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Screening for Depression and Suicide Risk in Children and Adolescents
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Depression, suicidal ideation, and self-harm behaviors in youth are associated with functional impairment and suicide.

OBJECTIVE To review the evidence on screening for depression or suicide risk in children and adolescents to inform the US Preventive Services Task Force (USPSTF).

DATA SOURCES PubMed, Cochrane Library, PsycINFO, CINAHL, and trial registries through July 19, 2021; references, experts, and surveillance through June 1, 2022.

STUDY SELECTION English-language, randomized clinical trials (RCTs) of screening for depression or suicide risk; diagnostic test accuracy studies; RCTs of psychotherapy and first-line pharmacotherapy; RCTs, observational studies, and systematic reviews reporting harms.

DATA EXTRACTION AND SYNTHESIS Two reviewers assessed titles/abstracts, full-text articles, and study quality and extracted data; when at least 3 similar studies were available, meta-analyses were conducted.

MAIN OUTCOMES AND MEASURES Test accuracy, symptoms, response, remission, loss of diagnosis, mortality, functioning, suicide-related events, and adverse events.

RESULTS Twenty-one studies (N = 5433) were included for depression and 19 studies (N = 6290) for suicide risk. For depression, no studies reported on the direct effects of screening on health outcomes, and 7 studies (n = 3281) reported sensitivity of screening instruments ranging from 0.59 to 0.94 and specificity from 0.38 to 0.96. Depression treatment with psychotherapy was associated with improved symptoms (Beck Depression Inventory pooled standardized mean difference, −0.58 [95% CI, −0.83 to −0.34]; n = 471; 4 studies; and Hamilton Depression Scale pooled mean difference, −2.25 [95% CI, −4.09 to −0.41]; n = 262; 3 studies) clinical response (3 studies with statistically significant results using varying thresholds), and loss of diagnosis (relative risk, 1.73 [95% CI, 1.00 to 3.00; n = 395; 4 studies). Pharmacotherapy was associated with improvement on symptoms (Children's Depression Rating Scale–Revised mean difference, −3.76 [95% CI, −5.95 to −1.57; n = 793; 3 studies), remission (relative risk, 1.20 [95% CI, 1.00 to 1.45]; n = 793; 3 studies) and functioning (Children's Global Assessment Scale pooled mean difference, 2.60 (95% CI, 0.78 to 4.42; n = 793; 3 studies). Other outcomes were not statistically significantly different. Differences in suicide-related outcomes and adverse events for pharmacotherapy when compared with placebo were not statistically significant. For suicide risk, no studies reported on the direct benefits of screening on health outcomes, and 2 RCTs (n = 2675) reported no harms of screening. One study (n = 581) reported on sensitivity of screening, ranging from 0.87 to 0.91; specificity was 0.60. Sixteen RCTs (n = 3034) reported on suicide risk interventions. Interventions were associated with lower scores for the Beck Hopelessness Scale (pooled mean difference, −2.35 [95% CI, −4.06 to −0.65]; n = 644; 4 RCTs). Findings for other suicide-related outcomes were mixed or not statistically significantly different.

CONCLUSION AND RELEVANCE Indirect evidence suggested that some screening instruments were reasonably accurate for detecting depression. Psychotherapy and pharmacotherapy were associated with some benefits and no statistically significant harms for depression, but the evidence was limited for suicide risk screening instruments and interventions.

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Depression and suicidal behaviors have long-term effects involving functional impairment, increased risk for substance abuse, and premature mortality.[1-4] Routine screening may result in early identification and treatment. In 2016, the US Preventive Services Task Force (USPSTF) issued a recommendation for screening for major depressive disorder (MDD) in adolescents aged 12 to 18 years (B recommendation).[5] The USPSTF also concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening in younger children. In 2014, the USPSTF concluded there was insufficient evidence to assess the balance of benefits and harms of screening for suicide risk in adolescents, adults, and older adults in primary care (I statement).[6] This review updated the evidence on screening for depression and suicide risk for children and adolescents to inform updated recommendations by the USPSTF.

Methods

Scope of the Review

The analytic framework and key questions (KQs) that guided the review are shown in **Figure 1**. Detailed methods, evidence tables, and contextual information are available in the full evidence report.[8]

Data Sources and Searches

PubMed, Cochrane Library, PsycINFO, CINAHL, and ClinicalTrials.gov were searched for English-language articles (eMethods in the Supplement). Depression searches were limited to articles published from January 1, 2015, through July 19, 2021; suicide risk searches were limited to articles published between June 1, 2012, and July 19, 2021. Evidence prior to these dates was identified from existing reviews.[9,10] Reference lists of pertinent articles and studies suggested by reviewers were also reviewed. Article alerts and targeted searches of journals to identify major studies published in the interim that may affect the conclusions or understanding of the evidence and the related USPSTF recommendation were used as part of ongoing surveillance. The last surveillance was conducted on June 1, 2022.

Study Selection

Two investigators independently reviewed titles, abstracts, and full-text articles using prespecified criteria for each KQ (eMethods in the Supplement); disagreements were resolved by discussion or by a third reviewer. English-language studies of persons 18 years or younger, on average, that met all study selection criteria, were fair or good methodological quality, and were conducted in countries categorized as very highly developed by the 2018 United Nations Human Development Index[11] were eligible. Studies included in the prior reviews for the USPSTF were reassessed against the study selection criteria. For screening, studies that included unselected participants without known risk of depression or increased risk of suicide were eligible. For depression, treatment studies that included at least half of participants with MDD were eligible. For suicide risk, treatment studies were restricted to participants with increased suicide risk. Eligible interventions included psychotherapy or first-line pharmacotherapy approved for pediatric use (eg, clonidine, duloxetine, fluoxetine, escitalopram, sertraline, fluvoxamine). Interventions were required to be relevant to or referable from primary care. Eligible outcomes for benefits of screening and treatment included depression symptoms as measured through validated instruments, clinical response, or remission; suicide deaths, suicide attempts, and deliberate self-harm or suicidal ideation; all-cause mortality; quality of life measured using validated instruments; and functioning (validated scales, days of missed school, sleep-related outcomes). Eligible harms of treatment included treatment avoidance, deterioration in patient-clinician relationship, labeling or stigma, unnecessary treatment, serious adverse effects, withdrawals due to adverse effects, and suicidality.

