JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Screening for Anxiety in Children and Adolescents
Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Anxiety in children and adolescents is associated with impaired functioning, educational underachievement, and future mental health conditions.

OBJECTIVE To review the evidence on screening for anxiety in children and adolescents to inform the US Preventive Services Task Force.

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; diagnostic test accuracy studies; RCTs of cognitive behavioral therapy (CBT) or US Food and Drug Administration–approved 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, all-cause mortality, functioning, suicide-related symptoms or events, adverse events.

RESULTS Thirty-nine studies (N = 6065) were included. No study reported on the direct benefits or harms of screening on health outcomes. Ten studies (n = 3260) reported the sensitivity of screening instruments, ranging from 0.34 to 1.00, with specificity ranging from 0.47 to 0.99. Twenty-nine RCTs (n = 2805) reported on treatment: 22 on CBT, 6 on pharmacotherapy, and 1 on CBT, sertraline, and CBT plus sertraline. CBT was associated with gains on several pooled measures of symptom improvement (magnitude of change varied by outcome measure), response (pooled relative risk [RR], 1.89 [95% CI, 1.17 to 3.05]; n = 606; 6 studies), remission (RR, 2.68 [95% CI, 1.48 to 4.88]; n = 321; 4 studies), and loss of diagnosis (RR range, 3.02-3.09) when compared with usual care or wait-list controls. The evidence on functioning for CBT was mixed. Pharmacotherapy, when compared with placebo, was associated with gains on 2 pooled measures of symptom improvement—mean difference (Pediatric Anxiety Rating Scale mean difference, −4.0 [95% CI, −5.5 to −2.5]; n = 726; 5 studies; and Clinical Global Impression–Severity scale mean difference, −0.84 [95% CI, −1.13 to −0.55]; n = 550; 4 studies) and response (RR, 2.11 [95% CI, 1.58 to 2.98]; n = 370; 5 studies)—but was mixed on measures of functioning. Eleven RCTs (n = 1293) reported harms of anxiety treatments. Suicide-related harms were rare, and the differences were not statistically significantly different.

CONCLUSIONS AND RELEVANCE Indirect evidence suggested that some screening instruments were reasonably accurate. CBT and pharmacotherapy were associated with benefits; no statistically significant association with harms was reported.

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Supplemental content

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Anxiety is a common condition in children and adolescents. The 2020 National Survey of Children's Health estimated that 7.8% of children aged 3 to 17 years had a current anxiety disorder; 0.7% had severe anxiety.[1] Longitudinal studies of anxiety disorders suggest that early anxiety may lead to an increased risk for secondary depression.[2-4] In addition, childhood anxiety often interferes with social, emotional, and academic development[5,6] that can result in substance abuse, dependence, or both; suicide; educational underachievement; and functional impairment.[7,8] The rationale for routine screening is to identify undiagnosed youth who may benefit from effective treatment for anxiety disorders. This systematic review evaluated the evidence on screening for anxiety in children and adolescents to inform a new recommendation by the US Preventive Services Task Force (USPSTF).

Methods

Scope of the Review

The analytic framework and key questions that guided the review are shown in **Figure 1**. Detailed methods, evidence tables, and contextual information are available in the full evidence report.[10]

Data Sources and Searches

PubMed, the Cochrane Library, PsycINFO, CINAHL, and ClinicalTrials.gov were searched for English-language articles (eMethods in the Supplement). Searches for treatment of anxiety were limited to articles published from January 1, 2017, to July 19, 2021, because evidence from prior to 2017 was identified from an existing comprehensive Agency for Healthcare Research and Quality (AHRQ) review.[11] Reference lists of pertinent articles and studies suggested by reviewers were also evaluated. 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 inclusion criteria for each key question (eMethods in the Supplement); disagreements were resolved by discussion or by a third reviewer. English-language studies that included children and adolescents 18 years or younger, were of fair or good methodological quality, and were conducted in countries categorized as very highly developed by the 2018 United Nations Human Development Index were eligible.[12] For screening, studies that included unselected participants without known anxiety were eligible. For treatment, selection was restricted to studies of participants diagnosed with at least 1 anxiety disorder (ie, generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, separation anxiety disorder, and selective mutism). For studies of nonpharmacological interventions, inclusion was restricted to cognitive behavioral therapy (CBT), the most common therapy.

