

Screening and Treatment for Major Depressive Disorder in Children and Adolescents: US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

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ABSTRACT

DESCRIPTION. This is an update of the 2002 US Preventive Services Task Force recommendation on screening for child and adolescent major depressive disorder.

METHODS. The US Preventive Services Task Force weighed the benefits and harms of screening and treatment for major depressive disorder in children and adolescents, incorporating new evidence addressing gaps in the 2002 recommendation statement. Evidence examined included the benefits and harms of screening, the accuracy of primary care–feasible screening tests, and the benefits and risks of treating depression by using psychotherapy and/or medications in patients aged 7 to 18 years.

RECOMMENDATIONS. Screen adolescents (12–18 years of age) for major depressive disorder when systems are in place to ensure accurate diagnosis, psychotherapy (cognitive-behavioral or interpersonal), and follow-up (B recommendation). Evidence is insufficient to warrant a recommendation to screen children (7–11 years of age) for major depressive disorder (I statement). *Pediatrics* 2009;123:1223–1228

THE US PREVENTIVE Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition. It bases its recommendations on a systematic review of the evidence of the benefits and harms and an assessment of the net benefit of the service.

The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policy-makers should understand the evidence but individualize decision-making to the specific patient or situation.

SUMMARY OF RECOMMENDATION AND EVIDENCE

The USPSTF recommends screening of adolescents (12–18 years of age) for major depressive disorder (MDD) when systems are in place to ensure accurate diagnosis, psychotherapy (cognitive-behavioral or interpersonal), and follow-up (B recommendation) (see “Clinical Considerations” below for additional information).

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening of children (7–11 years of age) for MDD (I statement).

See Fig 1 for a summary of the recommendation and suggestions for clinical practice. Table 1 describes the USPSTF grades, and Table 2 describes the USPSTF classification of levels of certainty about net benefits.

RATIONALE

Importance

MDD among youth is a disabling condition that is associated with serious long-term morbidities and risk of suicide. However, the majority of depressed youth are undiagnosed and untreated.

Detection

There is adequate evidence that screening tests accurately identify MDD in adolescents. The USPSTF found inadequate evidence that screening tests accurately identify MDD in children.

Benefits of Detection and Early Intervention

- Adolescents (12–18 years of age): The USPSTF found adequate evidence that treatment in adolescents with selective serotonin reuptake inhibitors (SSRIs), psychotherapy, and combined therapy (SSRIs and psychotherapy) results in decreases in MDD symptoms.

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Key Words

screening, treatment, depression, child and adolescent

Abbreviations

USPSTF—US Preventive Services Task Force

MDD—major depressive disorder

SSRI—selective serotonin reuptake inhibitor

PHQ-A—Patient Health Questionnaire for Adolescents

BDI-PC—Beck Depression Inventory-Primary Care Version

RCT—randomized, controlled trial

CI—confidence interval

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Population	Adolescents (12–18 y)	Children (7–11 y)
Recommendation	<p>Screen (when systems for diagnosis, treatment, and follow-up are in place)</p> <p>Grade B</p>	<p>No recommendation</p> <p>Grade I (insufficient evidence)</p>
Risk assessment	Risk factors for major depressive disorder (MDD) include parental depression, having comorbid mental health or chronic medical conditions, and having experienced a major negative life event.	
Screening tests	<p>The following screening tests have been shown to do well in teens in primary care settings:</p> <ul style="list-style-type: none"> • Patient Health Questionnaire for Adolescents (PHQ-A) • Beck Depression Inventory–Primary Care version (BDI-PC) 	Screening instruments perform less well in younger children.
Treatments	<p>Among pharmacotherapies, fluoxetine, a selective serotonin reuptake inhibitor (SSRI), has been found efficacious. However, because of risk of suicidality, SSRIs should be considered only if clinical monitoring is possible. Various modes of psychotherapy, and pharmacotherapy combined with psychotherapy, have been found efficacious.</p>	Evidence on the balance of benefits and harms of treatment of younger children is insufficient for a recommendation.

FIGURE 1

For a summary of the evidence systematically reviewed in making these recommendations, the full recommendation statement, and supporting documents, please go to www.preventiveservices.ahrq.gov.