Data Extraction and Quality Assessment

For each included study, 1 reviewer abstracted relevant study characteristics and outcomes into a structured form. A second reviewer checked all data for completeness and accuracy. Methodological quality ratings for studies included from a prior Agency for Healthcare Research and Quality (AHRQ) evidence review on depression treatment in youth[12] were spot-checked and carried forward. All other studies were assessed dually and independently using predefined criteria established by the USPSTF (eMethods in the Supplement) and others.[13-16]

Disagreements in study quality ratings were resolved through discussion or by a third senior reviewer. Detailed study quality assessments are provided in eTables 1 through 7 in the Supplement.

Data Synthesis and Analysis

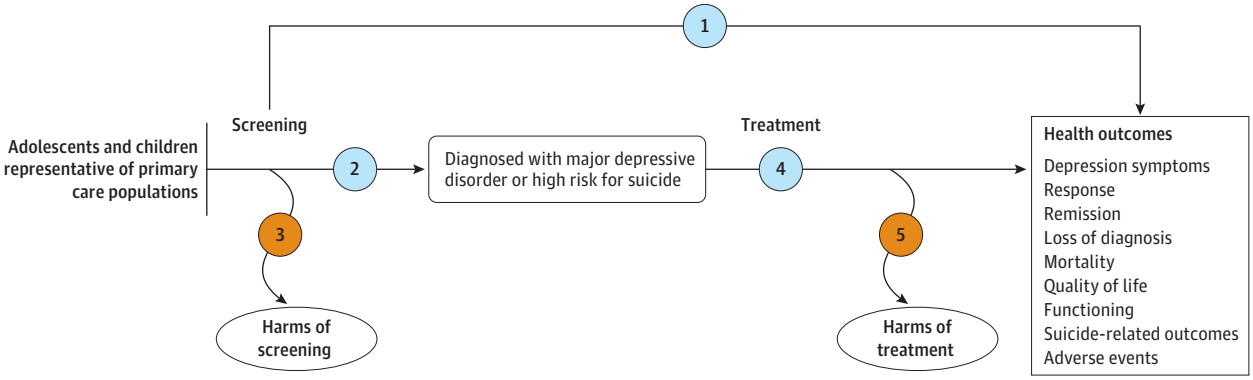
Data were synthesized in tabular and narrative forms. When at least 3 similar studies were available, a quantitative synthesis was performed using random-effects models with the inverse-variance weighted method of DerSimonian and Laird in Comprehensive Meta-Analysis version 3.3 to generate pooled estimates of effect.[17] The I^2 statistic was calculated to assess statistical heterogeneity in effects.[18] Significance testing was based on the exclusion of the null value by the 95% CI around the pooled estimate; all testing was 2-sided.

The strength of evidence was assessed as high, moderate, low, or insufficient using methods developed for the USPSTF and the AHRQ Evidence-based Practice Center program.[7,19] Two senior reviewers independently developed initial strength-of-evidence assessments; disagreements were resolved through discussion or input of a third senior reviewer.

Results

Forty studies in 54 publications (N = 11 220 from screening accuracy studies and randomized clinical trials [RCTs]) were eligible (**Figure 2**). For depression, 7 screening test accuracy studies[21-27] and 13 treatment RCTs[28-47] (N = 5433) were identified in addition to 1 meta-analysis.[48] Two studies of screening accuracy,[22,25] 7 treatment trials,[28,32,33,35,37,38,40,42,47] and the meta-analysis[48] are new to this update. For suicide risk, 1 screening test accuracy study,[49] 2 studies of screening harms,[50,51] and 16 treatment RCTs were identified (N = 6290).[52-74] Nine trials are new to this update.[52-55,58,60,64-72] The results in this publication focus on pooled analyses when available. Additional results are available in the full report.[8] A list of full-text articles that were screened but excluded is provided in the Supplement (List of Excluded Studies).

Figure 1. Analytic Framework: Screening for Depression or Suicide Risk in Children and Adolescents



Key questions

1. Do depression or suicide risk screening programs in primary care or comparable settings result in improved health outcomes in children and adolescents?
2. Do instruments to screen for depression or suicide risk accurately identify children and adolescents with depression and increased risk of suicide in primary care or comparable settings?
3. What are the harms associated with screening for depression or suicide risk in primary care or comparable settings in children and adolescents?
4. Does treatment (psychotherapy, pharmacotherapy, or collaborative care) of depression or suicide risk result in improved health outcomes in children and adolescents?
5. What are the harms of treatment (psychotherapy, pharmacotherapy, or collaborative care) in children and adolescents who are treated for depression or suicide risk?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions that the review addressed to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions and outcomes. Refer to the USPSTF Procedure Manual for interpretation of the analytic framework.[7] KQ indicates key question.

Benefits of Screening

Key Question 1. Do depression or suicide risk screening programs in primary care or comparable settings result in improved health outcomes in children and adolescents?

No trials directly assessing the benefits of screening children or adolescents in the primary care setting for MDD or suicide risk compared with no screening were found.

Accuracy of Screening Instruments

Key Question 2. Do instruments to screen for depression or suicide risk accurately identify children and adolescents with depression or increased risk of suicide in primary care or comparable settings?

Depression

Seven fair-quality studies of diagnostic test accuracy (n = 3316) were included[21-27]; 2 were new to this update.[22,25] Authors assessed 7 different screening instruments (eTables 8 and 9 in the Supplement describe index tests and reference standards, respectively). Some authors assessed more than 1 instrument or more than 1 threshold for a positive screen result for the same instrument, and few studies prespecified thresholds for a positive screen result. All but 1 study[25] were restricted to adolescents.

The prevalence of MDD based on reference standard diagnostic clinical interviews ranged from 3% to 9% across studies enrolling persons recruited from school or community-based settings[21,23,26,27] and was 11% in all 3 of the studies enrolling persons from nonpsychiatric clinical settings.[22,24,25] **Table 1** provides a summary of sensitivity and specificity (additional detail is provided in eTable 10 in the Supplement). Excluding 2 outliers,[26] the sensitivity across these instruments for identifying MDD ranged from 0.73 to 0.94, and the specificity ranged from 0.38 to 0.97.

