Depression in Children and Adolescents: Evaluation and Treatment

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The prevalence of major unipolar depression in children and adolescents is increasing in the United States. In 2016, approximately 5% of 12-year-olds and 17% of 17-year-olds reported experiencing a major depressive episode in the previous 12 months. Screening for depression in adolescents 12 years and older should be conducted annually using a validated instrument, such as the Patient Health Questionnaire-9: Modified for Teens. If the diagnosis is confirmed, treatment should be initiated for

persistent, moderate, and severe depression. Active support and monitoring may be sufficient for mild, self-limited depression. For more severe depression, evidence indicates greater response to treatment when psychotherapy (e.g., cognitive behavior therapy) and an antidepressant are used concurrently, compared with either treatment alone. Fluoxetine and escitalopram are the only antidepressants approved by the U.S. Food and Drug Administration for treatment of depression in children and adolescents. Fluoxetine may be used in patients older than eight years, and escitalopram may be used in patients 12 years and older. Monitoring for suicidality is necessary in children and ado-



lescents receiving pharmacotherapy, with frequency of monitoring based on each patient's individual risk. The decision to modify treatment (add, increase, change the medication or add psychotherapy) should be made after about four to eight weeks. Consultation with or referral to a mental health subspecialist is warranted if symptoms worsen or do not improve despite treatment and for those who become a risk to themselves or others. (Am Fam Physician. 2019;100(10):609-617. Copyright © 2019 American Academy of Family Physicians.)

Illustration by Jonathan Dimes

The prevalence of depression is increasing among youth in the United States. The 2005 to 2014 National Surveys on Drug Use and Health, which included 172,495 adolescents 12 to 17 years of age, found that the percentage of adolescents who experienced one or more major depressive episodes in the previous 12 months increased from 9% in 2005 to 11% in 2014. In 2016, this percentage was approximately 13% (5% in 12-year-olds, 13% in 14-year-olds, and 17% in 17-year-olds), and although 70% of youths

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 607.

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Patient information: A handout on this topic is available at https://www.aafp.org/afp/2019/1115/p609-s1.html.

experienced severe impairment from depression, only about 40% received treatment.¹ Treatment rates have changed little since 2005, raising concern that adolescents are not receiving needed care for depression.¹

Risk Factors

Increased risk of depression in children and adolescents may be due to biologic, psychological, or environmental factors (*Table 1*).²⁻³⁴ In children 12 years and younger, depression is slightly more common in boys than in girls (1.3% vs. 0.8%).³⁵ However, after puberty, adolescent girls are more likely to experience depression.³⁵

Screening for Depression

The U.S. Preventive Services Task Force (USPSTF) recommends screening children and adolescents 12 to 18 years of age for major depressive disorder with adequate systems in

TABLE 1

Risk Factors for Depression in Children and Adolescents

Biologic

Being overweight²

Chronic illness (e.g., lupus, diabetes mellitus, asthma)³⁻⁵

Early puberty (girls)6

Family history of depression⁷

Female sex8,9

 $High-functioning\ autism^{10,11}$

LGBTQ identified¹²

Polymorphisms in the serotonin, dopamine, or monoamine oxidase genes¹³

Psychological

Body dissatisfaction and early dieting^{2,14,15}; sweetened beverage consumption¹⁶

Dysfunctional emotional regulation¹⁷

Internet gaming disorder or video game addiction 18,19

Less attachment to parents and peers, or problems with peers^{6-8,17}

Low self-esteem and lack of self-kindness^{20,21}

Negative thinking and recall styles^{22,23}

Other mental health and behavior problems, including previous depression and cannabis or tobacco use^{6-8,10,13}

Problematic use of social media (e.g., Facebook)²⁴

Worried about school grades or standardized testing⁸

Environmental

Academic difficulties⁸

Being victimized or bullied or witnessing violence^{7,8,25,26}; physical, sexual, or emotional abuse or neglect^{27,28}

Exposure to natural disasters^{29,30}

Few opportunities for physical activity and sports³¹; low physical activity³²; greater than two hours per day of leisure-time screen use³¹

Foreign born or perceived discrimination^{8,13}

Loss of a loved one8

Low socioeconomic status^{7,8,33,34}

Parental rejection or low parental involvement^{6,8,13}

Poor family functioning or caretaker depression^{6,8,13}

LGBTQ = lesbian, gay, bisexual, transgender, queer/questioning. *Information from references 2-34*.

place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.³⁶ The American Academy of Family Physicians supports the USPSTF recommendation.³⁷ In 2018, the American Academy of Pediatrics endorsed the Guidelines for Adolescent Depression in Primary Care (GLAD-PC), which recommends screening adolescents 12 years and older annually for depressive disorders using a self-report screening tool.^{38,39}

