Effective Health Care

Depressive Disorders in Children and Adolescents

Results of Topic Selection Process & Next Steps

The nominator, AACAP is interested in using a new systematic review on childhood depression to inform an update of their clinical practice guideline.

This topic will go forward as a new systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase. When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to https://effectivehealthcare.ahrq.gov/email-updates.

Topic Brief

Topic Name: Depressive Disorders in Children and Adolescents, #679

Nomination Date: 8/16/2017

Topic Brief Date: October 19, 2017

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Conflict of Interest: The author does not have any affiliations or financial involvement that conflicts with the material in this report

Findings:

- This topic is a re-nomination by a stakeholder
- This nomination fulfilled all selection criteria
- Although the evidence base may be small for pervasive depressive disorder and difficult to disentangle from major depression, the topic is of great interest by a stakeholder group, thus the entire scope (major depressive disorder and pervasive depressive disorder) should be included

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Background

Approximately 1 in 10 adolescents aged 13-18 has either a major depressive disorder or dysthymic disorder.[1] Depressive disorders negatively impact social[2] and academic outcomes,[3] and are associated with poor long-term outcomes and increased risk of suicide.[4] Some believe that persistent depressive disorder (PDD), or dysthymia, is important to diagnose and manage for children and adolescents since the consequences of PDD are increasingly recognized as grave; and can include severe functional impairment, increased morbidity from physical disease, and increased risk of suicide. 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 care,[7] and outline steps for treating children and adolescents with acute mental health and behavioral problems presenting in EDs.[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.

AACAP is interested in using a systematic review process to inform an update of their 2007 American Academy of Child & Adolescent Psychiatry (AACAP) practice parameters[7] on depressive disorders in children and adolescents. This topic was nominated initially in June 2016. Due to limited resources AHRQ was unable to move forward with a systematic review. Due to continued to interest, AACAP has re-nominated this topic for consideration. The assessment of the previous nomination was used to inform this one.

Nominator and Stakeholder Engagement: AACAP was consulted because of the broad scope of the nomination. After input on their priorities and reviewing the results of the previous nomination assessment, this nomination was narrowed to focus on pharmacologic and nonpharmacologic treatment of depression, including dysthymia.

The key questions are:

Key Question 1. 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 2. 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.)?

Table 1. Key Questions and PICOs

	KQ1	KQ2
Key Question	1. 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.)?	2. 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.)?

	KQ1	KQ2
Population	Children and adolescents <18 years old with major depressive or persistent depressive (dysthymic) disorders	Children and adolescents <18 years old with major depressive or persistent depressive (dysthymic) disorders
Intervention	Any non-pharmacological treatment (eg, psychotherapy, CBT, online CBT, self-help, etc)	Any pharmacological treatment (eg, second generation antidepressants, tricyclic antidepressants)
Comparator	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	Depressive symptoms, adverse events	Depressive symptoms, adverse events

Methods

We assessed the nomination for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria (Appendix A). Assessment of each criteria determined the need for evaluation of the next one.

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.

Desirability of New Review/Duplication

We updated the search for high-quality, completed or in-process evidence reviews published since the previous assessment (June 1, 2016 to October 18, 2017). See Appendix B for sources searched.

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We used the literature search from the previous assessment, and did not update the search.

Value

We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.

Compilation of Findings
We constructed a table with the selection criteria and our assessments (Appendix A).

Results

Appropriateness and Importance
This is an appropriate and important topic. Depressive disorders are projected to be the second most important cause of loss of disability-adjusted life years by the year 2020

Desirability of New Review/Duplication
A new evidence review would not be duplicative of an existing product. While the update search identified additional reviews, they collectively did not cover the scope of the nomination. See Table 2, Duplication column.

Impact of a New Evidence Review
A new systematic review may have high impact. There is uncertainty around the best treatment and combination of treatments for children and adolescents, especially in those with comorbid conditions.

Feasibility of a New Evidence Review
A new evidence review is feasible. The previous assessment projected a large evidence base. See Table 2, Feasibility column.

Table 2. Key Questions and Results of Duplication Search and Feasibility Search

Key Question	Duplication (Completed or In-Process Evidence Reviews) with updated search	Feasibility (Published and Ongoing Research) Not updated
KQ 1: Non-pharmacological treatment	Total number of completed or in-progress systematic reviews: 7 • AHRQ: 1[10] • Cochrane- 1[11] • Other- 2[12,13] • In-process (Cochrane)- 1[14] • In-process (Other)- 3[15-17] Updated search: 7 • Cochrane-1 • Other-4 • In-process (other), -2	Size/scope of review Total number of identified published studies: 1 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and PDD) + 4 (search for PDD only) • RCTs: 1[18] + 4[19-22] Projected total: 101 + 4 Clinicaltrials.gov Relevant Trials: 7 • Recruiting – 3[23-25] • Active, not recruiting – 1[26] • Complete – 3[27-29]
KQ 1a: Benefits and harms of non-pharmacological treatment by patient subpopulation	Total number of completed or in-progress systematic reviews: 3 • AHRQ: 1[10] • Cochrane- 1[11] • In-process (Cochrane)- 1[14]	Size/scope of review Total number of identified published studies: 1 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and PDD) + 2 (search for PDD only) • RCTs: 1[18] + 2[19,20] Projected total: 202 + 2 Clinicaltrials.gov Relevant Trials: 3 • Recruiting – 3[23-25]