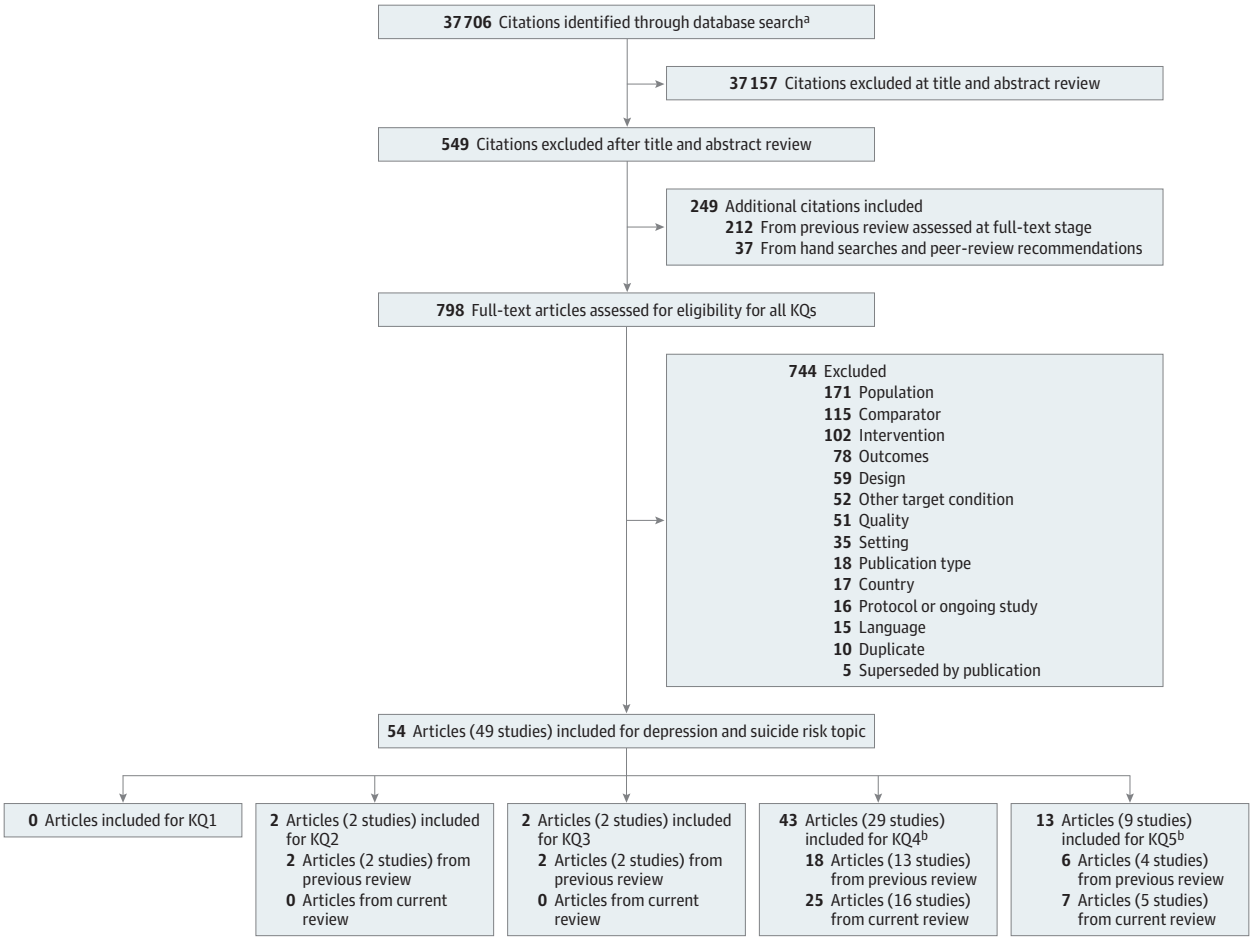
Suicide Risk

One fair-quality study (n = 580) conducted in the US that recruited potential high school dropouts aged 14 to 20 years evaluated the 20-item Suicide Risk Screen (SRS).[49] The prevalence of increased suicide risk ranged from 19% to 22%, depending on the reference standard used. The sensitivity and specificity of the SRS compared with one reference standard were 0.91 and 0.60, respectively, and were 0.87 and 0.60 against another reference standard.[49]

Harms of Screening

Key Question 3. What are the harms associated with screening for depression or suicide risk in primary care or comparable settings in children and adolescents?

Figure 2. Literature Search Flow Diagram: Screening for Depression or Suicide Risk in Children and Adolescents



Reasons for exclusion: Population: Study was not conducted in an included population. Comparator: Study did not use an included comparator. Intervention: Study did not use an included intervention. Outcomes: Study did not report relevant outcomes. Design: Study did not use an included design. Other target condition: Study reported on anxiety. Quality: Study was poor quality. Setting: Study was not conducted in settings representative of primary care. Publication type: Publication was a commentary. Country: Study was not conducted in a country relevant to US practice. Protocol or ongoing study: Study was a protocol or ongoing study and did not report eligible outcomes. Language: Study was not in English. Duplicate: Study was a duplicate of other studies in the review. Superseded by publication: Study findings were wholly superseded by another publication.

[a] Combined searches were conducted on anxiety, depression, and suicide risk. Results for anxiety are presented in a separate publication.[20]

[b] Study may address more than 1 key question (KQ).

Depression

No trials directly assessing the harms of screening children or adolescents in the primary care setting for MDD compared with no screening were found.

Suicide Risk

Two fair-quality RCTs (n = 2675) conducted in high schools reported no differences in harms in distress, transient mood states, or suicidal ideation after screening for suicide risk.[50,51]

Benefits of Treatment

Key Question 4. Does treatment (psychotherapy, pharmacotherapy, or collaborative care) of depression or suicide risk result in improved health outcomes in children and adolescents?

Benefits of treatment for depression and increased suicide risk are summarized in **Table 2**.

Depression

Thirteen fair-quality RCTs (20 publications) were identified (n = 2152).[28-47] Seven RCTs[28,32,33,35,37,38,40,42,47] were new in this update. Key characteristics of included depression studies are provided in eTable 11 in the Supplement, detailed outcomes are provided in eTables 12 through 27 in the Supplement, and results from meta-analyses are provided in eFigures 1 through 8 in the Supplement.