There are various instruments to screen adolescents for depression. One popular instrument for use in primary care is the Patient Health Questionnaire-9: Modified for Teens (also called PHQ-A) for patients 11 to 17 years of age. The PHQ-A is shown in *Figure 1* and *Table 2*, along with four questions not used in scoring that address suicidality, dysthymia, and severity of depression.^{40,41}

Clinical Presentation

The presenting sign of major depressive disorder may be insomnia or hypersomnia; weight loss or gain; difficulty concentrating; loss of interest in school, sports, or other previously enjoyable activities; increased irritability; or feeling sad or worthless. ⁴² To distinguish between normal grief, such as after the loss of a loved one, and a major depressive episode, it may be helpful to determine whether the predominant symptom is a sense of loss or emptiness (more

typical of grief) vs. a persistent depressed mood with the inability to anticipate future enjoyable events (more typical of depression).⁴²

Diagnosis

When a child or adolescent screens positive using a formal screening tool, such as the PHQ-A, or when he or she presents with symptoms indicating a possible depressive disorder, the primary care physician should assess whether the symptoms are a result of a major depressive episode or another condition that could present with similar symptoms. To diagnose major depressive disorder, criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. (DSM-5), must be met and not explained by substance abuse, medication use, or other medical or psychological condition. The full DSM-5 criteria are available at https://www.aafp.org/afp/2018/1015/p508.html#afp201810 15p508-t6. Some children may develop a cranky mood or irritability rather than sadness.

Medical conditions that may present similarly to depression include hypothyroidism, anemia, autoimmune disease, and vitamin deficiency. Laboratory tests that may be helpful in ruling out common medical conditions that could be mistaken for depression include complete blood count; comprehensive metabolic profile panel; an inflammatory

FIGURE 1					
Name:	Clinician:			Date:	
Instructions: How often have you been bothers symptoms during the past <i>two weeks?</i> For each box beneath the answer that best describes how	symptom put an "X" in the	0 Not at all	1 Several days	2 More than half the days	3 Nearly every day
1. Feeling down, depressed, irritable, or hopeles	ss?				
2. Little interest or pleasure in doing things?					
3. Trouble falling asleep, staying asleep, or sleep	ping too much?				
4. Poor appetite, weight loss, or overeating?					
5. Feeling tired or having little energy?					
6. Feeling bad about yourself – or feeling that y have let yourself or your family down?	ou are a failure, or that you				
7. Trouble concentrating on things like schoolw television?	ork, reading, or watching				
8. Moving or speaking so slowly that other peo opposite – being so fidgety or restless that y more than usual?					
9. Thoughts that you would be better off dead of other way?	or of hurting yourself in some				
In the past year, have you felt depressed or sad r \square Yes \square No	most days, even if you felt okay s	sometimes?			
If you are experiencing any of the problems on take care of things at home, or get along with of \Box Not difficult at all \Box Somewhat difficult	ther people?		made it for	you to do you	ır work,
Has there been a time in the past month when y \Box Yes \Box No	ou have had serious thoughts a	bout ending <u>y</u>	your life?		
Have you <i>ever</i> , in your <i>whole life</i> , tried to kill you \square Yes \square No	ırself or made a suicide attempt	?			
If you have had thoughts that you would be bett go to a hospital emergency room, or call 911.	er off dead or of hurting yoursel	lf in some way	y, discuss th	nis with your p	ohysician,
Patient Health Questionnaire-9: Modified fo	or Teens.				
Note: See Table 2 for scoring.					
Adapted from Patient Health Questionnaire (PHQ) scretion from reference 41.	eners. Accessed August 12, 2019. ht	tp://www.phqs	creeners.con	n, with additior	nal informa

biomarker, such as C-reactive protein or erythrocyte sedimentation rate; thyroid-stimulating hormone; vitamin B_{12} ; and folate.

Other psychological conditions that may present similarly to major depressive disorder include persistent depressive disorder (also called dysthymia) and disruptive mood dysregulation disorder. If a child or adolescent has a depressed mood for more days than not for at least one year,

the diagnosis may be persistent depressive disorder, which is often treated the same as a major depressive episode (e.g., antidepressants, psychotherapy).⁴² If a child or adolescent is predominantly angry with temper outbursts, the diagnosis may be disruptive mood dysregulation disorder or post-traumatic stress disorder.⁴²

Symptoms of bipolar disorder, eating disorders, and conduct disorders may also overlap with major depressive

disorder. Children and adolescents may have more than one psychiatric diagnosis concurrently, such as comorbid depression and anxiety. According to the Centers for Disease Control and Prevention, 74% of children three to 17 years of age who have depression also have anxiety, and 47% of children with depression also have a behavior problem. Therefore, a thorough assessment is needed, with possible mental health consultation or referral.