Eligible pharmacotherapy interventions included agents approved by the US Food and Drug Administration 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 anxiety symptoms measured by validated instruments, clinical response, or remission; all-cause mortality; quality of life measured using validated scales or instruments; and functioning measured by validated scales, missed days of school, or sleep-related outcomes. Eligible harms of treatment included treatment avoidance, deterioration in patient-clinician relationship, labeling or stigma, unnecessary treatment, serious adverse effects, withdrawal 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 included studies from a prior AHRQ evidence review on anxiety treatment in youth[11] were spot-checked and carried forward. All other studies were rated dually and independently using predefined criteria established by the USPSTF (eMethods in the Supplement) and others.[11,13-16] 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 6 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) software 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.[9,19] Two senior reviewers independently developed initial strength of evidence assessments; disagreements were resolved through discussion or input of a third senior reviewer.

Results

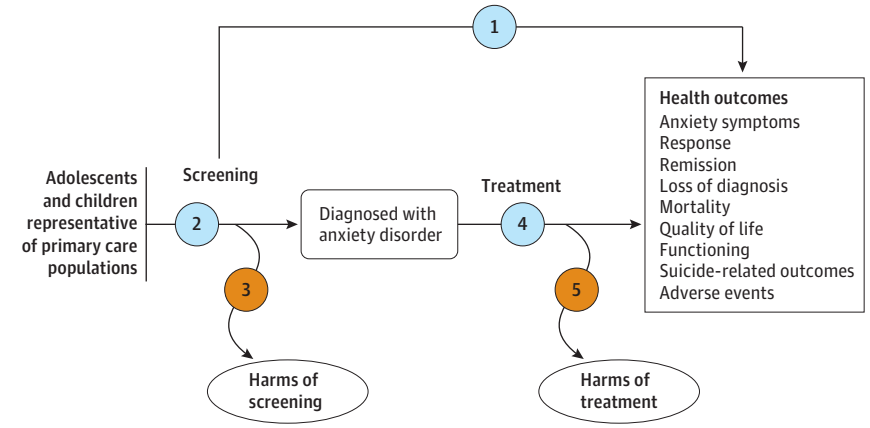
Thirty-nine studies (N = 6065) in 50 publications were eligible (**Figure 2**), including 10 studies reporting on screening test accuracy[21-30] and 29 randomized clinical trials (RCTs) reporting on treatment interventions.[31-70] The results in this publication focus on pooled analyses when available. Additional results are available in the full report.[10] A list of full-text articles that were screened but excluded is provided in the Supplement (List of Excluded Studies).

Benefits of Screening

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

No trial directly assessed the benefits of screening children or adolescents for anxiety in the primary care setting.

Figure 1. Analytic Framework: Screening for Anxiety in Children and Adolescents



Key questions

1. Do anxiety screening programs in primary care or comparable settings result in improved health outcomes in children and adolescents?
2. Do instruments to screen for anxiety accurately identify children and adolescents with anxiety in primary care or comparable settings?
3. What are the harms associated with screening for anxiety in primary care or comparable settings in children and adolescents?
4. Does treatment (cognitive behavioral therapy or pharmacotherapy) of anxiety result in improved health outcomes in children and adolescents?
5. What are the harms of treatment (cognitive behavioral therapy or pharmacotherapy) in children and adolescents who are treated for anxiety?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions that the review will address 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.[9]

Accuracy of Screening Instruments

Key Question 2. Do instruments to screen for anxiety accurately identify children and adolescents with anxiety in primary care or comparable settings?

Ten fair-quality studies assessed the accuracy of 12 different screening instruments for detecting anxiety[21-30] (n = 3260) (eTables 7 and 8 in the Supplement). Some studies assessed multiple instruments, some instruments were examined in multiple studies, and some studies examined instrument versions for children, adolescents, or both or included parents, youth, or both as respondents. Five studies[21,23,28-30] examined instrument accuracy for detection of social anxiety disorder, 3 studies[24-26] for generalized anxiety disorder, 2 studies[24,27] for panic disorder, 1 study[25] for separation anxiety disorder, and 1 study for global anxiety not specific to any given disorder.[22]

The prevalence of anxiety disorders in included studies, based on diagnostic clinical interviews, ranged from 2.5% to 24%. **Table 1** provides the sensitivity and specificity by screening instrument (additional detail is provided in eTable 9 in the Supplement). Across all instruments and respondents, sensitivity ranged from 0.34 to 1.00 and specificity ranged from 0.47 to 0.99.

Findings Within Age Groups

Seven studies of adolescents (mean age, 14.8 years) reported on 8 instruments,[21,23,24,27,28,30] and 4 studies on school-aged children and adolescents aged 7 to 17 years (mean age, 11.0 years) reported on 7 instruments.[21,22,71,72] No study included children younger than 7 years.

