



Effective Health Care

Treatments for Adults with Schizophrenia

Nomination Summary Document

Results of Topic Selection Process & Next Steps

- This topic will go forward for refinement by the EPC in preparation for assignment as a new systematic review.
 - 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 <http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/>.
 - Abou-Setta AM, Mousavi SS, Spooner C, Schouten JR, Pasichnyk D, Armijo-Olivo S, Beath A, Seida JC, Dursun S, Newton AS, Hartling L. First-generation versus second-generation antipsychotics in adults: comparative effectiveness. Rockville: Agency for Healthcare Research and Quality (AHRQ). Comparative Effectiveness Review No. 63. 2012.

Topic Description

Nominator(s): Health care professional association

Nomination Summary: According to the nominator, an up-to-date evidence-based review of the efficacy and comparative effectiveness of treatments for schizophrenia would inform development of clinical practice guidelines aimed at optimizing clinical interventions and patient outcomes for individuals with schizophrenia. The most recent American Psychiatric Association (APA) practice guideline on this topic was published in 2004 with an updated discussion of subsequent literature in 2009. A substantial body of literature has been published since that time. The nominator anticipates that an AHRQ review would result in modifications to the APA 2009 guideline recommendations that could consequently improve care for patients.

Staff-Generated PICOs

Key Question #1

- Population(s):** Male and female adults with schizophrenia or schizophrenia-related psychoses, with and without co-occurring disorders
- Intervention(s):** Any commercially available Food and Drug Administration (FDA)-approved antipsychotic
- Comparator(s):** Any commercially available FDA-approved antipsychotic; all other treatment options/variations (e.g., different dosage of the same antipsychotic)
- Outcome(s):** Social, occupational and functioning improvements; improvements

in health-related quality of life; reductions in hospitalizations; reductions in self-harm, including suicide and suicide attempts; reductions in agitation or aggressive behaviors; changes in the status of co-occurring disorders; ability to live independently; harms of treatments (e.g., diabetes mellitus, extrapyramidal symptoms); improvements in core illness symptoms (e.g., delusions, hallucinations)

Key Question #2

- Population(s):** Male and female adults with schizophrenia or schizophrenia-related psychoses, with and without co-occurring disorders
- Intervention(s):** Non-pharmacological treatments
- Comparator(s):** Non-pharmacological treatments; all other treatment options/variations (e.g., different dosage of the same non-pharmacological treatment)
- Outcome(s):** Social, occupational and functioning improvements; improvements in health-related quality of life; reductions in hospitalizations; reductions in self-harm, including suicide and suicide attempts; reductions in agitation or aggressive behaviors; changes in the status of co-occurring disorders; ability to live independently; harms of treatments (e.g., increased agitation and aggression); improvements in core illness symptoms (e.g., delusions, hallucinations)

Key Question #3

- Population(s):** Male and female adults with schizophrenia or schizophrenia-related psychoses, with and without co-occurring disorders
- Intervention(s):** Treatments to manage the side effects (e.g., weight gain, diabetes mellitus, extrapyramidal symptoms) of treatments for schizophrenia
- Comparator(s):** All other treatment options/variations (e.g., different dosage of the same antipsychotic)
- Outcome(s):** Harms of treatments used to manage side effects; reductions in the experience of side effects with a given treatment

Key Questions from Nominator:

1. What are the comparative benefits and harms of pharmacological treatments for adults with schizophrenia?
 - What patient characteristics (e.g., age, sex, race, ethnicity, socioeconomic status, time since illness onset, prior treatment history, co-occurring disorders) predict the benefits and harms of pharmacological treatments for adults with schizophrenia?
2. What are the comparative benefits and harms of non-pharmacological treatments for adults with schizophrenia?
 - What patient characteristics (e.g., age, sex, race, ethnicity, socioeconomic status, time since illness onset, prior treatment history, co-occurring disorders) predict the benefits and harms of non-pharmacological treatments for adults with schizophrenia?
3. What is the comparative effectiveness of treatments to manage the side effects of

Considerations

- Schizophrenia is a brain disorder in which people interpret reality abnormally; it typically results in hallucinations, delusions, and extremely disordered thinking and behavior. Signs and symptoms may vary, but usually impair a person's ability to function substantially.
- According to the Centers for Disease Control and Prevention, worldwide prevalence estimates for schizophrenia range between 0.5% and 1%. Although the exact cause of the disorder remains unknown, experts attribute schizophrenia to a combination of factors, including genetics and/or brain chemistry and structure.
- Currently, there is no cure for schizophrenia and therefore treatments, including pharmacological (e.g., antipsychotics) and non-pharmacological treatments (e.g., psychotherapy, electroconvulsive therapy). These therapies focus on eliminating the symptoms of the disease, and improving patient functioning and quality of life.
- Common adverse effects of many antipsychotics used for schizophrenia include: weight gain, diabetes mellitus, extrapyramidal symptoms (EPS; a set of side effects associated with antipsychotic medications, such as Parkinsonism, akathisia, dystonia, and tardive dyskinesia), prolactin elevation, sedation, anti-cholinergic side effects, orthostatic hypotension, and QTc prolongation. Common non-pharmacological interventions for adult schizophrenia include psychotherapy, multicomponent programs (e.g., Antipsychotic Treatment Improvement Program [ATIP]), and somatic therapies such as electroconvulsive therapy, or transcranial magnetic stimulation.
- The treatment success rate with antipsychotic medications and psychosocial therapies can be high. Patient characteristics (e.g., age, sex, race, ethnicity, socioeconomic status, time since illness onset, prior treatment history, co-occurring disorders) may predict treatment effectiveness as well as the side effects associated with treatments for adults with schizophrenia.
- Concerning pharmacological treatments, a scan of the literature identified an evidence-based 2012 AHRQ review that compares first-generation antipsychotics (FGAs) with second-generation antipsychotics (SGAs) in adults with schizophrenia, schizophrenia-related psychoses, or bipolar disorder, with a focus on core illness symptoms, functional outcomes, health care system utilization, and adverse events. Since the publication of this review, there have been eight recent Cochrane systematic reviews published, though they are not comprehensive. We also identified more than 600 potentially-relevant randomized controlled trials (RCTs) and more than 1,300 ongoing and completed clinical trials. Based on this scan of the literature, there appears to be enough evidence to update the AHRQ systematic review.
- For treatments to manage the side effects of pharmacological treatments for adults with schizophrenia, a scan of the literature found adequate research on treatments to manage antipsychotic-induced weight gain, as well as some limited evidence regarding other conditions and side effects associated with antipsychotic medication (e.g., diabetes mellitus, extrapyramidal symptoms / tardive dyskinesia, prolactin elevation, sedation, anti-cholinergic side effects, orthostatic hypotension, QTc prolongation). The scan also identified two relevant Cochrane systematic reviews (both on tardive dyskinesia), almost 100 potentially-relevant RCTs (the majority focused on antipsychotic-related weight gain) and nearly 80 ongoing and completed clinical trials. Based on the results of the scan an AHRQ systematic review that comprehensively examines the available evidence appears to be feasible at this time.

- For non-pharmacological treatments for adults with schizophrenia, a scan of the literature identified a large body of relevant evidence, including four recent Cochrane systematic reviews, more than 500 potentially-relevant RCTs, and more than 300 ongoing and completed clinical trials. However, the scan did not locate any comprehensive products that synthesized the comparative effectiveness of various non-pharmacological treatments (as most examined one treatment compared to placebo or different dosages of the same non-pharmacological treatment). Given the available evidence and absence of existing comprehensive systematic reviews on this topic, an AHRQ systematic review appears to be feasible at this time.