Irish Journal of Psychological Medicine (2025), **42**, 242–243
doi:10.1017/ipm.2025.5

CAMBRIDGE UNIVERSITY PRESS

Letter to the Editor

Towards optimized clozapine use: comparative reflections from Ireland and India

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Dear Sir,

We read the study by Grant et al with great interest. The Irish study surveyed 275 psychiatrists, of which only 28% completed the survey, with 55% practicing for over 15 years. Although the psychiatrists expressed familiarity with clozapine treatment guidelines, barriers persist due to patient-related concerns, specifically regarding blood monitoring and side effects. Notably, 69% of respondents highlighted patient concerns over clozapine's efficacy, and 50% cited issues with tolerability as common deterrents (Grant *et al.* 2024).

In India, similar barriers to clozapine use exist but are impacted heavily by the decentralized nature of psychiatric services and the socioeconomic diversity within the healthcare infrastructure. An Indian study surveyed 500 psychiatrists, with 117 responses, revealed widespread use of clozapine, particularly in treatment-resistant schizophrenia. Notably, 43% of psychiatrists reported achieving positive outcomes with clozapine, indicating its perceived clinical efficacy. However, unlike in Ireland, clozapine initiation in India often proceeds without centralized blood monitoring services due to resource limitations. Monitoring practices vary, with 80% of psychiatrists performing weekly monitoring in the initial month and monthly thereafter, although adherence declines over time and only 5% continue bi-weekly monitoring post one year (Shrivastava & Shah, 2009). Despite these challenges, the majority of Indian practitioners maintain single-drug therapy with clozapine and report low incidences of severe adverse events (Grover *et al.* 2010, 2015).

Studies from both the countries underscore significant barriers related to patient reticence and logistical complexities in blood monitoring. However, Ireland's system emphasizes the need for dedicated support and the potential for community-based initiation, whereas India adapts clozapine use within a less structured framework, leading to greater variability in monitoring practices. The reliance on gradual, flexible dose initiation in India, where psychiatrists often co-administer lower doses alongside other antipsychotics, contrasts with Ireland's structured guidelines that recommend rigid adherence to monitoring protocols before dose escalation. A critical difference lies in the infrastructural resources: Ireland's emphasis on a centralized, resource-intensive approach contrasts with the more decentralized, physician-dependent model in India. Despite limited resources, Indian psychiatrists exhibit a higher rate of direct initiation of clozapine in various psychiatric conditions beyond schizophrenia, including schizoaffective disorders and psychosis associated with Parkinson's disease. This broad application underscores a pragmatic approach likely driven by the absence of strict regulatory oversight on clozapine use and monitoring.

Recommendations and Future Directions

The Irish study advocates for structural reforms, particularly the development of specialized clozapine services, to improve clozapine accessibility and management in the community. Implementing such models in developing countries like India would be challenging but may benefit from an incremental approach, focusing on expanding monitoring resources and training for healthcare staff. The Irish recommendation for professional development programs is applicable to both contexts, as the Indian study similarly identified knowledge gaps among less-experienced psychiatrists regarding clozapine's adverse effects, such as agranulocytosis and seizure risk.

While both Ireland and India face challenges in optimizing clozapine use, the Indian model illustrates the feasibility of using clozapine flexibly within a decentralized framework, albeit with limitations on monitoring continuity. Conversely, Ireland's emphasis on establishing dedicated resources reflects an advanced, albeit resource-intensive, standard for clozapine management. Future studies may benefit from a focus on patient and caregiver education regarding clozapine's benefits and modifying the monitoring requirements to mitigate concerns that hinder initiation and adherence in both countries. Bridging the structural gaps through shared learning from both systems could foster better outcomes and access to clozapine for those in needs.

Acknowledgement. None.

Financial support. None.

Competing interests. None.

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Cite this article: Grover S and Patil AN. (2025) Towards optimized clozapine use: comparative reflections from Ireland and India. *Irish Journal of Psychological Medicine* **42**: 242–243, https://doi.org/10.1017/ipm.2025.5

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https://doi.org/10.1017/ipm.2025.5 Published online by Cambridge University Press

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https://doi.org/10.1017/ipm.2025.5 Published online by Cambridge University Press