Effective Health Care

Assessment, Treatment, and Prevention of Bipolar Disorder in Children and Adolescents

Results of Topic Selection Process & Next Steps

The nominator, the American Academy of Child & Adolescent Psychiatry (AACAP), is interested in using a rigorously developed systematic review to inform the update of 2007 American Academy of Child & Adolescent Psychiatry (AACAP) practice parameters pertaining to the prevention, assessment, and treatment of bipolar disorders in children and adolescents. 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: Assessment, Treatment, and Prevention of Bipolar Disorder in Children and Adolescents

Topic #: 0678

Nomination Date: 06/03/2016

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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 evidence review on the proposed topic would not be duplicative. We identified six systematic reviews related to key question 5 of the nomination, focused on pharmacologic treatment—four are complete and two are in-process. We did not identify systematic reviews related to the other key questions (KQ 1-4). An AHRQ review (draft currently posted for comment) examines use of first- and second-generation antipsychotics in children and young adults for a variety of conditions including bipolar disorder. Use of risperidone, olanzapine, aripiprazole, lithium, haloperidol, divalproex, anticonvulsants, ziprasidone, and clozapine in children are addressed in other systematic reviews.
- Impact: The nomination has high potential to impact clinical care by addressing uncertainty and knowledge gaps around identification of risk factors for bipolar disorder and prevention of bipolar disorder in children.
- Feasibility: A new evidence review on the proposed topic is feasible.

- *Size/scope of review:* From a random sample of 200 out of 1,398 results, we identified 11 studies and 1 clinical trial for KQ1 (risk factors), 2 published studies and 3 clinical trials for KQ2a (non-pharmacological prevention), 5 published studies and 5 clinical trials for KQ3 (diagnosis and screening), 3 published studies and 5 clinical trials for KQ4 (non-pharmacological interventions), 1 clinical trial for KQ 4a (non-pharmacological interventions by subgroup), 4 published studies and 5 clinical trials for KQ5 (pharmacologic interventions), and 1 clinical trial for KQ 5a (pharmacologic interventions by subgroup). We identified no studies for KQ 2b (pharmacologic prevention). We estimate that the total size of the relevant literature (2011-present) may be approximately 200 studies across key questions (low confidence).
- *ClinicalTrials.gov:* We identified 17 relevant trials on ClinicalTrials.gov.
- *Cochrane RCT filter results:* We identified 23 additional RCTs. One examined diagnostic tools, one examined preventative measures, five examined nonpharmacological treatments, and 16 examined pharmacologic interventions for bipolar spectrum disorder in children and adolescents.

- Value: The potential for value is high, given that AACAP will use a new AHRQ systematic review to update their 2007 practice parameters. AACAP has previously produced evidence-based guidelines.

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Introduction

Bipolar disorder, also known as manic-depressive disorder, is a serious brain illness.[1] It can develop in anyone, and is more prevalent in families with a history of mental illness. While it is usually first diagnosed in the late teens or early adulthood, young children can develop bipolar disorder.

Bipolar disorder is characterized by unusual mood changes known as manic episodes and depressive episodes.[1] According to the National Institute of Mental Health (NIMH), some symptoms may include children and teens experiencing a manic episode may act unusually happy or silly, talk in an erratic fashion, have trouble sleeping and focusing, and engage in risky behavior. At the other end of the spectrum, children and teens having a depressive episode may feel very sad, complain about pain a lot, sleep too little or too much, have little energy and no interest in activities, and think about death and suicide.[1] There are many pharmacological treatments for bipolar depression in children, as well as variations of psychotherapies.

Topic nomination #0678 was received on June 3, 2016. It was nominated by the 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 bipolar disorder?

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

- a. " Non-pharmacological
- b. " Pharmacological

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

Key Question 4. In adolescents and children, what are the benefits and harms and/or comparative benefits and harms of non-pharmacological interventions for bipolar disorder?

- 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/or comparative benefits and harms of pharmacological interventions for bipolar disorder?

