Effective Health Care

Depressive Disorders in Children and Adolescents

Results of Topic Selection Process & Next Steps

The nominator, the American Academy of Child & Adolescent Psychiatry (AACAP), is interested in a new systematic review to inform the update of their 2007 practice parameters pertaining to the prevention, assessment, and treatment of depressive disorders in children and adolescents. Specifically the nominator would like to know what factors increase the risk of developing depressive disorders, the benefits and harms of interventions to prevent the development of a depressive disorder, the accuracy of various approaches for screening and diagnosing depressive disorders, the benefits and harms of pharmacologic and/or non-pharmacologic treatments for depressive disorders, and how different treatment outcomes may vary by a range of individual characteristics.

Due to limited program resources, the program is unable to develop a review at this time. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Depressive Disorders in Children and Adolescents

Topic #: 0679

Nomination Date: June 3, 2016

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Summary of Key Findings:

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new review would be partly duplicative of existing reviews. Existing reviews do not fully address KQ 1-2; and children with dysthymia for KQ 3-5.
    - We identified a 2016 AHRQ review focused on MDD in children. It addresses the accuracy and comparative accuracy of screening and diagnostic tools (KQ3), effectiveness of non-pharmacological treatments (KQ4), and effectiveness of pharmacological treatments (KQ5). It did not include children with dysthymia. We also identified additional systematic reviews examining depression (both MDD and dysthymia) in children for

KQ3-5; however, these did not provide evidence on screening for and treating dysthymia alone.
    - We identified multiple systematic reviews related to risk factors for depressive disorders (KQ1) and interventions to prevent depressive disorders (KQ2). However they focused on specific risk factors and populations and did not address the broader range of individuals and factors of interest to the nominator. For example the two reviews related to KQ1 focused on populations after natural disasters, and LGBTQ youth.
- Impact: A new evidence review has high impact potential. There is practice variation because the standard for care is unclear. A new review could address this uncertainty and influence practice.
- Feasibility: Our feasibility scan was inclusive of all KQ except for MDD for KQ 3-5 as these were covered by the 2016 AHRQ review. A new review on this topic would be feasible.
    - *Size/scope of the review:* We identified 20 potentially relevant studies (7 for KQ1, 3 for KQ2, 5 for KQ3, 5 for KQ4, 3 for KQ4a, 4 for KQ5, and 3 for KQ5a) from our random sample of studies from the past 5 years.
    - *Clinicaltrials.gov:* We identified 15 on-going or recently completed, unpublished trials pertaining to the key questions.
- Value: The potential for value is high, given that AACAP will use a new AHRQ systematic review to update their 2007 practice parameters. This organization has previously produced high quality, evidence based guidelines, and are transparent about their methodology

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Introduction !

Approximately 1 in 10 adolescents aged 13-18 will develop either major depressive disorder or dysthymic disorder during their lifetime.[1] Depressive disorders negatively impact social[2] and academic[3] outcomes, and are associated with poor long-term outcomes and increased risk of suicide.[4] Current clinical guidelines recommend the use of psychotherapy with or without antidepressants for children and adolescents with depressive disorders seen in primary[5,6] and mental health[7] care, and outline steps for treating children and adolescents with acute mental health and behavioral problems presenting in Emergency Departments.[8] However, there continue to be concerns that antidepressants may be associated with higher rates of suicidality.[9] It is also unclear how non-pharmacological and pharmacological treatments compare to each other, whether certain treatments are more effective for certain population subgroups, and whether early interventions can effectively prevent the development of depressive disorders.

Topic nomination *#0679 Depressive Disorders in Children and Adolescents* was received on June 3, 2016. It was nominated by American Academy of Child & Adolescent Psychiatry (AACAP).The questions for this nomination are:

Key Question 1. In adolescents and children, what are the risk factors associated with the development of depressive disorders?

Key Question 2. In adolescents and children, what are the benefits and harms of interventions to prevent depressive disorders?

Key Question 3. What is the accuracy and comparative accuracy of diagnostic and screening tools for depressive disorders in children and adolescents?