Eleven RCTs enrolled youth meeting *Diagnostic and Statistical Manual* (*DSM*) criteria for MDD.[28,29,31,33-40] Two RCTs enrolled a sample in which more than 50% of participants met *DSM* criteria for MDD but also admitted youth with MDD, dysthymia, or depressive disorder not otherwise specified.[30,32] Mean ages ranged from 5 to 17.5 years.[33,38,42] One RCT focused on early childhood (3-6 years),[33,42] 2 focused on school-aged children and adolescents (ages ranged from 7-14 years and 6-17 years),[32,39] and

Table 1. Accuracy of Screening Instruments for Screening for Depression and Suicide Risk

Condition	Screener	Age range	No. of studies	Sensitivity	Specificity
Major depressive disorder	Beck Depression Inventory (threshold = 11)	15-18.5	2[21,27]	0.84-0.90	0.81-0.86
	Center for Epidemiologic Studies Depression Scale (various thresholds)	12-18	2[26]	0.18[a]-0.85	0.38-0.83
	Clinical Interview Schedule-Revised	Mean, 15.7	1[26]	0.18[a]	0.97[b]
	Hopkins Symptom Checklist	14-16	1[22]	0.85	0.78
	Patient Health Questionnaire-Adolescents	13-18	1[24]	0.73	0.94
	Paediatric Index of Emotional Distress-Depression subscale	8-17	1[25]	0.94	0.81
	World Health Organization 5-Item Well-being Index	14-16	1[22]	0.88	0.80
Suicide risk	Suicide Risk Screen	14-20	1[49]	0.87-0.91[c]	0.60

[a] Across the 2 studies, 5 thresholds were evaluated. The sensitivity for most ranged between 0.59 and 0.85 except for the thresholds of 20 or greater and 22 or greater among boys, which were 0.19 and 0.18, respectively.

[b] These estimates were from an analysis weighted for selection into the second phase of the study; calculated sensitivity without weighting was 0.74 and specificity was 0.78.

[c] This instrument was evaluated against 2 different reference standards.

10 focused on adolescents (ages ranged from 12-17 years and 15-19 years).[28-31,34-38,40] Two had majority male participants.[32,33,42]

Two pharmacotherapy trials compared escitalopram with placebo.[31,39] One 3-group trial compared fluoxetine, cognitive behavioral therapy (CBT), and placebo.[34] One trial compared collaborative care with enhanced usual care.[36] Six studies focused on CBT,[28-30,32,37,38] and 3 focused on counseling other than CBT.[33,35,40] Comparisons included treatment as usual, wait-list, placebo, attention control, and supportive contact. The results reported here focus on psychotherapy and pharmacotherapy trials; detailed results for collaborative care and combination therapy are available in the full report.[8]

Outcomes reported included (1) depression symptoms; (2) response, remission, or loss of diagnosis; and (3) quality of life and functioning. Regarding depression symptoms, pooled estimates suggested improved symptoms associated with psychotherapy (Beck Depression Inventory [BDI] pooled standardized mean difference, −0.58 [95% CI, −0.83 to −0.34]; n = 471; 4 RCTs[30,35,37,38] and Hamilton Depression Scale pooled mean difference, −2.25 [95% CI, −4.09 to −0.41]; n = 262; 3 RCTs[29,30,35]) or pharmacotherapy (Children's Depression Rating Scale–Revised mean difference, −3.76 [95% CI, −5.95 to −1.57]; n = 793; 3 RCTs[31,34,39]) in some but not all measures of symptom severity. Regarding clinical response, 3 studies reported responses on the BDI and BDI-II (BDI version 2) scale[35,37,38] favoring pharmacotherapy but results could not be pooled because of the various thresholds used. Results favored pharmacotherapy for remission (relative risk [RR], 1.20 [95% CI, 1.00 to 1.45]; n = 793; 3 RCTs[31,34,39,45]) and psychotherapy for loss of diagnosis (RR, 1.73 [95% CI, 1.00 to 3.00]; n = 395; 4 RCTs[30,34,37,38]), but CIs included the null. Studies reported improved functioning, measured by the Children's Global Assessment Scale for pharmacotherapy (mean difference, 2.60 [95% CI, 0.78 to 4.42]; n = 793; 3 RCTs[31,34,39]) but not for psychotherapy (mean difference, 1.52 [95% CI, −1.54 to 4.58]; n = 601; 4 RCTs).[28,29,34,35]

Two psychotherapy studies focused on or included children; 1 reported improvements in symptoms, loss of diagnosis, and functioning,[33] and a second reported no differences for symptoms or remission.[32] One pharmacotherapy study that included children reported no differences in symptoms, response, or functioning.[39]

Suicide Risk

Sixteen RCTs of good or fair quality (described in 23 articles) were identified.[52-74] Nine were new to this update (n = 3034).[52-55,58,60,64-72] Key characteristics of included studies are described in eTable 28 in the Supplement, detailed outcomes included in pooled results are provided in eTables 29 and 30 in the Supplement, and results from meta-analyses are provided in eFigures 9 through 15 in the Supplement.

Fourteen studies enrolled adolescents based on elevated suicide risk,[52-55,57-72,74] and 2 studies admitted adolescents with suicide risk and self-reported depressive symptoms (BDI >19[73] or BDI >20[56]). Mean ages ranged from 14 to 18 years. All included studies focused on adolescents[52-74] and included a majority of female participants.

All included studies examined psychotherapy, counseling, support, or a combination with variable intensity and duration. Fifteen studies compared these interventions with treatment as usual,[52-59,61-74] which often included active psychosocial treatment, and 1 study compared the intervention with attention control.[60] Duration of treatment ranged between 1 single session to weekly sessions over 12 months. No evidence was captured that examined pharmacotherapies.