- 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 with PICOs

Key Questions	1. In adolescents and children, what are the risk factors associated with the development of bipolar disorders?	2. In adolescents and children, what are the benefits and harms of interventions to prevent bipolar disorders?	3. What is the accuracy and comparative accuracy of diagnostic or screening tools for bipolar disorders in children and adolescents?	4. In adolescents and children, what are the benefits and harms and/or comparative benefits and harms of non-pharmacological interventions for bipolar 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/or comparative benefits and harms of pharmacological interventions for bipolar 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 bipolar disorder	Children and adolescents <18 years old with bipolar disorder
Interventions	Any risk factor (e.g., age, sex, race/ethnicity, family history of bipolar disorders, low socioeconomic status, comorbid mental or physical health disorder)	Any prevention intervention	Any diagnostic or screening tool	Any non-pharmacological treatment	Any pharmacological treatment
Comparators	NA	No intervention, wait list control, attention control, informational materials	Other screening tools	Any comparator (e. g., treatment as usual, wait list control, attention control, informational materials, other non-pharmacological interventions, pharmacological interventions)	Any comparator (e.g., placebo, wait list control, non-pharmacological interventions, other pharmacological interventions)
Outcomes	Diagnosis of bipolar disorders	Reduction in incidence of bipolar disorders	Accuracy (sensitivity, specificity)	Manic/depressive symptoms, adverse events	Manic/depressive symptoms, adverse events

Methods

To assess topic nomination *#0678 Assessment, Treatment, and Prevention of Bipolar Disorder 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 the reviews that were determined to address the key questions.

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 it was hypothetically 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 conducted a literature search in PubMed from July 2011 and July 2016. Because a large number of articles were identified, we reviewed a random sample of 200 abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review. See *Table 2, Feasibility Column, Size/Scope of Review Section* for the citations of included studies. See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov search.

Value

We assessed the nomination for value (see Appendix A). We considered whether or not the topic would inform clinical policy in community and/or clinical settings, and if there was a partner organization that would use this evidence review to influence practice.

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. According to the National Alliance on Mental Illness, approximately 3% of all individuals suffer from bipolar disorder.[2] Important premorbid problems

in childhood and adolescence are common, and the most prevalent and dysfunctional problems are with emotional and behavioral dysregulation, and may lead to increased rates of anxiety, mood, disruptive behavior, and substance abuse disorders.

Desirability of New Review/Duplication
A new evidence review on the proposed topic would not be duplicative. Six systematic reviews were identified related to key question 5 of the nomination—four are complete[3-6] and two are in-process.[7,8] One in-process evidence review is an AHRQ review[7] (draft currently posted for comment), which examines first- and second-generation antipsychotics in children and young adults, with an analysis of second-generation antipsychotics and quetiapine for bipolar disorder. Our search, however, did not find any evidence reviews which met inclusion criteria pertaining to risk factors, preventative interventions, diagnostic screening tools, non-pharmacological interventions, or subgroup analyses for bipolar disorder.

Other pharmacologic interventions covered in the identified evidence reviews include risperidone,[4,5,7] olanzapine,[5,7] aripiprazole,[3-5] lithium,[3,4,8] haloperidol,[3] divalproex,[4] anticonvulsants,[4] ziprasidone,[4] quetiapine,[4-7] and clozapine.[5]

Impact of a New Evidence Review
The nomination has high potential to impact clinical practice related to risk factors and preventing bipolar disorder—two things new areas in AACAP's proposed guideline.

Feasibility of a New Evidence Review
A new systematic review examining treatments for bipolar disorder in children and adolescents is feasible at this time. From a random sample of 200 out of 1,398 PubMed results, we identified 11 studies[9-19] and one clinical trial[20] for KQ1 (risk factors), two published studies[9,21] and three clinical trials[22-24] for KQ2a (non-pharmacological prevention), five published studies[11,25-28] and five clinical trials[20,29-32] for KQ3 (diagnosis and screening), three published studies[21,33,34] and five clinical trials[35-39] for KQ4 (non-pharmacological interventions), one clinical trial[36] for KQ 4a (non-pharmacological interventions stratifying by subgroup), four published studies[33,40-42] and five clinical trials[37,43-46] for KQ5 (pharmacologic interventions), and one clinical trial[45] for KQ5a (pharmacologic interventions stratified by subgroup). We identified no studies or clinical trials for KQ 2b (preventative pharmacology). We estimate that the total size of the relevant literature (2011-present) may be approximately 258 studies across key questions (low confidence).

Some of the non-pharmacologic interventions for prevention of bipolar disorder in children and adolescents are web-based positive parenting and family-focused therapies. The non-pharmacological interventions we identified to treat bipolar disorder were also family-centered therapy, which is indicative of the importance of family and social support in treating this condition in children and adolescents. There are several clinical trials studying the ability to and efficacy of retraining the brain of a child with bipolar disorder in order to alleviate symptoms.

The studies we identified that examined pharmacologic treatments included a wide-variety of treatments, most of which are also being examined by an in-process AHRQ review.[7] Some of the most popularly studied pharmacologic options in the identified studies include quetiapine, risperidone, aripiprazole, lithium, and valproate.