Risk Assessment for Suicide

Suicide is the second leading cause of death for people 10 to 24 years of age after unintentional injury.⁴³ Depression is a risk factor for suicide, but at-risk youth can be easily missed without specific suicide screening. In one study, nurses in a pediatric emergency department used the Ask Suicide-Screening Questions (ASQ) tool to assess suicide risk in 970 adolescents who presented with psychiatric problems.44 Of those who screened positive, 53% did not present with suiciderelated problems. The sensitivity and specificity for a return visit to the emergency department because of suicidality within six months were 93% and 43%, respectively, for a positive predictive value of 10% and a negative predictive value of 99%.44 The ASQ screening test is shown in Figure 2.45 The complete ASQ toolkit is available at https://www.nimh.nih.gov/research/researchconducted-at-nimh/asq-toolkit-materials/index. shtml#outpatient.

Treatment

INITIAL MANAGEMENT

The GLAD-PC guidelines recommend that primary care physicians counsel families and patients about depression and develop a treatment plan that includes setting specific goals involving functioning at home, at school, and with peers.³⁸ For example, a treatment plan might include treating others with respect, attending

family meals, keeping up with schoolwork, and spending time in activities with supportive peers. Additionally, a safety plan should be established that limits access to lethal means, such as removing firearms from the home or locking them up. It should also provide a way for the patient to communicate during an acute crisis (e.g., providing phone numbers for people to contact if suicidal thoughts occur, creating a list of coping skills, educating the parents on how to recognize if the patient is a risk to self or others).³⁸ If the

TABLE 2

Scoring the PHQ-9: Modified for Teens

Scoring is easy but involves thinking about several different aspects of depression.

To use the PHQ-9 as a diagnostic aid for major depressive disorder:

Question 1 or 2 needs to be endorsed as a 2 or 3.

Five or more positive* answers are needed.

The functional impairment question (How difficult...) needs to be rated at least as "somewhat difficult."

To use the PHQ-9 to screen for all types of depression or other mental illness:

All positive* answers should be followed by a clinical interview.

A total PHQ-9 score of 10 points or more has a good sensitivity and specificity for major depressive disorder.

To use the PHQ-9 to aid in the diagnosis of dysthymia:

The dysthymia question (In the past year...) should be endorsed as "ves."

To use the PHQ-9 to screen for suicide risk:

All positive answers to question 9 and the two additional suicide items must be followed by a clinical interview.

To use the PHQ-9 to obtain a total score and assess depressive severity: Add up the numbers endorsed for questions 1 to 9 and obtain a total score.

See the chart below.

20 to 27

lotal score	Depression severity
0 to 4	No or minimal depression
5 to 9	Mild depression
10 to 14	Moderate depression
15 to 19	Moderately severe depression

Note: See Figure 1 for the questionnaire.

Severe depression

PHQ = patient health questionnaire.

*-Positive is defined by a 2 or 3 in questions 1 to 8 and by a 1, 2, or 3 in question 9.

Adapted with permission from American Academy of Child & Adolescent Psychiatry. PHQ-9: Modified for Teens. Accessed August 12, 2019. http://www.aacap.org/App_Themes/AACAP/docs/member_resources/toolbox_for_clinical_practice_and_outcomes/symptoms/GLAD-PC_PHQ-9.pdf, with additional information from reference 40.

danger of suicide becomes imminent, psychiatric evaluation in a hospital emergency department or psychiatry crisis clinic is needed.

For mild depression, which may be short-lived, primary care physicians should consider active support such as counseling about depression and treatment options, facilitating caregiver/patient depression self-management, and monitoring the patient every week or two for six to eight weeks before initiating pharmacotherapy and/or

psychotherapy.⁴⁶⁻⁵⁰ According to the DSM-5, although the symptoms of mild depression are distressing, they are manageable and result in only minor impairment in functioning, whereas severe depression causes more seriously distressing, unmanageable symptoms that greatly impact functioning. See *Figure 3* for a suggested approach to the management of depression in children and adolescents. 43,50

ONGOING MANAGEMENT

Treatment options for children and adolescents with depression include psychotherapy and antidepressants. Cognitive behavior therapy (CBT) is a form of talk therapy that focuses on changing behaviors by correcting faulty or potentially harmful thought patterns and generally includes five to 20 sessions. Whereas CBT focuses on cognition and behaviors, interpersonal psychotherapy concentrates on improving interpersonal relationships and typically includes around 12 to 16 sessions.