Outcomes reported included (1) suicide deaths, (2) suicide attempts and deliberate self-harm or suicidal ideation, (3) all-cause mortality, and (4) functioning. Three studies reported no deaths or no statistically significant differences in suicide deaths at the end of treatment (19 weeks to 12 months).[57,62,65-68] Pooled results for suicide attempt, deliberate self-harm, or suicidal ideation generally indicated no statistically significant differences for self-harm events (RR of self-harm events, 0.88 [95% CI, 0.63 to 1.24]; n = 1040; 5 RCTs[53-55,57,59,72,74]; mean difference in self-harm events, −0.76 [95% CI, −2.15 to 0.63]; n = 972; 3 RCTs[53-55,65-68,74]) or suicide-related hospitalization or emergency use (RR, 1.00 [95% CI, 0.67 to 1.50]; n = 978; 3 RCTs[53-55,65-70]). The exception was measures of suicidal ideation: studies reported benefits associated with the intervention on the Beck Hopelessness Scale (mean difference, −2.35 [95% CI, −4.06 to −0.65]; n = 644; 4 RCTs[62,64-68,73]). Pooled results for the Suicidal Ideation Questionnaire (SIQ) and SIQ-Junior scales also favored the intervention group but were not statistically significantly different (standardized mean difference, −0.18 [95% CI, −0.36 to 0.01]; n = 1111; 7 RCTs[56,57,59,62,64-68,74]). Regarding all-cause mortality, a long-term follow-up of a study on a youth-nominated support team approach,[62] 11 to 14 years after psychiatric hospitalization for suicide risk (baseline for the study), found a higher number of deaths in the National Death Index in the treatment-as-usual group when compared with the active treatment group (13/225 vs 2/223; hazard ratio, 6.62 [95% CI, 1.49 to 29.35]).[63] The same study did not

Table 2. Benefits for Treatment for Screening for Depression and Suicide Risk

Intervention	Time of outcome measurement	Outcome measure, range, threshold	Outcome range	Outcome threshold indicating clinically meaningful effect	Treatment range at follow-up	Comparator range at follow-up	No. of studies (No. of participants)	Pooled results (95% CI)[a]; I^2
Depression—change in symptoms								
Internet-based individual CBT group; in-person CBT with and without parents; interpersonal psychotherapy[b]	8-12 wk	BDI or BDI-II	BDI: 0-39[35] BDI-II: 0-63[75]	BDI: Score <10: minimal depression Score 10-18: mild to moderate depression Score 19-29: moderate to severe depression Score ≥30: severe depression[21,27] BDI-II: Score 0-13: minimal depression Score 14-19: mild depression Score 20-28: moderate depression Score 29-63: severe depression[75]	BDI: 8.4-13.3 BDI-II: 16-19.9	BDI: 12.3-16 BDI-II: 24.8-25.2	4[30,35,37,38]	Standardized mean difference, −0.58 (−0.83 to −0.34) I^2 = 0%
Individual in-person youth CBT; group in-person CBT with and without parents; interpersonal psychotherapy[b]	8-52 wk from baseline	HAM-D	Unclear (2 studies used a 14-item version of HAM-D)	Unclear	4.9-8.7	6.5-12.8	3[29,30,35] (262)	Mean difference, −2.25 (−4.09 to −0.41) I^2 = 0%
Individual in-person CBT; family CBT	12-52 wk from baseline	CDRS-R	17-113	Score ≥40 indicates depression Score ≤28 indicates remission (minimal or no symptoms)	30.0-42.1	28.2-41.8	3[28,32,34] (471)	Mean difference, 0.77 (−0.97 to 2.48) I^2 = 0%
Escitalopram; fluoxetine	8-12 wk from baseline	CDRS-R	17-113	Score ≥40 indicates depression Score ≤28 indicates remission (minimal or no symptoms)		36.4-41.8	3[31,34,39] (793)	Mean difference, −3.76 (−5.95 to −1.57) I^2 = 49%
Depression—remission and loss of diagnosis								
CBT	8-12 wk from baseline	Loss of diagnosis measured by clinical interviews	0%-100% For proportion	NA	56%-71%	16%-60%	4[30,34,37,38] (395)	RR, 1.73 (1.00 to 3.00) I^2 = 81%
Escitalopram; fluoxetine	8-12 wk from baseline	Remission from depression symptoms (CDRS-R ≤28)	0%-100% For proportion	CDRS-R ≤28 indicates moderate marked improvement, proportion threshold unclear	23%-46%	17%-38%	3[31,34,39,45] (793)	RR, 1.20 (1.00 to 1.45) I^2 = 0%
Depression—change in functioning								
Individual in-person CBT; interpersonal psychotherapy	12-52 wk from baseline	CGAS	1-100	Score >70: no clinically significant functional impairment Score <41: major impairment to functioning in several areas	60.0-72.3	59.3-74.1	4[28,29,34,35] (601)	Mean difference, 1.52 (−1.54 to 4.58) I^2 = 66%
Escitalopram; fluoxetine	8-12 wk from baseline	CGAS	1-100	Score >70: no clinically significant functional impairment Score <41: major impairment to functioning in several areas	62.1-68.5	59.3-64.6	3[31,34,39] (793)	Mean difference, 2.60 (0.78 to 4.42) I^2 = 0%

(continued)

Table 2. Benefits for Treatment for Screening for Depression and Suicide Risk (continued)