Key Question 4. In adolescents and children, what are the benefits and harms and comparative benefits and harms of non-pharmacological interventions for depressive disorders?

a) "Do the benefits and harms differ by subpopulation (eg, patient characteristics, disorder characteristics, history of previous treatment, comorbid condition, etc.)?

Key Question 5. In adolescents and children, what are the benefits and harms and comparative benefits and harms of pharmacological interventions for depressive disorders?

a) "Do the benefits and harms differ by subpopulation (eg, patient characteristics, disorder characteristics, history of previous treatment, comorbid condition, etc.)?

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, and outcomes, (PICOs) of interest. See Table 1.

Table 1. Key Questions and PICOs

Key Question	1. In adolescents and children, what are the risk factors associated with the development of depressive disorders?	2. In adolescents and children, what are the benefits and harms of interventions to prevent depressive disorders?	3. What is the accuracy and comparative accuracy of screening and diagnostic tools for depressive disorders in children and adolescents?	4. In adolescents and children, what are the benefits and harms and comparative benefits and harms of non-pharmacological interventions for depressive disorders? a) Do the benefits and harms differ by subpopulation (eg, patient characteristics, disorder characteristics, history of previous treatment, comorbid condition, etc.)?	5. In adolescents and children, what are the benefits and harms and comparative benefits and harms of pharmacological interventions for depressive disorders? a) Do the benefits and harms differ by subpopulation (eg, patient characteristics, disorder characteristics, history of previous treatment, comorbid condition, etc.)?
Population	Children and adolescents <18 years old	Children and adolescents <18 years old	Children and adolescents <18 years old	Children and adolescents <18 years old with major depressive or dysthymic disorders	Children and adolescents <18 years old with major depressive or dysthymic disorders
Intervention	Any risk factor (eg, age, sex, race/ethnicity, family history of depression, low SES, comorbid mental or physical health disorder, negative life events)	Any prevention intervention (ie, psychotherapy, self-help, etc)	Any screening tool (ie, Beck Depression Inventory or Center for Epidemiologic Studies Depression Scale for Children, etc.)	Any non-pharmacological treatment (eg, psychotherapy, CBT, online CBT, self-help, etc)	Any pharmacological treatment (eg, second generation antidepressants, tricyclic antidepressants)
Comparator	NA	No intervention, wait list control, attention control, informational materials	Other screening tools	Any comparator (eg, treatment as usual, wait list control, attention control, informational materials, other non-pharmacological interventions, pharmacological interventions)	Any comparator (eg, placebo, wait list control, non-pharmacological interventions, other pharmacological interventions)
Outcome	NA	Reduction in incidence of depressive disorders	Accuracy (sensitivity, specificity)	Depressive symptoms, adverse events	Depressive symptoms, adverse events

Abbreviations: NA=Not applicable; CBT=Cognitive behavioral therapy; SES=socioeconomic status

Methods

To assess topic nomination *#0679 Depressive Disorders in Children and Adolescents* for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. " Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. " Establish the overall *importance* of a potential topic as representing a health or " healthcare issue in the United States. "
3. " Determine the *desirability of new evidence review* by examining whether a new " systematic review or other AHRQ product would be duplicative. "
4. " Assess the *potential impact* a new systematic review or other AHRQ product.
5. " Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. " Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Table 2 includes the citations for these reviews.

Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether a new review could influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.). See Appendix A.

Feasibility of New Evidence Review

We conducted two literature searches in both PubMed and PsycInfo. The first literature search looked for studies on all depressive disorders (June 2011 to June 2016), and the second looked for studies on dysthymic disorder specifically (August 2011 to August 2016). Our first search yielded 10,151 unique articles, so we reviewed a random sample of 200 articles. Our second search yielded 182 unique articles, so we reviewed all articles. We reviewed titles and abstracts for inclusion, and classified studies by study design to assess the size and scope of a potential evidence review. We then calculated the projected total number of included studies based on the proportion of studies included from the sample. We also searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Appendix B for the PubMed and PsycInfo search strategies and links to the ClinicalTrials.gov search.

Value

We assessed the nomination for value (see Appendix A). We considered whether a partner organization could use the information from the proposed evidence review to facilitate evidence-based change; or the presence of clinical, consumer, or policymaking context that is amenable to evidence-based change.

Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

Results

Appropriateness and Importance

This is an appropriate and important topic. Approximately 1 in 10 adolescents aged 13-18 will develop either major depressive disorder or dysthymic disorder during their lifetime.[1] According to AACAP, depression is projected to be the second leading cause of disability-adjusted life years in 2020.

Desirability of New Review/Duplication

A new review on this topic nomination would be partly duplicative of existing systematic reviews. Existing reviews do not address screening and treatment of dysthymia in children (KQ 3-5); and the range of risk factors and prevention for depressive disorders (KQ 1-2) across the spectrum of populations of interest to the nominator.

We identified a 2016 AHRQ review[10] that fully addresses KQ 3-5 in children with MDD. We also identified 11 reviews[9,11-20] related to screening and treatment for depression, several of which include children with dysthymia. However, these reviews do not fully address questions on screening and treatment of dysthymia because they did not analyze children with dysthymia separately.

We identified 5 reviews related to risk factors[21,22] and prevention[23-25] of depressive disorders (KQ 1-2). However these reviews looked at specific populations and did not include the full range of populations of interest to the nominator. For example, the two reviews identified for KQ 1 focused solely on children after a natural disaster; and on LGBTQ children.

Impact of a New Evidence Review

A new evidence review on this topic nomination would have high impact potential. There is practice variation because the standard of care for treating children and adolescents with depression is unclear. A new systematic review could address this uncertainty.

Feasibility of a New Evidence Review

A new evidence review on this topic nomination is feasible. Our literature search focused on KQ1, KQ2, the effectiveness of interventions for dysthymia for KQ 3-5, and the comparative effectiveness for interventions for dysthymia and depression for KQ 3-5. The effectiveness and comparative effectiveness of interventions for MDD (KQ3-5) was covered by an existing AHRQ review.[10]

We identified 20 potentially relevant studies (7 for KQ1[26,27 28-32], 3 for KQ2[33 34,35], 5 for KQ3[36-40], 5 for KQ4[41 42-45], 3 for KQ4a[41 42,43], 4 for KQ5[41-43,46], and 3 for KQ5a[41,46 42]) from our random sample of studies from the past 5 years. We project there may be 203 studies examining the key questions, though our confidence in this estimate is low. We also identified 15 on-going or recently completed, unpublished trials[47-61] pertaining to the key questions from Clinicaltrials.gov.

See Table 2, Feasibility column for the citations that were determined to address the key questions.

Table 2. Key Questions from Nomination, 2007 AACAP Depressive Disorders Practice Parameters, and Results of Duplication Search and Feasibility Search

Key Question	2007 Practice Parameter Recommendation	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
KQ 1: Risk Factors	Risk Factors & Prevention: Recommendation 16 Children With Risk Factors Associated With Development of Depressive Disorders Should Have Access to Early Services Interventions (SOR: CG)	Total number of completed or in-process systematic reviews: 2[21,22] • Other- 1[21] • Other (In process)- 1[22]	Size/scope of review Total number of identified published studies: 2 (overall search) + 5 (search for dysthymia only) • Cross-sectional: 2[26,27] + 2[28,29] • Prospective case series: 0 + 2[30,31] • Prospective cohort: 0 + 1[32] Projected total: 102 + 5 ClinicalTrials.gov Relevant Trials: 1 • Recruiting: 1[47]
KQ 2: Prevention	Risk Factors & Prevention: Recommendation 16 Children With Risk Factors Associated With Development of Depressive Disorders Should Have Access to Early Services Interventions (SOR: CG)	Total number of completed or in-process systematic reviews: 3 • Cochrane- 1[23] • Other- 2[24,25]	Size/scope of review Total number of identified published studies: 2 (overall search) + 1 (search for dysthymia only) • RCTs: 1[33] + 1[34] • nRCT: 1[35] + 0 Projected total: 102 + 1 Clinicaltrials.gov Relevant Trials: 4 • Recruiting – 3[48-50] • Complete – 1[51]