Only 1 study[21] reported results for adolescents and children separately for the same instruments; these results did not suggest consistent differences in sensitivity and specificity by age of the youth, and variations in instruments and thresholds may explain differences in results. Across instruments and conditions reported in other included studies, differences in reported accuracy between studies on adolescents alone vs studies including both adolescents and children did not suggest age-related patterns (eTable 9 in the Supplement).

Harms of Screening

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

No trial directly assessed the harms of screening children or adolescents for anxiety in the primary care setting.

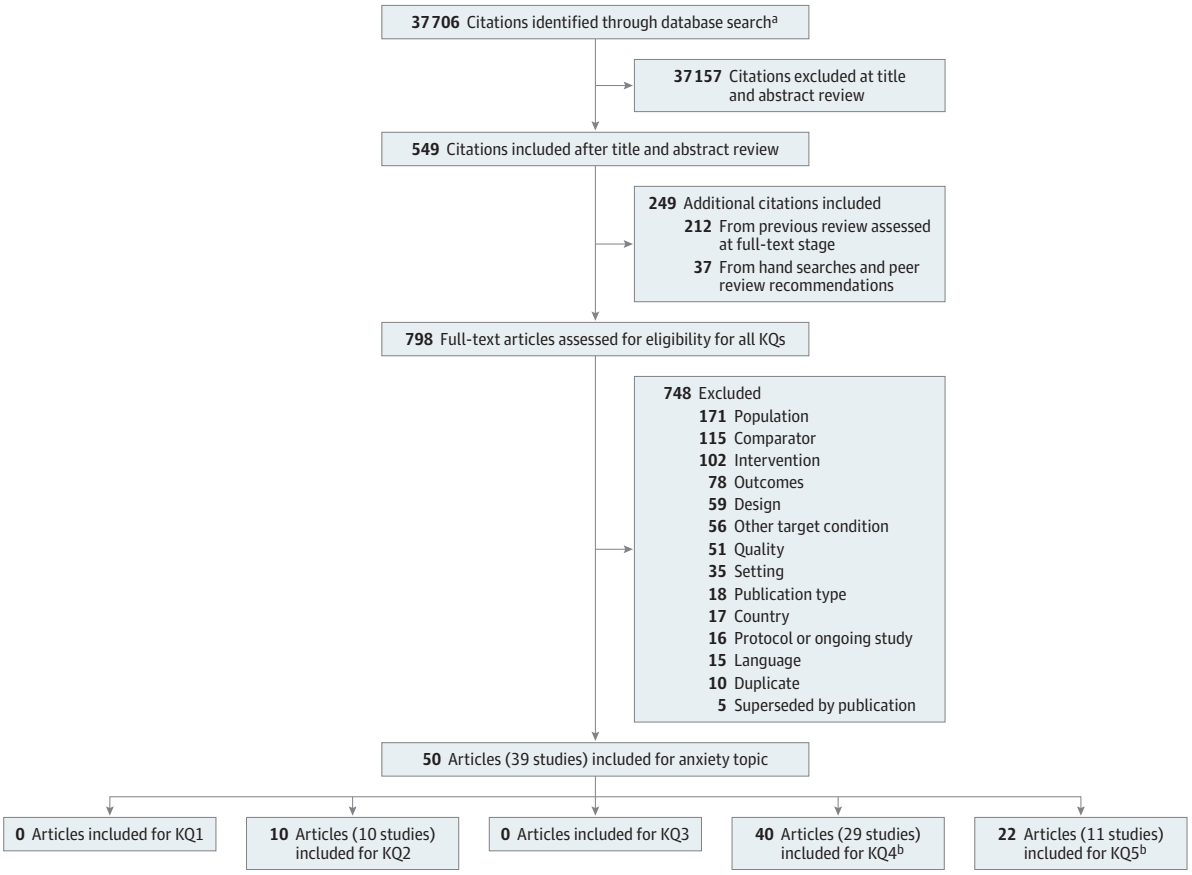
Benefits of Treatment

Key Question 4. Does treatment (cognitive behavioral therapy or pharmacotherapy) of anxiety result in improved health outcomes in children and adolescents?

Benefits of treatment for anxiety are summarized in **Table 2**.

Twenty-nine RCTs (described in 40 articles) of good or fair quality were eligible (n = 2805).[31-70] All studies are new to this

Figure 2. Literature Search Flow Diagram: Screening for Anxiety 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 depression or suicide risk. 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. KQ indicates key question.

