



Exploration of the Barriers to Clozapine Prescribing in Patients with Treatment-Resistant Schizophrenia: A Qualitative Study

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Abstract Treatment-resistance schizophrenia (TRS) is one of the psychiatric challenges. While clozapine is an effective treatment for patients with TRS, there are some barriers to clozapine prescribing in these patients. The study aims to explore the barriers from Iranian psychiatrists' points of view. The study was conducted by a qualitative approach using content analysis. The Participants included 12 psychiatrists who were selected purposefully. Data were collected using a semi-structured interview from May to December 2020. All interviews were recorded and transcribed and analyzed qualitatively using constant comparisons. Three main categories emerged concerning barriers to the use of clozapine: drug-related barriers, psychiatrist and health system-related barriers, and patient and family-related barriers. Additionally, specific subcategories within each main category were documented. The present study showed that there are three main groups of barriers to the use of clozapine in patients with TRS. Psychiatrist and health

system-related barriers may influence the other two groups of barriers. Further research to investigate the effective strategies to overcome the barriers is recommended

Keywords Treatment-resistant schizophrenia · Clozapine · Barriers · Qualitative study

Introduction

Schizophrenia is a complex and progressive psychiatric disorder that is characterized by disturbances in thinking, perception, emotion, speech, and behavioral function. It affects one percent of the world's population (McGrath et al. 2008). Despite the efficacy of antipsychotic medication in treatment of patients with schizophrenia, up to 30% of these patients are diagnosed with treatment-resistant schizophrenia (TRS). These patients do not respond to treatment attempts with two antipsychotic drugs, one of which is an atypical antipsychotic (Kane and Correll 2010; Kane et al. 2010). There is evidence that showed that patients with schizophrenia impose psychological and economic stress on the family and society due to problems caused by illness such as unemployment (Kane et al. 2010). Evidence shows that clozapine an atypical antipsychotic drug, can reduce symptoms and improves the quality of life among patients with TRS

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effectively. Moreover, studies have shown that patients treated with clozapine have lower rates of readmission and discontinuation than other antipsychotic drugs. However, clozapine has not yet been used in many countries, and there is an average delay of about four to ten years before starting clozapine. Despite the clear instructions for prescribing clozapine, it is less successful (Yoshimura et al. 2019; Lobos 2010).

The previous studies have indicated that part of the reluctance to prescribe clozapine is related to the prescribers. Accordingly, psychiatrists do not have a positive attitude towards this drug due to its potentially fatal side effects, such as agranulocytosis and myocarditis. Therefore, psychiatrists prefer to use other drugs (Baig 2021). In this regard, Farooq et al. (2019) conducted a systematic review to explore barriers to clozapine use for patients with TRS. They classified the barriers into three groups: (1) patients and drug-related barriers, (2) clinician-related barriers, and (3) health system-related factors. Patients and drug-related barriers stemmed from patients' non-commitment to blood work, delay in initiation of treatment, and concerns about dealing with complications of clozapine. Farooq et al. confirmed that lack of knowledge or experience regarding the management of side effects are the most common clinician-related barriers. Health system difficulties such as service fragmentation, lack of community support, short supply of inpatient beds (required to initiate clozapine), and registration difficulties for patients who need to do blood work are among the barriers mentioned in this report (Farooq et al. 2019).

In general, these studies, while expressing the barriers to clozapine prescription, highlight the importance of removing these barriers to prescribing it to patients with TRS so that these patients can also experience improvement and quality of life. Therefore, further studies are warranted to understand all probable barriers to clozapine prescribing.

In Iran, the focus of the present study the psychiatrists are responsible to prescribe clozapine for patients with TRS based on the current guidelines. Nevertheless, there is no formal report about the barriers to prescribing clozapine among Iranian psychiatrists and the studies on clozapine use have been focused on the efficacy of clozapine in the treatment of schizophrenia or other psychosis disorders. In addition to the common barriers, we do not know exactly what

barriers Iranian psychiatrists experience when prescribing clozapine. Therefore, it is helpful to do a study in this area. Given that qualitative studies have a greater ability to deeply understand the phenomenon under study, a current study is a qualitative approach to explaining barriers to clozapine administration in patients with TRS.

Methods

Procedure and Participants

Conventional content analysis was used for the present study. In this method, information is collected directly from the participants. The researcher's subjective presuppositions are not imposed on it. Moreover, the knowledge produced is based on data collected directly from the participants (Hsieh et al. 2005; Graneheim et al. 2004).

Participants were psychiatrists with at least three years of experience and a history of prescribing clozapine to patients with TRS and willing to participate in the study. The sampling method in the present study was purposeful and snowball. First, the team members selected their participants from the eligible psychiatrists in Kermanshah University of Medical Sciences Kermanshah, Iran, then each of these participants was introduced some of whom were from other cities. Finally, 12 eligible psychiatrists participated in the present study.

Data Collection

Data were collected using a semi-structured interview. Each interview was started with questions such as "Please tell us about your experiences with clozapine in the treatment of patients with TRS," "What are the barriers and problems for clozapine use," and how these barriers and problems can be managed. Next, the interview process continued based on the respondent's responses. The interviews each lasted about 45–60 min and continued until saturation (Dworkin 2012). All interviews were recorded and transcribed. It should be noted that participants living in Kermanshah were interviewed at Farabi Psychiatric Hospital under health protocols. However, other interviews were conducted using Skype Messenger due to the covid-19 pandemic, social distance protocol, and travel

restrictions. All interviews were conducted in the period from May to December 2020.