Key Question	2007 Practice Parameter Recommendation	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
KQ 3: Diagnosis and Screening	Screening/Evaluation: Recommendation 2 The Psychiatric Assessment of Children and Adolescents Should Routinely Include Screening Questions About Depressive Symptomatology (SOR: MS) Screening/Evaluation: Recommendation 3 If the Screening Indicates Significant Depressive Symptomatology, the Clinician Should Perform a Thorough Evaluation to Determine the Presence of Depressive and Other Comorbid Psychiatric and Medical Disorders (SOR: MS) Screening/Evaluation: Recommendation 4 The Evaluation Must Include Assessment for the Presence of Harm to Self or Others (SOR: MS) Screening/Evaluation: Recommendation 5 The Evaluation Should Assess for the Presence of Ongoing or Past Exposure to Negative Events, the Environment In Which Depression Is Developing, Support, and Family Psychiatric History (SOR: MS)	Total number of completed or in-process systematic reviews: 2 • AHRQ: 1[10] • In process (other): 1[11]	Size/scope of review Total number of identified published studies: 5 (search for dysthymia only) • Cross-sectional: 5[36-40] Projected total: 5 Clinicaltrials.gov: Relevant Trials: None identified
KQ 4: Non-pharmacological treatment	Treatment: Recommendation 6 The Treatment of Depressive Disorders Should Always Include an Acute and Continuation Phase; Some Children May Also Require Maintenance Treatment (SOR: MS) Treatment: Recommendation 7 Each Phase of Treatment Should Include Psychoeducation, Supportive Management, and Family and School Involvement (SOR: MS) Treatment: Recommendation 8 Education, Support, and Case Management Appear to Be Sufficient Treatment for the Management of Depressed Children and Adolescents With an	Total number of completed or in-progress systematic reviews: 7 • AHRQ: 1[10] • Cochrane- 1[12] • Other- 2[13,14] • In-process (Cochrane)- 1[15] • In-process (Other)- 3[11,16,17]	Size/scope of review Total number of identified published studies: 1 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and dysthymia) + 4 (search for dysthymia only) • RCTs: 1[41] + 4[42-45] Projected total: 101 + 4 Clinicaltrials.gov Relevant Trials: 7 • Recruiting – 3[55-57] • Active, not recruiting – 1[58] • Complete – 3[59-61]

Key Question	2007 Practice Parameter Recommendation	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
	Uncomplicated or Brief Depression or With Mild Psychosocial Impairment (SOR: CG) Treatment: Recommendation 9 For Children and Adolescents Who Do Not Respond to Supportive Psychotherapy or Who Have More Complicated Depressions, a Trial With Specific Types of Psychotherapy and/or Antidepressants Is Indicated (SOR: CG) Treatment: Recommendation 10 To Consolidate the Response to the Acute Treatment and Avoid Relapses, Treatment Should Always Be Continued for 6 to 12 Months (SOR: MS) Treatment: Recommendation 11 To Avoid Recurrences, Some Depressed Children and Adolescents Should Be Maintained in Treatment for Longer Periods of Time (SOR: CG) Treatment: Recommendation 14 Treatment: During All Treatment Phases, Clinicians Should Arrange Frequent Follow-up Contacts That Allow Sufficient Time to Monitor the Subject's Clinical Status, Environmental Conditions, and, If Appropriate, Medication Side Effects (SOR: MS)		
KQ 4a: Benefits and harms of non-pharmacological treatment by patient subpopulation	Treatment: Recommendation 13 Treatment Should Include the Management of Comorbid Conditions (SOR: MS) Treatment: Recommendation 15. During All Treatment Phases, for a Child or Adolescent Who Is Not Responding to Appropriate Pharmacological and/or Psychotherapeutic Treatments, Consider Factors Associated With Poor Response (SOR: MS)	Total number of completed or in-progress systematic reviews: 3 • AHRQ: 1[10] • Cochrane- 1[12] • In-process (Cochrane)- 1[15]	Size/scope of review Total number of identified published studies: 1 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and dysthymia) + 2 (search for dysthymia only) • RCTs: 1[41] + 2[42,43] Projected total: 101 + 2 Clinicaltrials.gov Relevant Trials: 3 • Recruiting – 3[55-57]

