Effective Health Care

Treatment of Major Depression After Initial Trial of Pharmacotherapy Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Treatment of major depression after an initial trial of pharmacotherapy was found to be addressed by an in-process AHRQ Effective Health Care (EHC) program comparative effectiveness review, an update to an existing EHC program comparative effectiveness review and an ongoing AHRQ DEcIDE Network research project. Given that the in-process reports and new research project cover this nomination, no further activity will be undertaken on this topic.
  - In-process Comparative Effectiveness of Treatment for Depression after Unsatisfactory Response to SSRIs as First-line Therapy. To see draft key questions, please go to http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displaytopic&topicid=156&search=SSRI%20fail.
  - In- process Comparative Effectiveness of Off-Label Use of Atypical Antipsychotics – Update. To see draft key questions, please go to http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displaytopic&topicid=150&search=atypical.

    This report will update an earlier comparative effectiveness research review titled "Comparative Effectiveness of Off-label Use of Atypical Antipsychotics." To read the earlier report and review associated products, please visit: http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=64.
  - In-process Original Research, Addressing Knowledge Gaps in the Treatment of Depression. To see the abstract and draft key questions, please go to http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=293.
- To sign up for notification when this and other EHC program and DEcIDE Network topics are posted, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominator: Individual

Nomination Summary: This nominator proposes new research in the form of a prospective cohort study looking at patients with major depression who do not have full treatment cure at 12 months of pharmacotherapy. In particular, he mentions the use of Selective Serotonin Reuptake Inhibitors (SSRIs) for an approximate 12-month duration. He would like to study the comparative effectiveness and cost effectiveness of different adjuvant pharmacotherapy

for these "non-responders" at this 12 month mark.

Population(s): Adults (>18 years) on SSRI medications for approximately 12 months with chronic major depressive disorder
Intervention(s): Standard of care pharmacotherapy for major depression (e.g., SSRI)
Comparator(s): Adjuvant therapies such as atypical antipsychotics, buproprion, mood stabilizers, and other medications that are used in combination with SSRIs
Outcome(s): Remission rates, cost, health care utilization, and patient outcomes
Timing: Approximately 12 months after initial pharmacotherapy

Key Questions from Nominator: None

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/.)

- Recent research has established that not all patients respond to current first-line monotherapy for depression, and that a significant proportion of patients treated for depression will become treatment resistant. For patients who continue to experience depressive symptoms despite an optimal antidepressant trial, multiple pharmacologic strategies have been described; however, evidence is limited to determine the optimal strategy for a given patient. Inadequately treated depression is associated with higher rates of relapse, poorer quality of life, harmful personal and societal economic outcomes, as well as increased mortality rates.

- Three in-process AHRQ products aim to review existing literature and address knowledge gaps surrounding some of the uncertainty described above.

- The topic is mainly addressed by an in-process AHRQ comparative effectiveness review titled *Comparative Effectiveness of Treatment for Depression after Unsatisfactory Response to SSRIs as First-line Therapy*. Draft key questions from this report include:
  1. Among adults and adolescents with major depressive disorder (MDD), dysthymia, and subsyndromal depression, who are started on a selective serotonin reuptake inhibitor (SSRI) for the index episode and who are adherent but fail to improve either fully, partially, or have no response, what is the benefit (efficacy or effectiveness) of:

     Monotherapy:
     - Changing the dose or duration of the same SSRI.
     - Changing from one SSRI to another SSRI.
     - Changing from an SSRI to another class of antidepressant.
     - Changing from an SSRI to a non-pharmacologic therapy.

     Combined therapy:
     - Adjunct therapy: augmentation by adding an adjunct drug (or supplement) that is meant to improve the response but has no formal indication for use for unipolar depression.
     - Adjunct therapy: adding another antidepressant (an SSRI or other class of antidepressant)

- Adjunct therapy: adding a non-pharmacological therapy
- Combinations of any of the interventions listed above or any other intervention

2. What are the harms of each of the monotherapies 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 (e.g., 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 an SSRI based on current (< 5 years) clinical practice guidelines (CPG)?

- The topic is also addressed by an in-process AHRQ comparative effectiveness review update titled *Comparative Effectiveness of Off-Label Use of Atypical Antipsychotics.* Draft key questions from this report include:
  1. What are the leading off-label uses of atypical antipsychotics in the literature? How have trends in utilization changed in recent years, including inpatient versus outpatient use? What new uses are being studied in trials?
  2. What does the evidence show regarding the efficacy and comparative effectiveness of atypical antipsychotics for off-label indications, such as depression?
  a) How do atypical antipsychotic medications compare with other drugs, including first generation antipsychotics, for treating off-label indications?
  3. What subset of the population would potentially benefit from off-label uses? Do effectiveness and harms differ by race/ethnicity, gender, and age group? By severity of condition and clinical subtype?
  4. What are the potential adverse effects and/or complications involved with off-label prescribing of atypical antipsychotics? How do they compare within the class and with other drugs used for the conditions?
  5. What is the effective dose and time limit for off-label indications?

- The topic is also addressed by an in-process DEcIDE Network original research project titled *Addressing Knowledge Gaps in the Treatment of Depression.* Draft key questions from this project include:
  1. Are outcomes better following a medication switch compared with augmentation with a second medication?
  2. Do the incidence and tolerability of specific adverse events differ following specific SGA monotherapy or combinations?
  3. Does health care utilization differ following specific SGA monotherapy or antidepressant combinations?
  4. Does the presence of accompanying symptom clusters differentiate the comparative effectiveness of SGAs for treating depression?