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

[b] Study may address more than 1 KQ.

report because this topic has not been addressed previously by the USPSTF. Detailed study, population, and intervention characteristics and results are reported in eTable 10 in the Supplement; detailed outcomes are reported in eTables 11 through 19 in the Supplement; and results from meta-analyses are provided in eFigures 1 through 17 in the Supplement. Sixteen studies enrolled children with any type of anxiety disorder.[31,43,45,46,52,54-59,62,64,66-68] The most common primary diagnoses in these studies were social anxiety disorder and generalized anxiety disorder. Of the studies requiring specific anxiety disorders for trial eligibility, 5 required generalized anxiety disorder,[41,53,63,65,70] 4 required social anxiety disorder,[42,47,60,69] 2 required selective mutism,[44,61] and 2 required either generalized anxiety disorder, social anxiety disorder, or separation anxiety disorder.[32-40,48-51] Nine studies set a threshold for severity.[41,48-50,57,58,60,62,63,65] Nine of 29 studies had a majority of male participants.[48-52,55-58,63,64]

The mean age of enrolled populations ranged from 4.1 to 17.4 years. Three studies focused on early childhood (ages 3-7 years),[57,66,68] 11 focused on school-aged children (6-14 years),[44,47,52,55,56,58,60,64,65,67,69] 11 spanned childhood and adolescence,[31-41,45,46,48-51,53,59,61-63] and 4 focused solely on adolescence.[42,43,54,70] Results below are summarized overall and then by age group when available.

Twenty-two RCTs evaluated CBT,[31,42-47,52-60,64-67] 6 evaluated pharmacotherapy,[41,48-51,61-63,70] and 1 evaluated CBT, sertraline, and CBT plus sertraline separately.[32-40] The results below focus on CBT and pharmacotherapy; detailed results for combination therapy are available in the full report.[10]

Reported outcomes included (1) anxiety symptoms, (2) clinical response or remission, and (3) functioning. CBT was associated with clinically important and statistically significant benefits on several pooled estimates of effect for end-of-treatment measures of anxiety symptoms (Table 2). These measures included the clinician severity rating on the Anxiety Disorders Interview Schedule (mean difference, −2.01 [95% CI, −2.74 to −1.29]; n = 579; 11 RCTs[31,43-45,53,54,57,59,65,68,73]), the child-rated Spence Children's Anxiety Scale (SCAS) (mean difference, −7.81 [95% CI, −10.99 to −4.63];

Table 1. Accuracy of Screening Instruments for Screening for Anxiety

Condition	Screener	Age range, y	No. of studies	Sensitivity	Specificity
Generalized anxiety disorder	PHQ-A	13-18	1[24]	0.50	0.98
	SCARED-GAD subscale	7-14	1[25]	0.64	0.63
	PI-ED-anxiety subscale	8-17	1[26]	0.88	0.85
Panic disorder	ANSQ (various thresholds)	12-18	1[27]	1.00	0.47-0.65
	PHQ-A	13-18	1[24]	0.42	0.99
Separation anxiety disorder	SCARED-SAD subscale	7-14	1[25]	0.88	0.73
Social anxiety disorder	SCARED-social phobia scale (various thresholds)	8-16	1[21]	0.78-0.83	0.69-0.81
	SAS (various thresholds)	8-18	2[21,23]	0.75-0.93	0.74-0.80
	SAS-A	12-18	1[23]	0.93	0.79
	SPAI-Brief	12-18	1[23]	0.86	0.88
	SPIN/Mini-SPIN (various thresholds)	12-17	3[28-30]	0.80-0.86	0.77-0.85
	SWQ (various thresholds)	13-17	1[21]	0.67-0.83	0.84-0.94
Any anxiety disorder	PHQ-A	13-18	1[24]	0.50	0.98
	SCARED	7-14	1[25]	0.88	0.56

Abbreviations: ANSQ, Autonomic Nervous System Questionnaire; PHQ-A, Patient Health Questionnaire for Adolescents; PI-ED, Paediatric Index of Emotional Distress; SAS, Social Anxiety Scale; SAS-A, Social Anxiety Scale for Adolescents; SCARED, Screen for Child Anxiety Related Disorders; SCARED-GAD, Screen for Child Anxiety Related Disorders–Generalized Anxiety Disorder; SCARED-SAD, Screen for Child Anxiety Related Disorders–Separation Anxiety Disorder; SPAI, Social Phobia and Anxiety Inventory; SPIN, Social Phobia Inventory; SWQ, Social Worries Questionnaire.

n = 668; 9 RCTs[31,43,45,52,54-56,59,65]), the parent-rated SCAS (mean difference, −6.06 [95% CI, −9.58 to −2.56]; n = 652; 9 RCTs[31,43,45,52,54-56,59,65]), and the Revised Children's Manifest Anxiety Scale (mean difference, −3.08 [95% CI, −5.91 to −0.24]; n = 241; 3 RCTs[56,64,67]). For pharmacotherapy, pooled estimates of effect suggested clinically important and statistically significant improvements for symptom improvement (Pediatric Anxiety Rating Scale mean difference, −4.0 [95% CI, −5.5 to −2.5]; n = 726; 5 RCTs[32-41,48-51,62,70]; Clinical Global Impression–Severity scale mean difference, −0.84 [95% CI, −1.13 to −0.55]; n = 550; 4 RCTs[32-41,63,70]) (Table 2).