Table 2. Key questions with the identified corresponding evidence reviews and original research

Key Question	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
KQ 1: Risk Factors	Total number of completed or in-progress evidence reviews – None identified.	<u>Size/scope of review</u> Relevant Studies Identified: 11 • RCT - 1[9] • nRCT - 1[10]

Key Question	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
		• Prospective Cohort - 2[11,12] • Retrospective Cohort - 1[13] • Observational - 4[14-17] • Cross-Sectional - 1[18] • Case-Control - 1[19] Projected total: 105 ClinicalTrials.gov Relevant Trials: 1[20] • Enrolling by invitation - 1[20]
KQ 2a: Non-Pharmacological Prevention	Total number of completed or in-progress evidence reviews – None identified.	Size/scope of review Relevant Studies Identified: 2 • RCT - 2[9,21] Projected total: 19 ClinicalTrials.gov Relevant Trials: 3 • Recruiting - 2[22,23] • Completed - 1[24]
KQ 2b: Pharmacological Prevention	Total number of completed or in-progress evidence reviews – None identified.	Size/scope of review Relevant Studies Identified: 0 Projected total: 0 ClinicalTrials.gov Relevant Trials: 0
KQ 3: Diagnosis and Screening	Total number of completed or in-progress evidence reviews: 1[47] • Meta-Analysis: 1[47]	Size/scope of review • Relevant Studies Identified: 6Prospective Cohort - 1[11] • Retrospective Cohort - 1[25] • Observational - 1[26] • Validity - 1[27] • Descriptive Validity - 1[28] Projected total: 57 ClinicalTrials.gov Relevant Trials: 5 • Enrolling by invitation - 1[20] • Active, not recruiting - 1[29] • Completed - 3[30-32]
KQ 4: Non-pharmacological treatment	Total number of completed or in-progress evidence reviews – None identified.	Size/scope of review Relevant Studies Identified: 3 • RCT - 3[21,33,34] Projected total: 29 ClinicalTrials.gov Relevant Trials: 5 • Recruiting - 3[35-37] • Enrolling by invitation - 1[38] • Completed - 1[39]
KQ 4a: Nonpharmacological Interventions (subgroups)	Total number of completed or in-progress evidence reviews – None identified.	Size/scope of review Relevant Studies Identified: 0 Projected total: 0 ClinicalTrials.gov Relevant Trials: 1

Key Question	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Research)
		• Recruiting - 1[36]
KQ 5: Pharmacological treatment	Total number of completed or in-progress systematic reviews: 7[3-8,48] • AHRQ – 1[7] • Other – 6[3-6,8,48]	Size/scope of review Relevant Studies Identified: 4 • RCT - 2[33,40] • Retrospective Cohort - 1[41] • Open Label - 1[42] Projected total: 48 ClinicalTrials.gov Relevant Trials: 5 • Recruiting - 3[37,43,44] • Active, not recruiting - 1[45] • Completed - 1[46]
KQ 5a: Pharmacological Treatment (subgroups)	Total number of completed or in-progress evidence reviews: 1 • Other: 1[48]	Size/scope of review Relevant Studies Identified: 0 Projected total: 0 ClinicalTrials.gov Relevant Trials: 1 • Active, not recruiting - 1[45]

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; nRCT=non-Randomized Controlled Trial; RCT=Randomized Controlled Trial

Value

The potential for value is high, given that AACAP will use a new AHRQ systematic review to update their 2007 practice parameters. AACAP has previously produced evidence based guidelines.

Summary of Findings

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: A new evidence review on the proposed topic would not be duplicative. We identified six systematic reviews related to key question 5 of the nomination—four are complete and two are in-process. Our search did not find any evidence reviews of risk factors (KQ 1), preventative interventions (KQ 2a and b), diagnostic and screening tools (KQ 3), non-pharmacological interventions (KQ 4), or subgroup analyses for bipolar disorder (KQ 4a and 5a). An AHRQ review (draft currently posted for comment) examines use of first- and second-generation antipsychotics in children and young adults for a variety of conditions including bipolar disorder. Use of risperidone, olanzapine, aripiprazole, lithium, haloperidol, divalproex, anticonvulsants, ziprasidone, and clozapine in children are addressed in other systematic reviews.
- Impact: The nomination has high potential to impact clinical care in addressing uncertainty about risk factors and preventing bipolar disorder.
- Feasibility: A new evidence review on the proposed topic is feasible.
    - *Size/scope of review:* A new systematic review examining treatments for bipolar disorder in children and adolescents is feasible at this time. From a random sample of 200 out of 1,398 PubMed results, we identified 11 studies and one clinical trial for KQ1 (risk factors), two published studies and three clinical trials for KQ2a (non-pharmacological prevention), five published studies and five clinical trials for KQ3 (diagnosis and screening), three published studies and five clinical trials for KQ4 (non-pharmacological

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    - *ClinicalTrials.gov:* We identified 17 relevant trials on ClinicalTrials.gov.
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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. AACAP has previously produced evidence-based guidelines.

