

Rationale for Clozapine Trial

To the Editor: The article by Andrade¹ regarding clozapine is informative and well-written, but it may do a disservice to patients with schizophrenia, especially in the US, where clozapine is so grossly underutilized and where many psychiatrists, including recently trained residents, have never or rarely used clozapine.²

I don't think anyone would disagree with the idea that very few patients with schizophrenia are "normalized" by antipsychotics (even clozapine); there are almost always residual symptoms, often social or vocational. In my experience (using clozapine even before it was FDA approved, and ever since), clozapine-treated patients are able to get closer to "normality." A patient stabilized on olanzapine or risperidone may be stable enough that a trial on clozapine is not absolutely required, and psychiatrists

may wish to avoid the hassle and risk of prescribing clozapine, but the patient might do better on clozapine; if it's not tried, there's no way to know.

Drug companies making other atypicals are strongly motivated to discourage use of clozapine; they may sometimes exaggerate side effects of competitors.³ The elimination of the Risk Evaluation and Mitigation Strategies (REMS) program, supposedly intended to increase clozapine use, will almost certainly reduce it, given the increased burden on the prescribing psychiatrist. The underutilization of clozapine is a sad example of the power of marketing over rational decision-making. Dr. Andrade, in India, may not be aware of all the relevant issues in the US.

References

1. Andrade C. The superiority of clozapine over second-generation antipsychotics in patients

with treatment-resistant schizophrenia: room for doubt. *J Clin Psychiatry*. 2025;86(3):25f16038.

2. Singh B, Hughes AJ, Roerig JL. Comfort level and barriers to the appropriate use of Clozapine: a Preliminary Survey of US psychiatric residents. *Acad Psychiatry*. 2020;44:53–58.
3. Mattes JA. How does drug company marketing affect physician prescribing? *J Clin Psychopharmacol*. 2025;45(4):305–309.

Jeffrey A. Mattes, MD

Scan Now



Cite and Share
this article at
[Psychiatrist.com](https://www.psychiatrist.com)

Article Information

Published Online: January 28, 2026.
<https://doi.org/10.4088/JCP.25f16256>
© 2026 Physicians Postgraduate Press, Inc.
J Clin Psychiatry 2026;87(1):25f16256

To Cite: Mattes JA. Rationale for clozapine trial. *J Clin Psychiatry* 2026;87(1):25f16256.

Author Affiliation: Private Practice, Princeton, New Jersey.

Corresponding Author: Jeffrey A. Mattes, MD, 1000 Herrontown Rd, Clock Bldg, 1st Floor, Princeton, NJ 08540 (jmattesmd@verizon.net).

Relevant Financial Relationships: None.

Funding/Support: None.