



Effective Health Care

Side Effects of Antidepressants in Adolescents Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Benefits and harms of antidepressants in adolescent low socioeconomic status and racial/ethnic groups could potentially be considered for new research in comparative effectiveness.

Topic Description

Nominator: Individual

Nomination Summary: The nominator would like to see a review of the evidence that compares side effects of psychotropic medications (antidepressants) for depression in white Caucasian adolescents versus ethnic minorities. They specifically mention a need for scientific analysis of various ethnic backgrounds involved in trials as well as scientific inquiry into the various chemistry differences among ethnic populations.

Staff-Generated PICO:

Population(s): Adolescents aged 12-17 years who are of low socioeconomic status (defined by eligibility for free school lunch program), diagnosed with depression, prescribed antidepressants, and compliant with medication and therapy

Intervention(s): Treatment with antidepressants for depression

Comparator(s): White Caucasian adolescents versus ethnic minority adolescents

Outcome(s): Side effects of antidepressants

Key Questions from Nominator: 1. What are the comparative side effects of antidepressant medications on low socio-economic ethnic/racial minority adolescents versus white low socio-economic adolescents?

Considerations

- The topic meets EHC Program appropriateness and importance criteria. (For more information, see [http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.](http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/))
- The general topic of antidepressants in adolescents is addressed by the following existing and in-process reviews:

- A 2009 AHRQ EPC Program review conducted for the US Preventive Services Task Force titled *Screening for Child and Adolescent Depression in Primary Care Settings* evaluated treatment outcomes and adverse effects of selective serotonin reuptake inhibitors (SSRIs) in children and adolescents <http://www.uspreventiveservicestaskforce.org/uspstf09/depression/chdepres.pdf>. Key questions from the review include:
 1. Does screening for depression among children and adolescents in the primary care setting improve health outcomes?
 - a. Does screening increase the proportion of patients identified with and/or treated for depression?
 2. Are depression screening instruments for children and adolescents accurate in identifying depression in primary care or school-based clinics?
 3. What are the harms of screening?
 4. Does treatment of depression (SSRIs and/or psychotherapy) among screen-detected children and adolescents identified in primary care or comparable populations improve health outcomes?
 5. What are the adverse effects of treatment?

- The AHRQ EHC program is conducting a review titled *Depression Treatment after Unsatisfactory Response to SSRIs when used as First-line Therapy* that will include a review of the adolescent population (12-18 years). This review will look at harms and subpopulations by race. Draft key questions include:
 1. Among adults and adolescents with Major Depressive Disorder (MDD), Dysthymia, and Subsyndromal Depression, who are started on an SSRI and who are compliant with treatment but fail to improve either fully, partially, or have no response, what is the benefit (efficacy or effectiveness) of monotherapy and combined therapy?
 2. What are the harms of each of the monotherapy or combined therapies among these adults and adolescents? How do the harms compare across different interventions?
 3. How do these therapies compare in different populations (for example, different depressive diagnoses, disease severity, ages, gender, racial and socioeconomic group, and medical or psychiatric co-morbidities)? These subgroups will be considered with respect to the different interventions.
 4. How does the efficacy/effectiveness vary between the different monotherapies and combined therapies?
 5. What is the range of recommended clinical actions following the failure of one adequate course of SSRI based on current (< 5 years) clinical practice guidelines (CPGs)?
 - To view a description and status of the research review, please go to: <http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/>
 - To sign up for notification when this and other EHC Program topics are posted, please go to <http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/>

- The Drug Effectiveness Review Project (DERP) has a 2011 publically available drug class review on second-generation antidepressants that included a review of the pediatric literature with an evaluation of benefits and harms. Available at http://derp.ohsu.edu/final/Antidepressants_final_report_update%205_MAR_11.pdf. Key questions include:

1. For outpatients with depressive, anxiety, and/or premenstrual dysphoric disorders, do second-generation antidepressants differ in efficacy or effectiveness?
2. For outpatients with depressive, anxiety, and/or premenstrual dysphoric disorders, do second-generation antidepressants differ in safety or adverse events?
3. Are there subgroups of patients based on demographics (age, racial groups, and sex), other medications, or comorbidities for which one second-generation antidepressant is more effective or associated with fewer adverse events than another?

Importance of New Research

- Adolescent depression is an important topic, and racial differences exist in the prevalence of disease and treatment. Additionally, minority status participants are underrepresented in trials of depression treatment. The nominator is interested in whether low socioeconomic and racial/ethnic minority status groups have greater potential harms from antidepressant use compared to other groups. A scan of the literature identified very few studies that include analysis of patient outcomes by race or ethnicity. It remains unclear whether race/ethnicity impacts treatment effects in terms of both benefits and harms, and new research is needed in order to bring clarity to this question.

Research Gaps

- Recent professional society clinical guidelines on major depression treatment recognize that ethnic groups may differ in their metabolism and response to medications but offer no specific treatment recommendations for these groups.
- No existing or in-process clinical trials were identified that aimed to look at the comparative benefits and harms of antidepressants among various racial/ethnic minority adolescent groups. Existing studies that have performed a subgroup analysis by race/ethnicity have found mixed results and are very limited. Outcomes reported in these few studies include:
 - Rate of positive treatment response by race/ethnicity in terms of whites versus nonwhites
 - Race/ethnicity as a potential predictor of earlier time to onset of suicidal event
 - Race/ethnicity as a potential predictor of variation in treatment and treatment improvement
 - Race/ethnicity as a potential predictor of remission status
 - Incidence of suicidal events by race/ethnicity