Bipolar Disorder and Antipsychotic Use in Children, Adolescents, and Young Adults
Workgroup Meeting Summary

February 2014

Overview

On December 20, 2013, PCORI’s Clinical Effectiveness Research program convened a workgroup in Washington, DC, to gain a multifaceted perspective on potential research topics addressing bipolar disorder and antipsychotic use in children, adolescents, and young adults.

The workgroup included patients, clinicians, researchers, and other stakeholders. Workgroup members provided feedback on a set of research questions and identified other research topics for PCORI to consider.

The workgroup participants provided feedback on research questions that PCORI had previously identified and offered ideas for other comparative effectiveness research topics. The workgroup then refined a list of research questions.

The participants reached consensus on the following high-priority topics:

- Diagnostic uncertainty for bipolar disorder in children, adolescents, and young adults
- Adverse effects of long-term medication exposure between and within classes of antipsychotic drugs
- Treatment of symptoms of bipolar disorder (especially depression)
- Comparative safety and effectiveness of different treatment strategies or algorithms for patients presenting with symptoms of bipolar disorder, focusing in particular on the maintenance phase of therapy.

Related Information

- List of Participants
- Participant Biographies
- September 2013 Advisory Panel Meeting
- April 2013 Advisory Panel Meeting

The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed healthcare decisions.

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Background

PCORI identified the topic “Bipolar Disorder and Antipsychotic Use in Children, Adolescents, and Young Adults” through a process in which patients and other healthcare stakeholders suggested research topics. The source of that concern is a rapid increase in use of second-generation antipsychotic medications in children. 1

In April 2013, PCORI’s Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options reviewed topics and assigned a high priority to “Bipolar Disorder and Antipsychotic Use in Adolescents and Young Adults.” In response, PCORI commissioned the Duke Evidence Synthesis Group to review evidence to identify research gaps in bipolar disorder. The advisory panel considered the resulting report at its meeting in September 2013 and identified several high-priority research questions.

PCORI then convened a workgroup to help identify research gaps and questions in this area. The workgroup participants 2 represent diverse perspectives, including clinicians, researchers, patients, other stakeholders, Staff from PCORI’s Science and Engagement teams also participated.

Discussion

The workgroup met on December 20, 2013, in Washington, DC, and was moderated by Dr. Ronald Means of Catholic Charities of Maryland and a member of the PCORI Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options. To set the stage for the discussion, Dr. Diane Bild of PCORI provided background information on the use of antipsychotics in children. She reported that approximately 14 to 20 percent of children and adolescents have a diagnosable mental illness 3 and that psychotropic medications are increasingly prescribed to children. 4 She also noted that other agencies, such as AHRQ 5, have proposed research in this area.

In preparation for the meeting, workgroup participants had provided feedback on PCORI’s proposed research questions and offered ideas for other comparative effectiveness research topics. The workgroup discussed the feedback and new ideas and refined and prioritized the list of research questions.

2 Available at pcori.org/assets/2014/01/PCORI-Bipolar-Workgroup-Participants-122013.pdf
5 Available at effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports

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To assign priorities, the workgroup emphasized the following considerations:

- Inclusion of children (ages 6 to 12 years).
- Both functional and symptomatic outcomes, including social, academic, and occupational functioning, as well as psychiatric symptoms. The group noted that:
  - Long-term outcomes (e.g., after at least two years) have been particularly understudied.
  - Outcomes should consider attainment of developmental milestones and symptom recurrence.
- Side effects of medication, particularly weight gain and development of metabolic syndrome with antipsychotic medication.
- Risk of substance abuse, imprisonment, and other mental health issues, including anxiety and attention deficit hyperactivity disorder.
- Whether to continue medications after the acute phase of the disorder, what medications to use at that time, and whether and how to discontinue medications.
- Non-pharmacologic approaches (which are of particular interest to patients and their families).
- Transitions in care and lack of care continuity. For example, recurrence of symptoms and disintegration of functioning as children move from pediatric to adult practices into college-based health clinics.

**Action**

The group agreed on the following high-priority research topics:

- Diagnostic uncertainty for bipolar disorder in children, adolescents, and young adults
  - Patients present with symptoms, not diagnoses, and mental illness presents as a spectrum of disorders.
  - A comparative effectiveness research question might include treatment based on full DSM criteria versus other symptom-based criteria.
- Adverse effects of long-term medication exposure between and within classes of antipsychotic drugs
- Treatment of symptoms of bipolar disorder (especially depression)
- The comparative safety (including side effects) and effectiveness of the different treatment strategies or algorithms for patients presenting with symptoms of bipolar disorder, focusing in particular on the maintenance phase of therapy. Strategies to be considered include:
  - Medications used alone or in combinations
  - Non-pharmacologic interventions (e.g., psychotherapy/counseling, peer and family support, supported employment, diet and physical activity interventions, assertive community treatment, and psychoeducational management)
  - Management strategies, such as targeted case management
  - Consideration of the timing of treatment (e.g., age at initiation)
Although the workgroup placed less emphasis on adjunct therapy, such as antidepressants, anxiolytics, and stimulants, it stated these could be part of a treatment algorithm. The group noted that the study of comparative safety and effectiveness of treatment depends on demographics (particularly race/ethnicity), as well as the patients’ symptoms (e.g., symptoms consistent with bipolar I, II, or not otherwise specified). Finally, the workgroup agreed that comparative effects of antipsychotics on core disease features (i.e., symptoms specific to bipolar disorder, such as grandiosity) versus nonspecific symptoms, such as irritability, is less important than the outcomes discussed above.

**Next Steps**

These recommendations will be presented to the PCORI Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options on January 14, 2014.