Fluoxetine (Prozac) and escitalopram (Lexapro) are the only two medications approved by the U.S. Food and Drug Administration to treat major depressive disorder in children and adolescents. Fluoxetine is approved for patients eight years and older, and escitalopram is approved for patients 12 years and older. There are concerns of increased suicidality with the use of fluoxetine and escitalopram in this population.⁵¹ Although there were no suicides in trials of children and adolescents taking antidepressants, suicidal thoughts and behaviors were increased compared with placebo (4% vs. 2%).51 Children and adolescents who are taking these medications should be monitored for suicidality. The frequency of monitoring should be based on the individual patient's risk (e.g., weekly monitoring at treatment onset, monthly monitoring in a child showing steady improvement on antidepressants).

PHARMACOTHERAPY ALONE

Three systematic reviews of randomized controlled trials including children and adolescents with major depressive disorder support the use of fluoxetine as the first-line antidepressant medication. 52-54 Two reviews also support the use of escitalopram as initial therapy. 52,54 However, the effects of fluoxetine and escitalopram as monotherapy were often similar to placebo, depending

FIGURE 2

Ask the patient: 1. In the past few weeks, have you wished you were dead? ☐ Yes ☐ No 2. In the past few weeks, have you felt that you or your family would be better off if you were dead? ☐ Yes ☐ No. 3. In the past week, have you been having thoughts about killing yourself? ☐ Yes ☐ No 4. Have you ever tried to kill yourself? ☐ Yes ☐ No If yes, how? When? If the patient answers "Yes" to any of the above, ask the following acuity question: 5. Are you having thoughts of killing yourself now? ☐ Yes ☐ No If yes, please describe: ___ Next steps: If the patient answers "No" to all of questions 1 to 4, screening is complete (not necessary to ask question 5). No intervention is necessary. (Note: clinical judgment can always override a negative screen.)

If the patient answers "Yes" to any of questions 1 to 4 or refuses to answer, it is considered a positive screen. Ask question 5 to assess acuity:

 \square "Yes" to question 5 = acute positive screen (imminent risk identified)

Patient requires an urgent safety assessment and full mental health evaluation. Patient cannot leave until evaluated for safety. Keep patient in sight. Remove all dangerous objects from room.

Alert physician or clinician responsible for patient's care. ☐ "No" to question 5 = nonacute positive screen (potential risk

identified)

Patient requires a brief suicide safety assessment to determine if a full mental health evaluation is needed. Patient cannot leave until evaluated for safety.

Alert physician or clinician responsible for patient's care.

Provide resources to all patients

24/7 National Suicide Prevention Lifeline: 800-273-TALK (8255), En Español: 888-628-9454

24/7 Crisis Text Line: text "HOME" to 741-741

Ask Suicide-Screening Questions Tool to assess for suicidality.

Adapted from National Institute of Mental Health. Suicide risk screening tool. Accessed August 12, 2019. https://www.nimh.nih.gov/research/researchconducted-at-nimh/asq-toolkit-materials/index.shtml#outpatient

on the outcome measured. Tricyclic antidepressants, other selective serotonin reuptake inhibitors, and serotonin-norepinephrine reuptake inhibitors have not been shown to be effective in treating depression in children and adolescents. 46,52-54 If neither fluoxetine nor escitalopram is effective and antidepressant therapy is desired, referral to a child or adolescent psychiatrist is recommended.

PSYCHOTHERAPY ALONE

Evidence is mixed for the use of CBT as monotherapy in children and adolescents with depression. A systematic review for the USPSTF found no benefit of CBT on remission or recovery and inconsistent effects on symptoms, response, and functioning.54 One trial of youth with major depression who declined antidepressants found that compared with self-selected treatment as usual, 12 weeks of CBT was associated with shorter time to treatment response and remission and improved depression scores through week 52 but not in weeks 53 to 104.55 In children and adolescents with subclinical depression, one systematic review (19 trials) found moderate-quality evidence that CBT is associated with a small effect on depressive symptoms vs. waitlist or no treatment.56

COMBINED THERAPY

Evidence from a good-quality randomized trial suggests that adolescents are most likely to achieve remission with 12 weeks of combined therapy with fluoxetine and CBT (37%; number needed to treat = 4) compared with either therapy alone (23% with fluoxetine; number needed to treat = 11; 16% with CBT) or placebo (17%). 47,57 Suicidality declined with duration of treatment for all therapies, but the decline was less steep for fluoxetine alone (26.2% at baseline to 13.7% at week 36) vs. combination therapy (39.6% to 2.5%) and CBT alone (25.2% to 3.9%). 47,57