CBT was also associated with a favorable clinical response (pooled relative risk [RR], 1.89 [95% CI, 1.17 to 3.05]; n = 606; 6 RCTs[32,44,46,54,57,66]), increased remission (pooled RR, 2.68 [95% CI, 1.48 to 4.88]; n = 321; 4 RCTs[31,43,56,59]), loss of any anxiety diagnosis (pooled RR, 3.09 [95% CI, 1.98 to 4.80]; n = 1414; 15 RCTs[31,43,45,46,52-54,58,59,64-68]), and loss of the primary anxiety diagnosis (pooled RR, 3.02 [95% CI, 1.84 to 4.95]; n = 1079; 13 RCTs[31,43-46,52-54,58-60,65,68,73]). Pharmacotherapy was also associated with a favorable clinical response (pooled RR, 2.11 [95% CI, 1.58 to 2.98]; n = 370; 5 RCTs[32-40,61-63,70]), but results from 3 studies were inconsistent for remission.[32-41,63] Regarding functioning, both CBT and pharmacotherapy were associated with statistically significant improvement on the Children's Global Assessment Scale (mean difference for CBT, 7.54 [95% CI, 2.84 to 12.23]; n = 811; 8 RCTs[32-40,44,46,53,54,58,65,68]; mean difference for pharmacotherapy, 5.14 [95% CI, 3.21 to 7.08]; n = 551; 3 RCTs[32-41,62]), whereas the evidence on other measures was not statistically significant.

Findings Within Age Groups

Three studies enrolled children aged 3 to 7 years[57,66,68] and 4 studies enrolled only adolescents aged 13 to 20 years.[42,43,54,70] The remaining studies focused on school-aged children aged 5 to 14 years (12 studies[44,45,47,55,56,58,60,64,65,67,69]) or children and adolescents aged 7 to 18 years (10 studies[31,32,41,46,48,53,59,61-63]).

No significant difference in results was observed between age groups enrolled. For younger children, all 3 studies focused on CBT and reported consistent statistically significant benefits for anxiety symptoms in 2[57,68] of 3[57,66,68] studies. Two studies reported on response, and both reported statistically significant differences favoring CBT.[57,66] One study reported on remission[57] and 1 reported on functioning,[68] and both suggested statistically significant differences favoring CBT. One[66] of 2[66,68] studies reported statistically significant differences favoring CBT for loss of diagnosis.

For studies enrolling only adolescents, 3 studies[42,43,54] reported on CBT and 1 reported on escitalopram.[70] Two[42,43] of the 3 CBT studies[42,43,54] reported consistent statistically significant improvement in anxiety symptoms, response, and remission; 1 reported no statistically significant differences.[54] Only 1 CBT study reported on loss of diagnosis and found no statistically significant differences.[54] Two studies reported on functioning, and neither consistently found statistically significant differences across a range of outcome measures.[43,54] The escitalopram study reported improvement in symptoms and response.[70]

Harms of Treatment

Key Question 5. What are the harms of treatment (cognitive behavioral therapy or pharmacotherapy) in children and adolescents who are treated for anxiety?

Eleven good- or fair-quality studies (described in 22 articles) that addressed benefits also addressed harms (n = 1293). In the Supplement, key characteristics of included studies for harms are provided in eTable 20, detailed outcomes are provided in eTables 21 and 22, and results from meta-analyses are provided in eFigures 18 and 19. Outcomes reported include (1) suicide-related harms, (2) withdrawal due to adverse events, (3) and serious adverse events. Regarding suicide-related harms, 2 CBT studies reported on suicidal ideation, attempts, or self-harm behavior.[32-40,54] One study of 60 participants[54] reported that 2 participants in the wait-list control group only withdrew from the study because of risk of suicide by 17 weeks. A second child-focused study comparing CBT with placebo reported on self-harm behavior without suicidal attempt (1/139 [0.7%] vs 0/76 [0%]), suicidal ideation (5/139 [3.6%] vs 1/76 [1.3%]), and suicidal attempts (no event in either group) by 12 weeks.[32-40] Three pharmacotherapy studies reported on suicide-related harms at the end of treatment at 8 to 12 weeks (duloxetine,[41] escitalopram,[70] and sertraline[32-40]). No study reported on suicide deaths, 2 studies reported on suicide attempts (1/26 events for