Intervention	Time of outcome measurement	Outcome measure, range, threshold	Outcome range	Outcome threshold indicating clinically meaningful effect	Treatment range at follow-up	Comparator range at follow-up	No. of studies (No. of participants)	Pooled results (95% CI)[a]; I^2
Suicide risk—suicide-related outcomes								
Group psychotherapy; family therapy; mentalization-based treatment; developmental group therapy	6-18 mo	Proportion with self-harm events	0-100	NA	0.55%-88%	1.1%-83%	5[53-55,57,59,72,74] (1040)	RR, 0.88 (0.63 to 1.24) I^2 = 80%
Family therapy; DBT; developmental group therapy	19 wk to 18 mo	Mean No. of self-harm events	NA	NA	0.6-9.0	1.2-22.50	3[53-55,65-68,74] (972)	Mean difference, −0.76 (−2.15 to 0.63) I^2 = 68%
Youth-nominated support team; motivational interviewing; DBT; IPT-A-IN	2 mo to 19 wk	Suicidal ideation: BHS	0-20	Score >9 indicative of suicide intentions	5.66-7.74	7.80-12.42	4[62,64-68,73] (644)	Mean difference, −2.35 (−4.06 to −0.65) I^2 = 46%
Attachment-based family therapy; group psychotherapy; group therapy; youth-nominated support team; motivational interviewing; DBT; developmental group therapy	2 mo to 71 wk	SIQ or SIQ-JR	SIQ: 0-180 SIQ-JR: 0-90	SIQ score >41 indicative of suicidal ideation SIQ-JR score >31 indicative of suicidal ideation	SIQ: 41.3-74.11 SIQ-JR: 5.2-25.55	SIQ: 39.7-76.40 SIQ-JR: 16.2-29.71	7[56,57,59,62,64-68,74] (1111)	SMD, −0.18 (−0.36 to 0.01) I^2 = 45%
Family therapy; DBT; therapeutic assessment	18 mo to 2 y	Proportion with suicide-related hospitalization or emergency department use	NA	NA	1%-88%	1%-94%	3[53-55,65-70] (978)	RR, 1.00 (0.67 to 1.50) I^2 = 21%
Attachment-based therapy and internet CBT	8-24 wk	Clinical response: SIQ-JR or perceived burdensomeness	SIQ-JR: 0-90; Perceived burden-someness: 6-42	Clinical response: SIQ-JR scores (defined as <13) Perceived burdensomeness <14.61	SIQ-JR: 87% Perceived burden-someness: 24%	SIQ-JR: 52% Perceived burden-someness: 10%	2[56,60] (146)	Results from individual studies: OR for SIQ-JR clinical response, 6.30 (1.76-22.61)[56] No significant differences at 24 wk for perceived burdensomeness (OR, 2.82 [0.80-9.91])[60]
Suicide risk—change in functioning								
Group psychotherapy; group therapy; developmental group therapy; psychoeduca-tion for parents	8 wk to 7 mo	Functioning: Health of the Nation Outcome Scales for Children and Adolescents	0-52	Scores >13 indicate impairment of clinical significance	8.4-16.8	6.9-17.6	4[57,59,71,74] (509)	Mean difference, −0.40 (−2.55 to 1.78) I^2 = 56%
Therapeutic assessment; individual and family DBT; group therapy	8-71 wk	Functioning: CGAS	1-100	Score >70: no clinically significant functional impairment Score <41: major impairment to functioning in several areas	58.5-65.7	60.1-64.22	3[59,66,70] (195)	Mean difference, 1.30 (−2.52 to 5.12) I^2 = 30%

Abbreviations: BDI, Beck Depression Inventory; BDI-II, Beck Depression Inventory version 2; Beck Hopelessness Scale, CBT, cognitive behavioral therapy; CDRS-R, Children's Depression Rating Scale–Revised; CGAS, Children's Global Assessment Scale; DBT, dialectical behavior therapy; HAM-D, Hamilton Depression Rating Scale; IPT-A-IN, intensive interpersonal bxpsychotherapy for depressed adolescents with suicidal risk; NA, not applicable; OR, odds ratio; RR, relative risk; SIQ, Suicidal Ideation Questionnaire; SIQ-JR, Suicidal Ideation Questionnaire–Junior; SMD, standardized mean difference.

[a] Results from pooled analyses unless otherwise specified.

[b] The results across groups for the study were averaged (mean values calculated), with multiple treatment groups (group in-person CBT with or without parents[30]) compared with wait-list.

demonstrate an effect on the primary outcome of suicidal ideation; as a result, findings by chance or through other mechanisms of action (such as improved problem solving) cannot be ruled out. The studies reported no statistically significant differences in functioning on the Health of the Nation Outcome Scales for Children and Adolescents (mean difference, −0.40 [95% CI, −2.55 to 1.78]; n = 509; 4 RCTs[57,59,71,74]) or the Children's Global Assessment Scale (mean difference, 1.30 [95% CI, −2.52 to 5.12]; n = 195; 3 RCTs[59,66,70]).

Harms of Treatment

Key Question 5. What are the harms of treatment (psychotherapy, pharmacotherapy, or collaborative care) in children and adolescents who are treated for depression or suicide risk?

Depression

Seven studies (described in 12 articles) were included (n = 1408 from primary studies).[28,31,34,36,39-41,43-46,48] All 7 studies are also included in the discussion of benefits except for 1 meta-analysis, which was new to this update.[48] Key characteristics of included depression studies are provided in eTable 31 in the Supplement, and detailed outcomes are provided in eTables 32 through 40 in the Supplement. Studies reported on suicide-related events (suicide deaths, attempts, deliberate self-harm, or suicidal ideation) and other adverse events. Regarding psychotherapy, the Treatment of Adolescents With Depression (TADS) trial with 2 active interventions (CBT and fluoxetine) reported varying results in the placebo group in different publications; as a result, the relative risk of suicide-related outcomes could not be calculated with certainty. A second trial reported 5 of 106 (4.7%) suicide-related events for CBT plus treatment as usual vs 2 of 106 (1.9%) for treatment as usual alone[28]; differences were not statistically significant. For pharmacotherapy, inconsistent reporting across different publications on harms from the TADS trial led to uncertainty regarding the relative risk of suicide-related outcomes with fluoxetine vs placebo. Other evidence for escitalopram studies indicated rates of suicide-related outcomes that are not statistically significantly different compared with placebo (1/129 [0.8%] vs 2/132 [1.5%][39]; 6/57 [3.8%] vs 6/155 [3.9%][31]). The meta-analysis also reported similar rates for escitalopram vs placebo (15/290 [5%] vs 15/294 [5%]; 2 studies) and fluoxetine vs placebo (51/521 [10%] vs 44/514 [9%]; 7 studies).[48] No statistically significant differences were reported for other harms for psychotherapy (deteriorated on the Quick Inventory of Depressive Symptomatology for Adolescents: 1 vs 3[40]; harm-related adverse events: 5/111 participants [4.5%] vs 6/112 participants [5.4%]; OR, 0.80 [95% CI, 0.25 to 2.81][34]). For pharmacotherapy, 2 escitalopram trials reported no statistically significant differences for withdrawals (4/155 [2.6%] vs 1/157 [0.6%][31]; 2/131 [1.5%] vs 2/133 [1.5%][39]) or serious adverse events (4/155 [2.6%] vs 2/157 [1.3%][31]; 2/131 [1.5%] vs 3/133 [2.3%][39]). The TADS trial reported a higher but not statistically significant difference in adverse events for fluoxetine compared with placebo (13/109 participants [11.9%] vs 6/112 [5.4%]; OR, 2.4 [95% CI, 0.87 to 6.54]).[34]