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Appendices

Appendix A: Selection Criteria Summary (

Appendix CB: 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. AACAP states that between 3-6% of all individuals suffer from bipolar disorder. AACAP also states that important premorbid problems in childhood and adolescence are common, and the most prevalent and dysfunctional problems are with emotional and behavioral dysregulation, and may lead to increased rates of anxiety, mood, disruptive behavior, and substance abuse disorders.
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 treatments for bipolar disorder.
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 this mental health diagnosis represents high cost due to the high rate of recurrence. AACAP states that approximately one-third of patients remain symptomatic and functionally impaired between episodes.
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)	Six systematic reviews were identified related to the key questions of the nomination—four are complete[3-6] and two are in-process.[7,8] All six pertain to pharmacologic treatments for bipolar disorder (KQ 5). One in-process evidence review is an AHRQ review[7] (draft currently posted for comment), which examines first- and second-generation antipsychotics in children and young adults, with an analysis of second-generation antipsychotics and quetiapine for bipolar disorder. Other pharmacologic interventions covered in the identified evidence reviews include risperidone,[4,5,7] olanzapine,[5,7]

	aripiprazole,[3-5] lithium,[3,4,8] haloperidol,[3] divalproex,[4] anticonvulsants,[4] ziprasidone,[4] quetiapine,[4-7] and clozapine.[5] Our search did not find any evidence reviews which met inclusion criteria pertaining to risk factors, preventative interventions, diagnostic screening tools, non-pharmacological interventions, or subgroup analyses for bipolar disorder.
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 conflicting data and recommendations among authors and experts.
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 conflicting data and existing recommendations.
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 review:* From a random sample of 200 out of 1,398 results, we identified 11 studies and 1 clinical trial for KQ1 (risk factors), 2 published studies and 3 clinical trials for KQ2 (prevention), 6 published studies and 5 clinical trials for KQ3 (diagnosis and screening), 4 published studies and 5 clinical trials for KQ4 (non-pharmacological interventions), and 6 published studies and 5 clinical trials for KQ5 (pharmacologic interventions). We estimate that the total size of the relevant literature (2011-present) may be approximately 293 studies across key questions (low confidence). *ClinicalTrials.gov:* We identified 17 relevant trials on ClinicalTrials.gov.
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 bipolar disorder 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 bipolar disorder among children and adolescents.

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

Appendix B. Search Strategy & Results (Feasibility)

Topic: Bipolar in Children and Adolescents Date: June 10th, 2016 Database Searched: PubMed	
Concept	**Search String**
Bipolar Disorder	("Bipolar Disorder"[Mesh]) OR ((bipolar[Title] OR manic[Title] OR mania[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 Human English kids	Filters activated: published in the last 5 years, Humans, English, Child: birth-18 years.
N=1398	
Systematic Review **N=72**	PubMed subsection "Systematic [sb]"
Randomized Controlled Trials **N=589**	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=737**	

Topic: Bipolar in Children and Adolescents Date: June 10th, 2016 Database Searched: PsycINFO (Ovid) 1806 to June Week 2 2016	
Concept	**Search String**
Bipolar Disorder	1 exp BIPOLAR DISORDER/ 2 (bipolar or manic or mania).m_titl. 3 1 or 2
Children and Adolescents	4 limit 3 to (100 childhood <birth to age 12 yrs> or 200 adolescence <age 13 to 17 yrs>)
Not Editorials, etc.	5 limit 4 to ("column/opinion" or "comment/reply" or editorial or letter or review-book) 6 4 not 5
Limit to last 5 years Human English	7 limit 6 to (english and human and last 5 years)
N=809	
Systematic Review **N=19**	8 limit 7 to ("0830 systematic review" or 1200 meta analysis)
Randomized Controlled Trials **N=47**	9 7 not 8 10 limit 9 to "2000 treatment outcome/clinical trial"
Other **N=743**	11 9 not 10

ClinicalTrials.gov Searched on 06/10/2016
84 studies found for: Bipolar Disorder | Child | received from 06/10/2011 to 06/10/2016
Link to results:
https://clinicaltrials.gov/ct2/results?term=&recr=&rslt=&type=&cond=Bipolar+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=