TABLE 1 What the USPSTF Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if there are other considerations in support of the offering/providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking or is of poor quality or conflicting, and the balance of benefits and harms cannot be determined.	Read "Clinical Considerations" (in the statement). If offered, patients should understand the uncertainty about the balance of benefits and harms.

- Children (7–11 years of age): The USPSTF found inadequate evidence to support the benefits of treatment in children. SSRIs (fluoxetine) reduce MDD symptoms in children; however, there are limited data on the benefits of psychotherapy and the benefits of psychotherapy plus SSRIs in children.

Harms of Detection and Early Treatment

- Adolescents (12–18 years of age): There is convincing evidence that there are harms of SSRIs (risk of suicid-

ality [ie, suicide ideation, preparatory acts, or suicide attempts]) in adolescents. Limited evidence exists regarding the harms of combining SSRIs and psychotherapy. However, there is inadequate evidence about the harms of screening and psychotherapy in adolescents, which are probably small.

- Children (7–11 years of age): SSRIs (fluoxetine) demonstrated harms in children (risk of suicidality); however, there is limited evidence on the harms of psychotherapy and on the harms of combining psychotherapy and

TABLE 2 USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion, therefore, is unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: <ul style="list-style-type: none"> • the number, size, or quality of individual studies; • inconsistency of findings across individual studies; • limited generalizability of findings to routine primary care practice; or • lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: <ul style="list-style-type: none"> • the limited number or size of studies; • important flaws in study design or methods; • inconsistency of findings across individual studies; • gaps in the chain of evidence; • findings not generalizable to routine primary care practice; or • a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.

SSRIs (fluoxetine) in children. There is also limited evidence about the harms of screening children. The USPSTF judged that the overall evidence is inadequate regarding the harms of screening and treatment in children.

USPSTF Assessment

The USPSTF concludes that:

- In adolescents (12–18 years of age), there is moderate certainty that the net benefit of psychotherapy is moderate.
- In children (7–11 years of age), the evidence is lacking, and the balance of benefits and harms of psychotherapy cannot be determined.

CLINICAL CONSIDERATIONS

Patient Population Under Consideration

This USPSTF recommendation addresses screening for MDD in adolescents (12–18 years of age) and children (7–11 years of age) in the general population. There is a spectrum of depressive disorders. This report focuses only on screening for MDD and does not address screening for various less-severe depressive disorders.

Assessment of Risk

A variety of factors contribute to the development of MDD. Most people who develop MDD have multiple risk factors. However, risk factors for MDD can be difficult to assess. As a result, researchers have focused on identifying youth subgroups at increased risk of developing MDD. Important risk factors that can be assessed relatively accurately and reliably include parental depression, having comorbid mental health or chronic medical conditions, and having experienced a major negative life event.

Screening Tests

Instruments developed for primary care (Patient Health Questionnaire for Adolescents [PHQ-A] and the Beck Depression Inventory-Primary Care Version [BDI-PC]) have been used successfully in adolescents. There are limited data describing the accuracy of using MDD screening instruments in younger children (7–11 years of age).

Treatment

Among pharmacotherapies available for the treatment of MDD in children and adolescents, SSRIs have been found to be efficacious. Treating depressed youth with SSRIs is associated with an increased risk of suicidality and, therefore, should only be considered if judicious clinical monitoring is possible. Psychotherapy trials indicate that a variety of psychotherapy types are efficacious among adolescents (including cognitive-behavioral and interpersonal therapies). Harms of psychotherapy are felt to be small.

OTHER CONSIDERATIONS

Research Needs/Gaps

Studies are needed to address the comparative effectiveness of pharmacologic and nonpharmacologic treatments for MDD in children and adolescents, particularly those at high risk for suicidality or nonadherence to pharmacotherapy. Also needed are studies to examine collaborative care management approaches compared with usual clinical care, as well as descriptive epidemiologic studies describing the prevalence of MDD in children and adolescents in primary health care settings according to age, gender, and race/ethnicity. Observational studies of risks for longer-term outcomes, including mania precipitation, with use of antidepressants (particularly SSRIs) would contribute to addressing current evidence gaps.