Key Question	2007 Practice Parameter Recommendation	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
KQ 5: Pharmacological treatment	Treatment: Recommendation 6 The Treatment of Depressive Disorders Should Always Include an Acute and Continuation Phase; Some Children May Also Require Maintenance Treatment (SOR: MS) Treatment: Recommendation 9 For Children and Adolescents Who Do Not Respond to Supportive Psychotherapy or Who Have More Complicated Depressions, a Trial With Specific Types of Psychotherapy and/or Antidepressants Is Indicated (SOR: CG) Treatment: Recommendation 10 To Consolidate the Response to the Acute Treatment and Avoid Relapses, Treatment Should Always Be Continued for 6 to 12 Months (SOR: MS) Treatment: Recommendation 11 To Avoid Recurrences, Some Depressed Children and Adolescents Should Be Maintained in Treatment for Longer Periods of Time (SOR: CG) Treatment: Recommendation 14 Treatment: During All Treatment Phases, Clinicians Should Arrange Frequent Follow-up Contacts That Allow Sufficient Time to Monitor the Subject's Clinical Status, Environmental Conditions, and, If Appropriate, Medication Side Effects (SOR: MS)	Total number of completed or in-progress systematic reviews: 8 • AHRQ: 1[10] • Cochrane- 4[9,12,18,19] • Other- 2[13,20] • In-process (other)- 2[11,17]	Size/scope of review Total number of identified published studies: 2 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and dysthymia) + 2 (search for dysthymia only) • RCTs: 2[41,46] + 2[42,43] Projected total: 202 + 2 Clinicaltrials.gov Relevant Trials: 3 • Recruiting – 3[52-54]
KQ 5a: Benefits and harms of pharmacological treatment by patient subpopulation	Treatment: Recommendation 13 Treatment Should Include the Management of Comorbid Conditions (SOR: MS) Treatment: Recommendation 15 During All Treatment Phases, for a Child or Adolescent Who Is Not Responding to Appropriate Pharmacological and/or Psychotherapeutic Treatments, Consider Factors	Total number of completed or in-progress systematic reviews: 8 • AHRQ: 1[10] • Cochrane- 2[18,19] • Other- 1[20]	Size/scope of review Total number of identified published studies: 2 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and dysthymia) + 1 (search for dysthymia only) • RCTs: 2[41,46] + 1[42] Projected total: 202 + 1

Key Question	2007 Practice Parameter Recommendation	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
	Associated With Poor Response (SOR: MS)		Clinicaltrials.gov Relevant Trials: None identified

Abbreviations: AACAP= American Academy of Child and Adolescent Psychiatry; AHRQ=Agency for Healthcare and Research Quality; CG=Clinical Guideline; KQ=Key Question; MDD= Major Depressive Disorder; MS=Minimal Standards; nRCT=Non-Randomized Controlled Trial; RCT=Randomized Controlled Trial; SOR=Strength of Recommendation

Notes on Table 2: The AACAP grades its recommendations according to the strength of evidence: minimal standard (MS) is applied to recommendations that are based on rigorous empirical evidence (eg, RCTs) and/or overwhelming clinical consensus, clinical guideline (CG) is applied to recommendations that are based on strong empirical evidence (eg, nRCTs) and/or strong clinical consensus, option (OP) is applied to recommendations that are acceptable based on emerging empirical evidence (eg, uncontrolled trials or case series/reports) or clinical opinion, but lack strong empirical evidence and/or strong clinical consensus.

Value

The potential for value is high, given that AACAP will use a new AHRQ systematic review to update their 2007 practice parameters. This organization has previously produced high-quality evidence-based guidelines, and they are transparent about their methodology.