Suicide Risk

Two studies[53-55,58] reported on adverse events (n = 885). One study[53-55] reported on adverse events, serious adverse events, and other harms during the 12- to 18-month follow-up period. Similar numbers of adverse events, including attendance at minor injury units, walk-in centers, and accident and emergency centers and referral to mental health services, occurred in the family therapy group (54%) and treatment-as-usual group (52%). Serious adverse events, defined as hospital attendance, also occurred at similar rates across the intervention (38%) and control (34%) groups. Two participants assigned to the family therapy group died between 3 and 4 years after randomization. Neither death was related to self-harm. One additional study[58] reported 5 adverse events among 4 participants, but the occurrences were not considered trial-related and were not reported by group.

Discussion

This systematic review evaluated screening for depression and suicide risk in children and adolescents. **Table 3** summarizes the evidence, including strength-of-evidence ratings. No studies reported on the direct benefits or harms of screening. The discussion below focuses on the indirect evidence from studies describing test accuracy, benefits of treatment, and harms of treatment.

Depression

The standard of evidence for test accuracy was rated as low to moderate for sensitivity and moderate for specificity.

The depression module (Patient Health Questionnaire 9 [PHQ-9]) of the full PHQ is the instrument highlighted for use in screening for depression by the American Academy of Pediatrics.[76] One study of the accuracy of the full PHQ modified for adolescents was included, but no studies evaluating the PHQ-9 were identified. Based on the accuracy characteristics for the 1 included study of the Patient Health Questionnaire—Adolescents (PHQ-A),[24] per 1000 screening tests conducted, 58 false-positives and 8 false-negatives would be generated at the low end of MDD prevalence (3%) observed in this updated review, and 53 false-positives and 30 false-negatives would be generated at the high end of prevalence (11%). Positive screening results would require additional diagnostic evaluation to determine true-positives from false-positives, but it is likely that some youth screening positive but not meeting diagnostic criteria for MDD may have persistent depressive disorder (formerly known as dysthymia) or other behavioral health conditions with symptoms similar to depression. The consequences of a false-negative would largely depend on the severity of the missed diagnosis; the likelihood of missing a severely depressed youth is small because most screen-detected depression is likely to be mild to moderate. However, even mildly to moderately depressed youth may have suicidal ideation, and the consequences of missing such symptoms could be serious.

The updated evidence on psychotherapy suggested some benefits for symptom improvement and clinical response, but the results were not consistent across all measures for other outcomes. The evidence for pharmacotherapy suggested benefit for symptom improvement, but the results were not consistent across all measures for other outcomes. Thus, the strength of evidence for psychotherapy and pharmacotherapy was rated as low for benefit. The evidence on harms was very limited; no statistically significant differences were observed. One multigroup trial (TADS) with inconsistent reporting on suicide-related events across its various publications contributed to the evidence on psychotherapy,

Table 3. Summary of Evidence

No. of studies, study designs (No. of participants)	Summary of findings	Consistency and precision	Limitations	Strength of evidence	Applicability
KQ1: Benefits of screening					
None	NA	NA	NA	Insufficient	NA
KQ2: Accuracy of screening					
Depression: 7 studies (n = 3281)[21-27]	Varies by screener and threshold, excluding outliers Sensitivity range, 0.59-0.94 Specificity range, 0.38-0.96 PHQ-A: Sensitivity, 0.73 (95% CI, 0.58-0.85) Specificity, 0.94 (95% CI, 0.91-0.96)	Consistent when multiple studies are available; precise for specificity, precision varies for sensitivity	Unclear whether thresholds were established a priori or whether index and reference standard results were blinded; no replication of approaches for most screeners	Low to moderate for sensitivity (varies by instrument); moderate for specificity	Primarily adolescents, as only 1 study included children younger than 12 y; 7 different screeners evaluated but most not being used in practice
Suicide: 1 study (n = 581)	Sensitivity, 0.87 and 0.91 (varies by reference standard) Specificity, 0.60	Consistency unknown; imprecise	Unclear whether thresholds were established a priori or whether interviewers were blinded; single study	Insufficient	Participants were potential high school dropouts; instrument was a 20-item screener embedded into a longer questionnaire, so unclear whether feasible in primary care
KQ3: Harms of screening tests					
Depression: none	NA	NA	NA	Insufficient	NA
Suicide: 2 RCTs[50,51] (n = 2675)	No significant difference in suicidal ideation between students exposed to screening items and those not exposed (1 RCT) No significant differences in measures of short-term distress/emotions for students exposed to suicide screening items compared with those not exposed (2 RCTs)	Consistent; precise	Fair-quality trials with some attrition; only evaluated measures of immediate and short-term emotions (over 1-2 d)	Low for no short-term harms from screening for suicide risk; insufficient for screening for depression and anxiety	High school students; 1 study entirely comprised boys
KQ4: Benefits of treatment					
Depression: 13 RCTs[28-40,42] (2 on pharmacotherapy; 9 on psychotherapy; 1 on CBT, fluoxetine, and their combination; 1 on collaborative care) (n = 2152)	Psychotherapy Varied by measure, with some pooled estimates of effect favoring psychotherapy for symptoms, clinical response, and loss of diagnosis, but other outcome measures did not consistently demonstrate a statistically significant difference Pharmacotherapy: Statistically significant differences favoring pharmacotherapy for 1 measure of symptoms Pooled differences favored pharmacotherapy but were not statistically significant for remission Other outcome measures did not demonstrate a statistically significant difference Collaborative care: Statistically significant differences favoring collaborative care for symptoms at 6 mo and clinical response by 12 mo; remission at 6 mo; no benefits for functioning	Mostly consistent; mostly imprecise	Psychotherapy cannot mask treatment, leading to the potential for bias in outcome reporting	Psychotherapy: low for benefit for all outcomes other than remission Pharmacotherapy: low for benefit for all outcomes other than response Collaborative care: low for benefit for symptoms, response, and remission; insufficient for functioning	Studies addressed youth aged 3 to 19 y, but 9 were conducted exclusively in adolescents Pharmacotherapy studies were limited to first-line drugs with FDA approval for pediatric use