DISCUSSION

Burden of Disease

Clinical depression is characterized by persistent sadness, irritability, or a loss of interest or pleasure in most activities. Additional symptoms may include social isolation, decline in school work, anger, sleep and appetite disturbances, or nonspecific pain. MDD may be present when these symptoms cluster together and persist for 2 weeks or more.

MDD is estimated to occur in 2.8% of children younger than 13 years of age. The estimated prevalence of MDD among adolescents aged 13 to 18 years is 5.6%, with a higher prevalence among girls than boys (5.9% vs 4.6%, respectively). Lifetime prevalence among adolescents may be as high as 20%. Point prevalence of MDD among adolescents is reported as ranging from 9% to 21% in primary care settings.¹

MDD is associated with significant morbidity and mortality. Morbidity in children and adolescents may be demonstrated through decreased school performance, poor social functioning, early pregnancy, increased physical illness, and substance abuse. Depressed adolescents have more psychiatric and medical hospitalizations than adolescents who are not depressed. Children with depressive disorders have increased health care costs (including general medical care and mental health care) compared with children without mental health diagnoses or children with other mental health diagnoses (except conduct disorder). Depressed youth are at an increased risk of suicide, which is the third leading cause of death among those aged 15 to 24 years and the sixth leading cause among those aged 5 to 14 years. Adolescent MDD is particularly associated with increased risk of MDD occurrence in early adulthood.¹

Scope of Review

The USPSTF updated its 2002 recommendation on screening for child and adolescent MDD among average-risk primary care populations. The objective was to review the literature to summarize the current state of evidence and identify new evidence addressing previously identified gaps. Evidence examined included the benefits and harms of screening, the accuracy of primary care–feasible screening tests, and the benefits and risks of treating depression by using psychotherapy and/or medications in patients aged 7 to 18 years.

Accuracy of Screening Tests

There is adequate evidence that screening tests can accurately identify MDD in adolescents. Nine fair-quality studies of MDD screening-instrument accuracy in children and adolescents addressed 6 depression instruments. Two of these studies were conducted in primary care settings, 1 in a community setting, and 6 in school settings. Although 1 study included children younger than 10 years of age, most studies focused on adolescents 12 years of age or older.¹ Studies that involved younger children demonstrated poorer performance of the screening instruments.

Two instruments demonstrated good sensitivity and specificity in primary care settings in adolescents: a sensitivity range of 73% for the PHQ-A to 91% for the BDI-PC and a specificity range from 91% for the BDI-PC to 94% for the PHQ-A.

In school settings, studies examined the Beck Depression Inventory (BDI), the Center for Epidemiologic Study-Depression Scale (CES-D), and the Revised Clinical Interview Scale (CIS-R). In this setting, cutoffs of both 11 and 16 performed reasonably to very well on the

BDI, with sensitivity ranging from 84% to 100% (BDI \geq 11) or 77% to 100% (BDI \geq 16) and specificity ranging from 77% to 86% (BDI \geq 11) or 65% to 96% (BDI \geq 16). Confidence in the school-setting results is quite limited, however, because of methodologic problems within each study.

The large number of instruments and sample and setting heterogeneity makes generalization across studies difficult and may explain the wide range of performance characteristics reported (sensitivity ranged from 18% to 100% and specificity ranged from 38% to 97%). Each of the studies had methodologic limitations such as high levels of attrition, nonrandom selection, excessive delays between screening and diagnostic interviews, poor reporting of methods, small samples, and the lack of a criterion standard for the diagnosis of depression.

Effectiveness of Early Detection and/or Treatment

Several fair- or good-quality randomized, controlled trials (RCTs) were identified that reported health outcomes among children or adolescents with MDD treated with SSRIs, psychotherapy, or both. The reviewed trials evaluated the short-term efficacy of 5 SSRIs (fluoxetine, citalopram, paroxetine, escitalopram, sertraline) compared with placebo, 10 different group or individually delivered psychotherapies compared with control conditions, and combined therapy (cognitive-behavioral psychotherapy and an SSRI). Trials were conducted in community- or school-based clinical settings, academic research centers, and schools. The majority of SSRI trials included children as young as 8 years or younger in their study samples. The majority of trials that tested psychotherapy interventions included adolescents 12 to 14 years and older. Two psychotherapy trials included 9- or 10-year-olds, and no completed trials included children 7 or 8 years of age.