Table 2. Benefits of Treatment for Anxiety

Intervention (mode of delivery for psychotherapy interventions	Time of outcome measurement (from baseline)	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 effect size (95% CI); I^2
Change in symptoms								
CBT								
Individual-, group/child-, parent-, or child + parent-focused (in-person, email, telephone, or internet)	4-17 wk	Primary diagnosis of ADIS-CSR or all diagnoses	0-8	Score of 4 (moderate degree of impairment) or greater indicates a clinical diagnosis	1.9-4.2	3.6-6.2	11[31,43-45,53,54,57,59,65,68,73] (579)	Mean difference, −2.01 (−2.74 to −1.29) I^2 = 83%
	6-17 wk	SCAS-C	0-114	Cutoffs vary by age and sex, from 33 to 50 (higher scores represent worse outcomes)	21.6-34.9	29.4-42.1	9[31,43,45,52,54-56,59,65] (668)	Mean difference, −7.81 (−10.99 to −4.63) I^2 = 29%
	6-17 wk	SCAS-P	0-114	Cutoffs vary by age and sex, from 33 to 50 (higher scores represent worse outcomes)	18.8-33.1	24.2-41.3	9[31,43,45,52,54-56,59,65] (652)	Mean difference, −6.06 (−9.58 to −2.56) I^2 = 58%
Individual/child-focused or parent-led (in-person)	5-12 wk	CGI-S	1-7	Score of 2: borderline ill; 3, mildly ill; 4, moderate illness	2.0-4.0	3.3-4.2	3[32-40,46,57] (453)	Mean difference, −0.60 (−1.14 to −0.06) I^2 = 75%
Individual-, group/child-, or child + parent-focused (in-person)	12 wk	MASC	0-117	Cutoff scores may not be possible to establish	40.9-48.8	42.9-54.7	3[32-40,58,60,73] (435)	Mean difference, −4.66 (−9.66 to 0.34) I^2 = 66%
Individual-, group/child-, or child + parent-focused (in-person, email, telephone, or internet)	10-12 wk	RCMAS	0-28	Score ≥19 indicates clinically significant levels of anxiety	6.6-10.9	9.8-15.7	3[56,64,67] (241)	Mean difference, −3.08 (−5.91 to −0.24) I^2 = 71%
Pharmacotherapy								
Fluoxetine, fluvoxamine, duloxetine, escitalopram, or sertraline	8-12 wk	PARS	0-25	Score >11.5 discriminates youth without anxiety disorders from those with anxiety disorders	8.1-9.8	9.3-15.9	5[32-41,48-51,62,70] (726)	Mean difference, −4.0 (−5.5 to −2.5) I^2 = 81%
Duloxetine, escitalopram, or sertraline	8-12 wk	CGI-S	1-7	Score of 2: borderline ill; 3, mildly ill; 4, moderate illness	2.4-3.0	3.1-3.9	4[32-41,63,70] (550)	Mean difference, −0.84 (−1.13 to −0.55) I^2 = 75%

(continued)

Table 2. Benefits of Treatment for Anxiety (continued)