Summary of Findings

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new review would be partly duplicative of existing reviews. Existing reviews do not fully address KQ 1-2; and children with dysthymia for KQ 3-5.
    - We identified a 2016 AHRQ review focused on MDD in children. It addresses the accuracy and comparative accuracy of screening and diagnostic tools (KQ3), effectiveness of non-pharmacological treatments (KQ4), and effectiveness of pharmacological treatments (KQ5). It did not include children with dysthymia. We also identified additional systematic reviews examining depression (both MDD and dysthymia) in children for KQ3-5; however, these did not provide evidence on screening for and treating dysthymia alone.
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- Value: The potential for value is high, given that AACAP will use a new AHRQ systematic review to update their 2007 practice parameters. This organization has previously produced high quality, evidence based guidelines, and are transparent about their methodology

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Appendices

Appendix A: Selection Criteria Summary *

Appendix B: Search Strategy & Results (Feasibility)

Appendix A. Selection Criteria Summary (

Selection Criteria	Supporting Data
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents a health care drug and intervention available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on both effectiveness and comparative effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. Approximately 1 in 10 adolescents aged 13-18 will develop either major depressive disorder or dysthymic disorder during their lifetime.[1]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, this topic affects heath care decisions for a large, vulnerable population.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers.
2d. Incorporates issues around both clinical benefits and potential clinical	Yes, this nomination addresses both benefits and potential harms of prevention interventions, pharmacological interventions, and non-pharmacological interventions for depression.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, according to the AACAP, depressive disorders are projected to be the second most important cause of loss of disability-adjusted life years by the year 2020.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	A new review would be partly duplicative of existing reviews. Existing reviews do not fully address KQ 1-2; and children with dysthymia for KQ 3-5. We identified existing and in process reviews for all key questions: two for KQ1 (2014[21], expected completion Dec 2015[22]), three for KQ2 (2015[24], 2013[25], 2011[62]), two for KQ3 (2016[10], expected completion August 2014[11]), seven for KQ4 (2015[14], 2015[15], 2014[12], 2014[13], expected completion April 2016[16], September 2015[17], and August 2014[11]) and eight for KQ5 (2015[20],

	2014[12], 2014[13], 2013[18], 2012[9], 2012[19], expected completion September 2015[17], August 2014[11]).
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, the standard of care is unclear, due to limited guidance on the comparative effectiveness of treatments in general, and for specific population subgroups.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, there is practice variation due to limited guidance on the comparative effectiveness of treatments.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	A new review is feasible. *Size/scope of the review:* We identified 20 potentially relevant studies (7 for KQ1[26,27 28-32], 3 for KQ2[33 34,35], 5 for KQ3[36-40], 5 for KQ4[41 42-45], 3 for KQ4a[41 42,43], 4 for KQ5[41-43,46], and 3 for KQ5a[41,46 42]) from our random sample of studies from the past 5 years. We project there may be 203 studies examining the key questions, though our confidence in this estimate is low. *Clinicaltrials.gov:* We identified 15 on-going or recently completed, unpublished trials[47-61] pertaining to the key questions.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, this topic will inform clinical decision-making on screening, diagnosing, treating, and preventing depression among children and adolescents across community and clinical settings.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes, AACAP will use a systematic review to update their 2007 clinical practice guidelines on the assessment and treatment of depression among children and adolescents.

Abbreviations: AACAP=American Academy of Child and Adolescent Psychiatry; KQ=Key Question; RCT=Randomized Control Trial

Appendix B. Search Strategy & Results (Feasibility)

Topic: Depressive disorders Date: June 10, 2016 Database Searched: PubMed	
Concept	**Search String**
Depression	("Depressive Disorder"[Mesh]) OR ((depression[Title] OR depressive[Title] OR melancholia[Title] OR depressions[Title]))
NOT Editorials, etc.	((((((("Letter"[Publication Type]) OR "News"[Publication Type]) OR "Patient Education Handout"[Publication Type]) OR "Comment"[Publication Type]) OR "Editorial"[Publication Type])) OR "Newspaper Article"[Publication Type]
Limit to last 5 years Children Human English	Filters activated: published in the last 5 years, Humans, English, Child: birth-18 years
N=6605	
Systematic Review **N=233**	PubMed subsection "Systematic [sb]"
Randomized Controlled Trials **N=2092**	Cochrane Sensitive Search Strategy for RCT's "(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])"
Other **N=4280**	