(continued)

Table 3. Summary of Evidence (continued)

No. of studies, study designs (No. of participants)	Summary of findings	Consistency and precision	Limitations	Strength of evidence	Applicability
Suicide: 16 RCTs[52-62,64-74] (3034)	Statistically significant difference favoring interventions for suicidal ideation on the Beck Hopelessness Scale, nonstatistically differences favoring suicide risk interventions on the SIQ and SIQ-JR, mixed on other measures No statistically significant differences on suicide deaths, hospitalization or emergency department visits, number of self-harm events, proportion with self-harm events, or functioning All-cause mortality: statistically significant difference favoring interventions (hazard ratio for treatment as usual, 6.62 [95% CI, 1.49-29.35]; n = 448; 1 study)	Consistent; imprecise	Interventions cannot mask treatment, leading to the potential for bias in outcome reporting; all comparison groups are treatment-as-usual comparisons, which in many cases were active treatments and could bias results toward null effects	Psychotherapy: Low for benefit for suicidal ideation and clinical response; insufficient for all other outcomes	Applicable to adolescents (predominantly females); no studies recruited children younger than 11 y; most recruited from mental health or specialist settings
KQ5: Harms of treatment					
Depression: 6 RCTs[28,31,34,36,39-41,43-46] (3 on pharmacotherapy; 2 on psychotherapy; 1 on CBT, fluoxetine, and their combination; 1 on collaborative care) (n = 1408 from trials) and 1 meta-analysis[48]	Psychotherapy: no statistically differences in negative effects in 2 trials; however, precise effects unclear because 1 trial had inconsistent reporting Pharmacotherapy: nonsignificant but higher risk of suicide-related outcomes, withdrawal due to adverse events and serious adverse events, precise effects unclear owing to inconsistent study reporting Collaborative care: inconsistent results for psychiatric hospitalizations and emergency department visits	Consistent to inconsistent; imprecise	Psychotherapy trials cannot mask treatment, leading to the potential for bias in outcome reporting, inconsistent results across publications from 1 trial	Psychotherapy: insufficient Pharmacotherapy: low for harms Collaborative care: insufficient	Studies addressed youth aged 6 to 18 y, but 5 were conducted exclusively in adolescents Pharmacotherapy studies were limited to first-line drugs with FDA approval for pediatric use
Suicide: 2 RCTs[53,58] (885)	No statistically significant differences on adverse events (such as minor injury, walk-in, accident and emergency centers, re-referral to mental health service, and hospital attendance)	Consistent; imprecise	Interventions cannot mask treatment, leading to the potential for bias in outcome reporting; all comparison groups are treatment-as-usual comparisons, which in many cases were active treatments and could lead to bias toward null effects	Insufficient	Applicable to adolescents, primarily females, recruited from mental health or specialist settings

Abbreviations: CBT, cognitive behavioral therapy; FDA, US Food and Drug Administration; KQ, key question; NA, not applicable; PHQ-A, Patient Health Questionnaire-Adolescents; RCT, randomized clinical trial; SIQ, Suicidal Ideation Questionnaire; SIQ-JR, Suicidal Ideation Questionnaire–Junior.

pharmacotherapy, and their combination. These discrepancies increased the uncertainty regarding harms of treatment and have led to a call for independent reanalysis of the TADS results.[77,78] The US Food and Drug Administration (FDA) noted a higher frequency of suicide-related events in boxed warnings for antidepressants.[79] The underlying FDA review for this warning relied on drug trials in populations ineligible for this review.[80]

Suicide

Only 1 eligible study assessed the accuracy of screening for suicide risk in adolescents evaluated against a clinical diagnostic interview reference standard; the instrument used was the SRS, a 20-item instrument embedded in a longer questionnaire, and the study population was recruited from youth identified as potential high school dropouts.[49] The strength of evidence for screening was rated as insufficient because of inconsistencies in estimates based on the reference standard used, imprecision, and study limitations. Given that many depression screening instruments include an assessment of suicidal ideation, it is unclear whether a separate, stand-alone instrument to screen for increased suicide risk has value for universal screening in primary care practice. The Ask Suicide Screening Questions (ASQ) is a brief 4-item instrument that was initially developed for youth 8 years or older in emergency department settings but has since been evaluated in other medical settings, including outpatient specialty and primary care.[81,82] The Joint Commission recommends suicide risk screening for all medical patients in all medical settings, including outpatient practices.[83] The National Institute for Mental Health developed an ASQ toolkit to support implementation of suicide risk screening in medical settings, including for youth in primary care.[84] One study evaluating the ASQ in outpatient settings, including primary care, was identified, but it was excluded because its accuracy was compared against another suicide risk screening instrument and not against a diagnostic clinical interview by a qualified professional.[82]

The updated evidence base suggests improvements in suicidal ideation resulting from psychotherapy interventions, but this finding was statistically significant for only 1 measure. The evidence suggested no statistically significant differences on all other measures. All trials included treatment-as-usual comparators, which for ethical reasons must be active comparators, such as standard psychotherapy, individual counseling, family sessions, medication assessment and review, medication, and other care coordination activities. Comparable intensity of therapy in study groups, coupled with low event rates for some outcomes (such as suicide deaths, hospitalizations, and suicide attempts), is likely to make differences between study groups difficult to detect. The evidence was rated as low for benefit on suicidal ideation; insufficient for evaluating outcomes such as suicide attempts, hospitalizations, and deaths; and low for no harm.

Limitations

This study has several limitations. First, no studies were available that compared screening with no screening. Second, only limited evidence was available on long-term outcomes, test accuracy, and suicide risk and depression treatment in children. Third, treatment-as-usual comparators for suicide risk interventions included active treatments, which may have led to lack of statistically significant differences between study groups. Fourth, the review was limited to first-line drugs approved for pediatric use by the FDA.

Conclusions

Indirect evidence suggested that some screening instruments were reasonably accurate for detecting depression. Psychotherapy and pharmacotherapy were associated with some benefits and no statistically significant harms for depression, but the evidence was limited for suicide risk screening instruments and interventions.

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