Intervention (mode of delivery for psychotherapy interventions)	Time of outcome measurement (from baseline)	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 effect size (95% CI); I^2
Clinical response, remission, and loss of diagnosis								
CBT								
Individual-, group/child-, parent-, or child + parent-focused (in-person)	4 wk to 6 mo	Proportion with a clinical response (CGI score of 1 or 2)	0%-100%	CGI-I scores of 1 and 2 indicate moderate marked improvement, proportion threshold unclear	40%-83%	0%-37%	6[32,44,46,57,66] (606)	RR, 1.89 (1.17 to 3.05) I^2 = 64%
Individual-, group/child-, parent-, or child + parent-focused (in-person, email, telephone, or internet)	8-16 wk	Remission from anxiety symptoms on SCAS-C	0%-100%	Unclear; "clinically significant change"	43%-62%	6%-38%	4[31,43,56,59] (321)	RR, 2.68 (1.48 to 4.88) I^2 = 48%
	8-16 wk	Loss of all anxiety diagnoses	0%-100%	No diagnosis following a structured clinical interview	15%-80%	0%-35%	15 Studies[31,43,45,46,52-54,58,59,64-68] (1414)	RR, 3.09 (1.98 to 4.80) I^2 = 65%
	6 wk to 12 mo	Loss of primary anxiety diagnosis	0%-100%	No diagnosis following a structured clinical interview	7%-80%	0%-43%	13[31,43-46,52-54,58-60,65,68,73] (1079)	RR, 3.02 (1.84 to 4.95) I^2 = 75%
Pharmacotherapy								
Escitalopram, fluoxetine, or sertraline	8-12 wk	Proportion with a clinical response (CGI score of 1 or 2)	0%-100% for proportion	CGI-I scores of 1 and 2 indicate moderate marked improvement, proportion threshold unclear	50%-91%	9%-44%	5[32-40,61-63,70] (370)	RR, 2.11 (1.58 to 2.98) I^2 = 18%
Functional status								
CBT								
Individual-, group/child-, parent-, or child + parent-focused (in-person, telephone, internet, or combination)	8-12 wk	CAIS	0-81	Score <7: no anxiety diagnosis	6.4-21.8	15.2-19.6	3[33,52,54] (403)	Mean difference, −2.23 (−5.88 to 1.43) I^2 = 38%
	4-12 wk	CGAS	1-100	Score >70: no clinically significant functional impairment Score <41: major impairment to functioning in several areas	53.6-82.1	52.5-61.9	8[32-40,44,46,53,54,58,65,68] (811)	Mean difference, 7.54 (2.84 to 12.23) I^2 = 90%
Pharmacotherapy								
Duloxetine, fluoxetine, or sertraline	10-12 wk	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[32-41,62] (551)	Mean difference, 5.14 (3.21 to 7.08) I^2 = 0%

Abbreviations: ADIS-CSR, Anxiety Disorders Interview Schedule–Clinician Severity Rating; CAIS, Children's Anxiety Impact Scale; CBT, cognitive behavioral therapy; CGAS, Children's Global Assessment Scale; CGI, Clinical Global Impression scale; CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impression–Severity; MASC, Multidimensional Anxiety Scale for Children; PARS, Pediatric Anxiety Rating Scale; RCMAS, Revised Children's Manifest Anxiety Scale; RR, relative risk; SCAS, Spence Children's Anxiety Scale; SCAS-C, Spence Children's Anxiety Scale–Child-rated; SCAS-P, Spence Children's Anxiety Scale–Parent-rated.

Table 3. Summary of Evidence

No. of studies, study designs	No. of participants	Summary of findings	Consistency, precision	Limitations	Strength of evidence	Applicability
KQ1: Benefits of screening						
None		NA	NA	NA	Insufficient	NA
KQ2: Accuracy of screening instruments						
10 Studies[21-30]	3260	Varies by screener, threshold, and condition Sensitivity range, 0.34-1.00 Specificity range, 0.47-0.99	Consistency unknown for individual screeners; imprecise	No replication of results for specific thresholds and screeners; unclear whether thresholds were established a priori or whether index and reference standard results were blinded	Low to moderate (varies by instrument)	Participants were primarily adolescents, but school-aged children were included in 4 studies Applicable to both primary care and school-based settings A variety of different screeners were used, of which only 2 (SCARED and SPIN) are used widely in practice for detecting anxiety
KQ3: Harms of screening						
None		NA	NA	NA	Insufficient	NA
KQ4: Benefits of treatment						
29 RCTs (22 on CBT; 6 on pharmacotherapy; 1 on CBT, sertraline, and combination)[31-70]	2805	CBT: Statistically significant differences favoring CBT on several pooled measures of symptom improvement Statistically significant improvement on CGAS but not on CAIS Pharmacotherapy: Statistically significant differences favoring pharmacotherapy on pooled measures of symptom improvement and response Statistically significant differences favoring pharmacotherapy on pooled CGAS but not on other measures of functioning	Mostly consistent; mostly precise	Potential for bias from attrition Additionally, CBT studies cannot mask treatments, leading to the potential for bias in outcome reporting	Moderate for anxiety symptoms, response, remission, and loss of diagnosis; low for functioning	15 CBT studies targeted any anxiety disorders; only 1 pharmacotherapy study targeted any anxiety disorders Studies addressed youth aged 3 to 20 y, but 11 were conducted exclusively in adolescents Psychotherapy studies were limited to CBT; pharmacotherapy studies were limited to drugs with FDA approval for pediatric use
KQ5: Harms of treatment						
11 RCTs (4 on CBT; 6 on pharmacotherapy; 1 on CBT, sertraline, and combination)[32-43,48-51,53,54,61-63,70]	1293	Psychotherapy: Inconsistent results on suicide-related events; harms were events and were not statistically significant Pharmacotherapy: More suicide-related events and withdrawals due to adverse events in the pharmacotherapy group, but harms were rare and not statistically significant	Consistent to mostly consistent; imprecise	CBT interventions cannot mask treatment, leading to the potential for bias in outcome reporting	Psychotherapy: insufficient evidence Pharmacotherapy: low for harms	Two of 4 CBT studies included any anxiety disorders; 1 of 7 pharmacotherapy studies included any anxiety disorders Studies addressed children aged 5 to 20 y, but 4 were conducted exclusively in adolescents Psychotherapy studies were limited to CBT; pharmacotherapy studies were limited to drugs with FDA approval for pediatric use