Topic: Depressive disorders Date: June 10, 2016 Database Searched: PsycINFO (EBSCOhost)	
Concept	**Search String**
Depression	DE "Major Depression"
Children and Adolescents	Narrow by SubjectAge: - childhood (birth-12 yrs) Narrow by SubjectAge: - adolescence (13-17 yrs)
Methodological Limits	Narrow by Methodology: scientific simulation field study focus group experimental replication systematic review clinical case study twin study mathematical model meta analysis brain imaging retrospective study qualitative study clinical trial treatment outcome

	literature review prospective study followup study longitudinal study quantitative study empirical study
Date, and language limits	Limiters - Publication Year: 2011-2016 Narrow by Language: - english
N=1455	
Systematic Review **N=39**	Narrow by Methodology: - systematic review Narrow by Methodology: - meta analysis
Randomized Controlled Trials **N=37**	
Other **N=1503**	

Clinicaltrials.gov searched on June 10, 2016 $
280 studies found for: $
Depressive Disorder | Child | received from 06/10/2011 to 06/10/2016 $
Link to Results: $
https://clinicaltrials.gov/ct2/results?term=&recr=&rslt=&type=&cond=Depressive+Disorder&intr= $
&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn= $
&gndr=&age=0&rcv_s=06%2F10%2F2011&rcv_e=06%2F10%2F2016&lup_s=&lup_e $

Topic: Dysthmic Disorder Date: August 22, 2016 Database Searched: MEDLINE (PubMed)	
Concept	Search String
Dysthymia	("Dysthymic Disorder"[Mesh]) OR ((Dysthymia[Title/Abstract] OR Dysthymic[Title/Abstract]))
NOT	
Not Editorials, etc.	((((("Letter"[Publication Type]) OR "News"[Publication Type]) OR "Patient Education Handout"[Publication Type]) OR "Comment"[Publication Type]) OR "Editorial"[Publication Type])) OR "Newspaper Article"[Publication Type]
Limit to last 5 years ; human ; English ; birth – 18 years	Filters activated: published in the last 5 years, Humans, English, Child: birth-18 years.
N=151	
Systematic Review N=5	PubMed subsection “Systematic [sb]”
Randomized Controlled Trials N=45	Cochrane Sensitive Search Strategy for RCT’s “(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])”
Other N=101	

Topic: Dysthymic Disorder Date: August 22, 2016 Database Searched: PsycINFO (EBSCOhost)	

Concept	Search String
Dysthymia	DE "Dysthymic Disorder"
Limit to Children and Adolescents ; English ; Last 5 years	Limiters - Publication Year: 2011-2016 Narrow by SubjectAge: - childhood (birth-12 yrs) Narrow by SubjectAge: - adolescence (13-17 yrs) Narrow by Language: - english
N=29	
Systematic Review N=0*	*no studies were marked as systematic review ; review ; or meta-analysis
Randomized Controlled Trials N=0**	** no studies were marked as clinical trial (or similar)
Other N=29***	*** methodology types available: Interview ; follow up study ; longitudinal study ; prospective study ; brain imaging ; clinical case study ; qualitative study ; treatment outcome

Clinical Trials.gov searched on August 22, 2016 $

no studies found for:
Recruiting | Dysthymic Disorder | Child | Studies received from 08/22/2011 to 08/22/2016 $

1 study found for:
Active, not recruiting | Dysthymic Disorder | Child | Studies received from 08/22/2011 to $
08/22/2016 $
https://clinicaltrials.gov/ct2/show/NCT02423733?recr=Active%2C+not+recruiting&cond=Dysthy $
mic+Disorder&age=0&rcv_s=08%2F22%2F2011&rcv_e=08%2F22%2F2016&rank=1 $

5 studies found for: $
Completed | Dysthymic Disorder | Child | Studies received from 08/22/2011 to 08/22/2016 $
https://clinicaltrials.gov/ct2/results?term=&recr=Completed&type=&rslt=&age_v=&age=0&gndr= $
&cond=Dysthymic+Disorder&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2= $
&cntry2=&state3=&cntry3=&locn=&rcv_s=08%2F22%2F2011&rcv_e=08%2F22%2F2016&lup_s $
=&lup_e=