Trial outcomes included treatment response, which was defined differently across studies. Additional outcomes reported included global functioning. Depression outcomes were reported after 8 to 12 weeks of SSRI treatment or 4 to 16 weeks of psychotherapy. No controlled data were available for longer-term outcomes.

Selective Serotonin Reuptake Inhibitors

SSRI users had higher response rates than those who were taking placebo medication, with an absolute risk difference between treatment and control groups of 12% (95% confidence interval [CI]: 7%–16%). Fluoxetine and citalopram yielded statistically significant higher response rates than did other SSRIs. Data from meta-analyses of efficacy among children and adolescents, analyzed separately, suggested that SSRIs were less effective among children. However, meta-analyses of SSRI treatment also demonstrated that fluoxetine is efficacious for treating both child and adolescent populations. Fluoxetine is the only drug that is approved by the US Food and Drug Administration for treating MDD among youth. The absolute risk difference in the response between treatment and intervention groups was ~20% for both age groups, which would mean that ~5 children or

adolescents would need to be treated for 1 to benefit.¹ Fluoxetine was studied in an effectiveness trial among adolescents (the Treatment for Adolescents With Depression Study) and also was found to be effective.²

Psychotherapy

The majority of psychotherapy RCTs revealed that treated patients had higher response rates, remission rates, or greater reductions in MDD symptoms after intervention, as compared with a control group. Results of psychotherapy RCTs have demonstrated that different psychotherapy types are efficacious among adolescents, including group cognitive-behavioral therapy and interpersonal therapy.¹

SSRIs Combined With Psychotherapy

In 1 study (the Treatment for Adolescents With Depression Study), the group that received combined therapy of fluoxetine and individual cognitive-behavioral therapy showed a 71% response rate versus a 35% response in adolescents who were taking placebo and receiving weekly clinical monitoring.² Nearly 3 of 4 patients responded to combined therapy, compared with 1 in 3 who responded in the placebo group. These results indicate that 2 to 3 adolescents would need to be treated with combined therapy for 1 adolescent to benefit from the therapy.

Potential Harms of Screening and/or Treatment

The USPSTF found no evidence on the harms of screening for MDD in youth.

Selective Serotonin Reuptake Inhibitors

The USPSTF examined data from fair-quality RCTs and meta-analyses. Pooled absolute risk differences were calculated. Conservative estimates from analyses show that treatment with antidepressants leads to a 1% to 2% absolute increase in the risk of suicidality. No suicide deaths are associated with these studies. Pooled data for individual drugs did not show statistically significant increases in suicide-related outcomes; however, this may be a result of insufficient power. For fluoxetine, 6% of treated patients and 4% of placebo-control patients experienced either suicidal ideation or behavior during a trial, resulting in an absolute risk difference of 2%. This result, however, was not statistically significant. On the basis of study estimates of increased absolute risk of 1% to 2%, for 1 patient to develop suicidality attributable to antidepressant therapy, ~50 to 112 patients would need to be treated. Long-term effects of SSRIs are unknown.¹

Antidepressant use can increase the risk of conversion from a unipolar depressive disorder to a bipolar disorder. In a large, good-quality cohort study of patients aged 5 to 29 years, the conversion rate in patients using antidepressants was 7.7% per year, compared with 2.5% per year in those who did not use antidepressants. In addition, the difference in conversion rates between antidepressant users and nonusers was even greater in younger children; the rate ratio between users and nonusers was 2.9% (95% CI: 2.8–3.1) in the 5- to 14-year

age group compared with 1.4% (95% CI: 1.3–1.5) in the 15- to 29-year age group.³

Psychotherapy

The USPSTF found no evidence on the harms of psychotherapy.