Key Question	Duplication (Completed or In-Process Evidence Reviews) with updated search	Feasibility (Published and Ongoing Research) Not updated
KQ 2: Pharmacological treatment	Total number of completed or in-progress systematic reviews: 8 • AHRQ: 1[10] • Cochrane- 4[9,11,30,31] • Other- 2[12,32] • In-process (other)- 2[16,17] Updated search: 2 • Other-1 • In-process (other)-1	Size/scope of review Total number of identified published studies: 2 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and PDD) + 2 (search for PDD only) • RCTs: 2[18,33] + 2[19,20] Projected total: 202 + 2 Clinicaltrials.gov Relevant Trials: 3 • Recruiting – 3[34-36]
KQ 2a: Benefits and harms of pharmacological treatment by patient subpopulation	Total number of completed or in-progress systematic reviews: 8 • AHRQ: 1[10] • Cochrane- 2[30,31] • Other- 1[32]	Size/scope of review Total number of identified published studies: 2 (overall search; effectiveness for dysthymia and comparative effectiveness for MDD and PDD) + 1 (search for PDD only) • RCTs: 2[18,33] + 1[19] Projected total: 202 + 1 Clinicaltrials.gov Relevant Trials: None identified

Abbreviations: AACAP= American Academy of Child and Adolescent Psychiatry; AHRQ=Agency for Healthcare and Research Quality; KQ=Key Question; MDD= Major Depressive Disorder; Persistent Depressive Disorder; RCT=Randomized Controlled Trial

Value

The potential for value is high. Mental illness, including depression, is a priority for the DHHS and this topic is of interest to multiple groups, including research agencies, healthcare provider and patients. A provider group is interested in using the findings of a systematic review to inform clinical care.

Summary of Findings

- This topic is a re-nomination by a stakeholder group
- This nomination meets all selection criteria.
- Previous reviews covered treatment for MDD, but not PDD, which is a clinically important area.
- Although the evidence base may be small for PDD and difficult to disentangle from major depression, the topic is of great interest by a stakeholder group, thus the entire scope should be considered

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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 has a depressive disorder.
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 pharmacological interventions and non-pharmacological interventions for depressive disorders.
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, 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)	The previous assessment identified seven reviews for KQ1 (2015[13], 2015[14], 2014[11], 2014[12], expected completion April 2016[15], September 2015[16], and August 2014[17]) and eight for KQ2 (2015[32], 2014[11], 2014[12], 2013[30], 2012[9], 2012[31], expected completion September 2015[16], August 2014[17]). Update: We updated the duplication search. Additional reviews did not cover the scope of the nomination.

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)	*Size/scope of the review:* We identified 15 relevant studies (5 for KQ1, 3 for KQ1a, 4 for KQ2, and 3 for KQ2a) from our random sample of 200 studies from the past 5 years. We project there may be a large evidence base
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. Mental illness, including depression, is a priority for the DHHS and this topic is of interest to multiple groups, including research agencies, healthcare provider and patients.
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.

AACAP = American Academy of Child and Adolescent Psychiatry; DHHS = Department of Health and Human Services; KQ = Key Question

Appendix B. Search for Evidence Reviews (Duplication)
Update (June 1, 2016 to October 18, 2017):

Sources Searched

AHRQ: Evidence reports and technology assessments, USPSTF recommendations
VA Products: VA/DoD EBCPG Program
Cochrane Systematic Reviews and Protocols http://www.cochranelibrary.com/
PubMed Health http://www.ncbi.nlm.nih.gov/pubmedhealth/
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
DoPHER (Database of promoting health effectiveness reviews) http://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=9
PsycINFO (Ovid)

Additional systematic reviews

1. Efficacy and Safety of Selective Serotonin Reuptake Inhibitors, Serotonin-Norepinephrine Reuptake Inhibitors, and Placebo for Common Psychiatric Disorders Among Children and Adolescents: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2017 Oct 1;74(10):1011-1020. https://www.ncbi.nlm.nih.gov/pubmed/28854296

2. Evidence Base Update of Psychosocial Treatments for Child and Adolescent Depression. J Clin Child Adolesc Psychol. 2017 Jan-Feb;46(1):11-43. https://www.ncbi.nlm.nih.gov/pubmed/27870579

3. Brief Behavioral Therapy for Pediatric Anxiety and Depression in Primary Care: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Jun 1;74(6):571-578. https://www.ncbi.nlm.nih.gov/pubmed/28423145

4. What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. Am Psychol. 2017 Feb-Mar;72(2):79-117 https://www.ncbi.nlm.nih.gov/pubmed/28221063

5. Psychological therapies for anxiety and depression in children and adolescents with long-term physical conditions Hiran Thabrew , Karolina Stasiak , Sarah E Hetrick , Stephen Wong , Jessica H Huss and Sally N Merry Online Publication Date: January 2017 Cochrane. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012488/full

6. Psychological treatments for depression in pre-adolescent children (12 years and younger): systematic review and meta-analysis of randomised controlled trials. Eur Child Adolesc Psychiatry. Oct 2016. https://www.ncbi.nlm.nih.gov/pubmed/26969618

7. A systematic review of combination antidepressant medication and psychotherapy in children and adolescents with unipolar depression https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=60191

8. A systemic review and meta-analysis of the effectiveness of interpersonal psychotherapy for adolescents with depression. https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=33888