In another trial of adolescents who achieved at least a 50% decrease in depression scores following six weeks of fluoxetine treatment, those who were randomized to receive the addition of CBT to fluoxetine therapy for six months were less likely to relapse at 78 weeks compared with continued fluoxetine monotherapy (36% vs. 62%).⁵⁸

Children and adolescents with moderate or severe depression or persistent mild depression

FIGURE 3 Major depressive disorder diagnosed Mild? No Yes Active support and monitoring (every one to two weeks) Adequate improvement after six to eight weeks? No Yes If the patient has persistent mild, mod-Routine care erate, or severe depression, consider and monitoring mental health consultation or referral Manage in primary care setting? No Yes Mental health Initiate antidepressant and/or psychotherapy referral Monitor closely Consider ongoing mental health consultation Adequate improvement after four to eight weeks? No Yes Go to A Reassess diagnosis Confirm major depressive disorder? No Yes Determine Consider adding, increasing, or changing medication new diagnosis Consider adding psychotherapy Manage/refer Consider mental health consultation or referral as appropriate Provide additional education and monitoring Adequate improvement after four to eight weeks? No Mental A Continue medication for one year after symptom resolution health Monitor monthly for six months, then regularly for 18 months referral Maintain contact with mental health specialist if ongoing treatment Management of depression in children and adolescents. Information from references 43 and 50.

SORT: KEY CLINICAL RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments	
Adolescents should be screened annually for depression. ^{36,38}	В	Recommendation from evidence-based guidelines	
For children and adolescents with mild depression, consider delaying pharma- cotherapy and psychotherapy for six to eight weeks while providing supportive care and close monitoring, because patients may improve without further treatment. 46-50		Evidence from response in placebo arms of trials and recommendation from consensus guidelines	
Children and adolescents with moderate or severe depression or persistent mild depression should be treated with fluoxetine (Prozac) or escitalopram (Lexapro) in conjunction with cognitive behavior therapy or other talk therapy. 47.57-59		Consistent evidence from several randomized trials	
For those who do not initiate combination therapy, monotherapy with an antidepressant or psychotherapy is recommended, although the likelihood of benefit is lower. 46,52-56		Evidence from several randomized trials and systematic reviews	
A - consistant, good quality nations oriented evidence: P - inconsistant or limited quality nat			

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, diseaseoriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.

should be treated with fluoxetine or escitalogram in conjunction with CBT or other talk therapy. 47,57-59 If combination therapy is not used, monotherapy with an antidepressant or psychotherapy is recommended, although the likelihood of benefit is lower. 46,52-56

Reassessing Treatment and Treatment **Duration**

One trial found that early reassessment of depression is valuable.43 In this study, all youth received interpersonal psychotherapy and were randomized to a four- or eightweek follow-up assessment for treatment modification. If additional treatment was needed because of inadequate response, patients were further randomized to add-on fluoxetine or more intense (twice weekly) psychotherapy. Those who were reassessed at four weeks improved the most at 16 weeks (a difference of 5.7 points on the Hamilton Rating Scale for Depression; scores on this scale can range from 0 to 58 points, with a score of 0 to 7 considered normal and a score of 20 associated with moderate depression; P < .05). Additionally, those who began add-on fluoxetine at four weeks had better posttreatment depression scores than those who began intense interpersonal psychotherapy at eight weeks, although there was no difference in global assessment scores between the two groups.

Treatment duration for talk therapy in adolescents with unipolar depression is typically six months or less, but longer treatment may be necessary. Although good evidence regarding the duration of medication treatment in adolescents with depression is lacking, the GLAD-PC guidelines recommend continuing medication for one year beyond the resolution of symptoms.⁵⁰

Referral to a Mental Health Subspecialist

If a child or adolescent does not improve after initial treatment for depression, the primary care physician may add, change, or increase a medication and may consider referral for psychotherapy. Referral to a licensed mental health professional is appropriate at any point in the treatment process. However, if the depression does not improve or the child deteriorates even with treatment, consultation with or referral to a child or adolescent psychiatrist is necessary.

This article updates previous articles on this topic by Clark, et al.60; Bhatia and Bhatia61; and Son and Kirchner.62

Data Sources: We conducted general and targeted searches using Essential Evidence Plus, Ovid Medline, PubMed, the Cochrane Database of Systematic Reviews, the U.S. Preventive Services Task Force, the Agency for Healthcare Research and Quality, and UpToDate, including the key words children or adolescents with depression. Search dates: November 2018 to January 2019, and September 27, 2019.

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