Abbreviations: CAIS, Children's Anxiety Impact Scale; CBT, cognitive behavioral therapy; CGAS, Children's Global Assessment Scale; FDA, US Food and Drug Administration; KQ, key question; NA, not applicable; RCT, randomized clinical trial; SCARED, Screen for Anxiety Related Emotional Disorders; SPIN, Social Phobia Inventory.

escitalopram vs 0/25 events for placebo[70]; no event occurred for sertraline or placebo in 1 study[32-40]), 3 studies reported on suicidal ideation or worsening of suicidality (1/135 for duloxetine vs 0/137 for placebo[41]; 6/26 for escitalopram vs 2/25 for placebo[70]; 0/133 for sertraline vs 1/76 for placebo[32-40]), and 2 studies reported on self-injurious behavior (2/26 for escitalopram vs 1/25 for placebo[70]; 1/133 for sertraline vs 0/76 for placebo[32-40]). Suicide-related harms were rare, and the differences between treatment and placebo groups were not statistically significantly different.

Regarding withdrawal due to adverse events, the pooled RR for CBT trials was 0.39 (95% CI, 0.08 to 1.87; n = 372; 4 studies[32-40,43,53,54]). The pooled RR across all pharmacotherapy trials was 1.72 (95% CI, 0.57 to 5.18; n = 734; 5 RCTs[32-41,48-51,62,70]).

For both CBT and pharmacotherapy, serious adverse events were rare and the differences between treatment and placebo groups were not statistically significantly different.

Findings Within Age Groups

No study reported on harms in young children. Results for studies of adolescents were consistent with results for the overall body of evidence: outcomes were rare and differences between treatment and comparison groups were not statistically significant.

Discussion

This systematic review evaluated screening for anxiety in children and adolescents. **Table 3** summarizes the evidence, including strength-of-evidence ratings. No study 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. Two of the most widely used screeners (ie, Screen for Anxiety Related Emotional Disorders and the Social Phobia Inventory) were reasonably accurate, leading to low-to-moderate strength of evidence.

Consistent, precise, statistically significant differences for most anxiety outcomes for CBT and pharmacotherapy led to strength-of-evidence ratings of moderate for benefit for nearly all outcomes. Treatment studies covered a wide range of ages, from preschool through adolescence, although 4 studies focused exclusively on adolescents (13-20 years[42,43,54,70]). Studies focusing on younger children aged 3 to 7 years[57,66,68] were consistent with the overall findings in demonstrating benefits for symptoms and clinical response.

Few CBT trials reported on harm outcomes leading to a strength-of-evidence rating of insufficient. The evidence suggests that suicide-related harms, serious adverse events, and withdrawal due to adverse events are rare in pharmacotherapy studies but more frequent in the treatment group; thus, strength of evidence for pharmacotherapy was rated as low for harms.

Few studies reported analyses for populations of interest. Studies reporting on analyses of anxiety symptoms consistently reported no differences in effect of treatment by age, but there is insufficient evidence available on effect of treatment on anxiety symptoms by race or ethnicity.

Limitations

This review has several limitations. First, no available study compared screening with no screening. Second, only limited evidence was available on long-term outcomes and on test accuracy and treatment in children. Third, the review was limited to CBT and drugs approved for pediatric use by the US Food and Drug Administration.

Conclusions

Indirect evidence suggested that some screening instruments were reasonably accurate for detecting anxiety. CBT and pharmacotherapy were associated with benefits; no statistically significant association with harms was reported.

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Concept and design: Viswanathan, Kahwati.
Acquisition, analysis, or interpretation of data: Viswanathan, Wallace, Cook Middleton, Kennedy, McKeeman, Hudson, Rains, Vander Schaaf, Kahwati.
Drafting of the manuscript: Viswanathan, Kennedy, Rains.
Critical revision of the manuscript for important intellectual content: Viswanathan, Wallace, Cook Middleton, Kennedy, McKeeman, Hudson, Rains, Vander Schaaf, Kahwati.
Statistical analysis: Viswanathan, Wallace, Kahwati.
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