SSRIs Combined With Psychotherapy

There is limited evidence on the harms of combined treatment with psychotherapy and SSRIs (fluoxetine) in children and adolescents.

Estimate of Magnitude of Net Benefit

The USPSTF considered indirect evidence of benefit because of a lack of direct evidence on the effectiveness of screening for MDD in children and adolescents.

The USPSTF found adequate evidence that screening tests can accurately identify MDD in adolescents. Adequate evidence also supports beneficial decreases in MDD symptoms associated with treatment of adolescents with SSRIs, psychotherapy, and therapy combining SSRIs with psychotherapy. The USPSTF found inadequate evidence of harms of screening adolescents. There is adequate evidence on the harms of SSRIs (risk of suicidality), but there is no evidence on the harms of psychotherapy or combined treatment of adolescents with psychotherapy and SSRIs (fluoxetine), which is bounded to be low. The USPSTF found moderate certainty that the net benefit is moderate for screening followed by treatment with psychotherapy in adolescents.

The USPSTF found inadequate evidence that screening tests can accurately identify MDD in children. Inadequate evidence exists on the benefits of psychotherapy or combined psychotherapy and SSRIs in children (7–11 years of age). The USPSTF found adequate evidence that fluoxetine reduces MDD symptoms in children. The USPSTF found inadequate evidence on the harms of screening for MDD in children. There is adequate evidence on the harms of SSRIs (risk of suicidality). As a result, the USPSTF concluded that the evidence is insufficient to make a recommendation regarding screening for MDD in children aged 7 to 11 years.

Update of Previous USPSTF Recommendation

This recommendation updates the previous recommendation released in 2002.⁴ The major change in the current recommendation is that the USPSTF now recommends screening of adolescents (12–18 years of age) for MDD when systems are in place to ensure accurate diagnosis, psychotherapy (eg, cognitive-behavioral, interpersonal), and follow-up. In 2002, the USPSTF concluded that there was insufficient evidence to recommend for or against routine screening of children or adolescents for MDD (I recommendation). The basis for this change in recommendation for adolescents is a result of new evidence that demonstrates treatment benefit.

RECOMMENDATIONS OF OTHERS

Routine screening for emotional and behavioral problems has been recommended by Medicaid's Early and

Periodic Screening, Diagnosis, and Treatment (EPSDT) program. The American Academy of Pediatrics recommends that pediatricians ask questions about depression in routine history-taking throughout adolescence. The American Medical Association recommends screening for depression among adolescents who may be at risk as a result of family problems, drug or alcohol use, or other indicators of risk. In 2004, the Canadian Task Force on Preventive Health Care concluded that there was insufficient evidence to recommend for or against routine screening for depression among children or adolescents in primary care settings.⁵ The Society for Adolescent Medicine supports the initiation and continued use of antidepressant medications for adolescents when clinically warranted, with close monitoring for emergent suicidality, hostility, agitation, mania, or unusual changes in behavior.⁶

MEMBERS OF THE US PREVENTIVE SERVICES TASK FORCE

The USPSTF is considered the collective author of its recommendations. The members of the USPSTF at the time that this recommendation was finalized were Ned Calonge, MD, MPH, chair, USPSTF (Colorado Department of Public Health and Environment, Denver, CO); Diana B. Petitti, MD, MPH, vice-chair, USPSTF (Arizona State University, Phoenix, AZ); Thomas G. DeWitt, MD (Children's Hospital Medical Center, Cincinnati, OH); Allen Dietrich, MD (Dartmouth Medical School, Lebanon, NH); Leon Gordis, MD, MPH, DrPH (Johns Hopkins Bloomberg School of Public Health, Baltimore, MD); Kimberly D. Gregory, MD, MPH (Cedars-Sinai Medical Center, Los Angeles, CA); Russell Harris, MD, MPH (University of North Carolina School of Medicine, Chapel Hill, NC); George Isham, MD, MS (HealthPartners, Minneapolis, MN); Michael L. LeFevre, MD, MSPH (University of Missouri School of Medicine, Columbia, MO); Rosanne Leipzig, MD, PhD (Mount Sinai School of Medicine, New York, NY); Carol Loveland-Cherry, PhD,

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