-20.
81. Hazell P, O'Connell D, Heathcote D, Henry D. Tricyclic drugs for depression in children and adolescents. Cochrane Database Syst Rev 2000;3:CD002317.
82. Emslie GJ, Heiligenstein JH, Wagner KD, 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(10):1205-15.
83. Emslie GJ, Rush AJ, Weinberg WA, et al. A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. Arch Gen Psychiatry 1997:54(11):1031-7.
84. Wagner KD, Ambrosini P, Rynn M, et al. Efficacy of sertraline in the treatment of children and adolescents with major depressive disorder: two randomized controlled trials. JAMA Aug 27 2003;290(8):1033-41.
85. Keller MB, Ryan ND, Strober M, et al. Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial. J Am Acad Child Adolesc Psychiatry 2001;40(7):762-72.
86. 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 Jun 2004;161(6):1079-83.
87. Emslie GJ, Hughes CW, Crismon ML, et al. A feasibility study of the childhood depression medication algorithm: The Texas Children's Medication Algorithm Project (CMAP). J Am Acad Child Adolesc Psychiatry May 2004;43(5):519-27.
88. Axelson DA, Perel JM, Birmaher B, et al. Sertraline pharmacokinetics and dynamics in adolescents. J Am Acad Child Adolesc Psychiatry Sep 2002;41(9):1037-44.
89. Joffe RT, Levitt AJ, Sokolov ST, Young LT. Response to an open trial of a second SSRI in major depression. J Clin Psychiatry Mar 1996;57(3):114-5.
90. Brent DA, Holder D, Kolko D, et al. A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. Arch Gen Psychiatry 1997;54(9):877-85.
91. Wood A, Harrington R, Moore A. Controlled trial of a brief cognitive-behavioural intervention in adolescent patients with depressive disorders. J Child Psychol Psychiatry Sep 1996;37(6):737-46.
92. Levinson W. In context: physician-patient communication and managed care. J Med Pract Manage 1999;14(5):226-30.
93. Clarke GN, Hornbrook M, Lynch F, et al. A randomized trial of a group cognitive intervention for preventing depression in adolescent offspring of depressed parents. Arch Gen Psychiatry 2001;58(12):1127-34.
94. Clarke GN, Rohde P, Lewinsohn PM, Hops H, Seeley JR. Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. J Am Acad Child Adolesc Psychiatry 1999;38(3):272-9.
95. Mufson L, Dorta KP, Wickramaratne P, Nomura Y, Olfson M, Weissman MM. A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. Arch Gen Psychiatry Jun 2004;61(6):577-84.
96. Mufson L, Weissman MM, Moreau D, Garfinkel R. Efficacy of interpersonal psychotherapy for depressed adolescents. Arch Gen Psychiatry Jun 1999;56(6):573-9.
97. Rossello J, Bernal G. The efficacy of cognitive-behavioral and interpersonal treatments for depression in Puerto Rican adolescents. J Consult Clin Psychol Oct 1999;67(5):734-45.
98. Thase ME, Friedman ES, Howland RH. Management of treatment-resistant depression: psychotherapeutic perspectives. J Clin Psychiatry 2001;62(Suppl.):18-24.
99. Keller MB, McCullough JP, Klein DN, et al. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. N Engl J Med May 18 2000; 342(20):1462-70.
100. Kroll L, Harrington R, Jayson D, Fraser J, Gowers S. Pilot study of continuation cognitive-behavioral therapy for major depression in adolescent psychiatric patients. J Am Acad Child Adolesc Psychiatry Sep 1996;35(9):1156-61.