



Topic Brief: Treatment Resistant Psychosis

Date: 12/9/2020

Nomination Number: 0914

Purpose: This document summarizes the information addressing a nomination submitted on June 27, 2020 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: The nominator recommends that research on effective pharmaceutical interventions targeting the dopaminergic system in schizophrenic patients be conducted.

Program Decision: The EPC Program will not develop a new evidence synthesis product because the nominator is requesting that primary research be conducted to develop a new treatment, which is outside of the scope of the program.

Background

Schizophrenia is a mental disorder that causes disruptions in thought processes, perceptions, emotional responsiveness and social interactions.¹ It is one of the top 20 causes of disability worldwide.² Mortality rates in individuals with schizophrenia are two to three times higher than those in the general population³, and financial costs associated with the condition are high due to indirect costs related to lost productivity, criminal justice involvement, and social service needs, for example.⁴

Schizophrenia involves abnormalities associated with the neurotransmitter dopamine, and antipsychotic medications target activity of this and other neurotransmitters.⁵ The American Psychiatric Association recommends that individuals with schizophrenia be treated with antipsychotics and continue to be treated with the type of antipsychotic that is associated with improvement for the individual. For individuals with treatment-resistant schizophrenia, they recommend treatment with the antipsychotic clozapine.⁶ Clozapine interacts with the dopaminergic system, binding transiently to dopamine (D2) receptors.⁷ Side effects of clozapine include a risk of seizures.⁸

Assessment Methods

We assessed nomination for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one.

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.

References

1. Mental Health Information, Schizophrenia. National Institute of Mental Health. doi: <https://www.nimh.nih.gov/health/statistics/schizophrenia.shtml>.
 2. James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*. 2018;392(10159):1789-858. doi: [https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7).
 3. Auquier P, Lançon C, Rouillon F, et al. Mortality in schizophrenia. *Pharmacoepidemiol Drug Saf*. 2007 Dec;16(12):1308-12. doi: <https://doi.org/10.1002/pds.1496>. PMID: 17944000.
 4. Desai PR, Lawson KA, Barner JC, et al. Estimating the direct and indirect costs for community-dwelling patients with schizophrenia. *Journal of Pharmaceutical Health Services Research*. 2013;4(4):187-94. doi: <https://doi.org/10.1111/jphs.12027>.
 5. Brisch R, Saniotis A, Wolf R, et al. The role of dopamine in schizophrenia from a neurobiological and evolutionary perspective: old fashioned, but still in vogue. *Frontiers in psychiatry*. 2014;5:47-. doi: <https://doi.org/10.3389/fpsy.2014.00047>. PMID: 24904434.
 6. Practice Guideline for the Treatment of Patients With Schizophrenia. The American Psychiatric Association. 2021; Third Edition. doi: <https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841>.
 7. Seeman P. Clozapine, a fast-off-D2 antipsychotic. *ACS chemical neuroscience*. 2014;5(1):24-9. doi: <https://doi.org/10.1021/cn400189s>. PMID: 24219174.
 8. Williams AM, Park SH. Seizure Associated with Clozapine: Incidence, Etiology, and Management. *CNS Drugs*. 2015 2015/02/01;29(2):101-11. doi: <https://doi.org/10.1007/s40263-014-0222-y>.
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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.

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