Data Analysis

Data were analyzed based on Lundman and Grane-hime methods (Graneheim et al. 2004). For this purpose, all interviews were transcribed first. Then, to get familiarized with the text, they were read several times, important sentences were underlined, and semantic units were identified. Then, the related codes were devoted to the semantic units. The similar codes were then named in the subcategory, which has different levels of abstraction. Finally, the most similar subcategories were placed in the same category. The classification was done so that there was the most homogeneity within the categories and the most heterogeneity between the subcategories. In the present study, recommended strategies by Lincoln and Guba were used to ensure the accuracy of the collected data (Lincoln 1995). One of the strategies used was the member check method. In this strategy, the analyzed interviews are returned to the participants to comment on them. The use of different specialties in the research team (psychiatrist and researcher of qualitative research method) also increased the validity of the data. Another strategy used was the constant comparison of data, which was done in weekly and continuous meetings of the research team.

This study was approved by the Research Committee of Kermanshah University of Medical Sciences

Kermanshah, Iran (IR.KUMS.REC.1398.1067) which was conducted by the ethical principles laid down in the Declaration of Helsinki and its later amendments. All eligible participants were informed about the study protocol and signed informed consent.

Results

In total, 12 psychiatrists (6 females and six males) with an average work experience of 8.33 years participated in this study. Sample characteristics and social and demographic background are listed in Table 1. To maintain confidentiality, the city of residence and work experience of participants are not listed in Table 1.

Data analysis in this study led to the extraction of three main categories of drug-related barriers, psychiatrists and health system-related barriers, and patients and family-related barriers. The categories and subcategories are included in Table 2.

Drug-Related Barriers

According to interviews, clozapine has properties that prevent it from being easily prescribed by psychiatrists. These features were mainly related to the side effects of the drug and were classified into two subcategories, which we describe:

Table 1 Demographic characteristics of study participants

Participants number	Gender	Faculty member (yes/no)	Work experience (year)	Work type (governmental/privet/ both)
1	Male	yes	18	Both
2	Male	Yes	11	governmental
3	Female	yes	8	governmental
4	Male	yes	11	Governmental
5	Female	yes	8	Governmental
6	Female	Yes	6	Governmental
7	Female	Yes	5	Both
8	Male	No	6	Private
9	Male	No	6	Private
10	Female	No	3	Both
11	Female	No	9	Both
12	Male	No	9	Both

Table 2 Extracted categories, subcategories, and codes

Codes	Subcategories	Categories
Agranulocytosis	Serious and life- threatening side effect	Drug- related barriers
Convulsion	Need to manage and control of drug	
Myocarditis		
Drooling		
Hypotension		
Weekly lab test		
Education to family		
Need to make family cooperation		
Need to make patients cooperation		
Fear and worry	Lack of positive attitude	Psychiatrist and health system –related barriers
Modeling	Personality traits of psychiatrist	
Harm avoidance	Work palace	
Lack of bed in hospital	Work experience	
Positive feedback from clozapine	Fear from legal and ethical challenge	
Malpractice	Lack of follow up team	
Guilt feeling		
Poor social worker team		
Low awareness	<i>The low level of economic, social status and poor awareness of the family in regards to illness</i>	Patients and family – related barriers
Economic problem		
Apathy to treatment importance	Lack of access to health system	
Distance from health system	Lack of patient cooperation	
Poor adherence		

Serious and Life-Threatening Side Effects

Participants in this study stated that the presence of severe and dangerous side effects such as agranulocytosis for clozapine is one of the main reasons that psychiatrists are usually reluctant to prescribe this drug. A participant says:

“When you read about the side effects of clozapine, it says agranulocytosis, seizures, and pancytopenia. A doctor thinks that if I come to prescribe clozapine, my patient goes to this place and becomes expired. What should I do? And that makes me afraid to prescribe.” (p 6).

The Need for Drug Management and Control

According to interviews, the use of clozapine requires special management in terms of the starting dose of the drug and repeated lab tests, satisfaction and cooperation of the family and the patient, as well as education

to them, which makes psychiatrists are usually reluctant to prescribe. A participant says:

“Overall, clozapine is much more difficult to administer than other medications because of the same specific conditions that clozapine has, weekly test, family training for side effects such as hypotension, runny mouth and anxiety, risk of agranulocytosis and other ailments.” It creates a challenge for the psychiatrist, while there are no challenges with prescribing olanzapine.” (p 1).

Psychiatrists and Health System-Related Barriers

This category describes the conditions and characteristics of the psychiatrists and the health system in which the psychiatrist works and could be potential barriers to prescribing clozapine. This category had six sub-categories, which we describe below.

Lack of a Positive Attitude Towards Drugs

Study participants believed that psychiatrists who do not have a positive attitude towards clozapine are less likely to prescribe it, which can be due to the course of residency and personal experiences and the experiences of others. One of the participants says in this regard:

“The fact is that the experiences of the residency course are very effective. In general, the attitude towards clozapine is inherited from our attending. Some attending in some universities are very cautious about clozapine, which is why the residents also look closely. ”They should be scared, and they should consider clozapine equivalent to agranulocytosis and not prescribe it after residency.“ (p 5).

Psychiatrist Personality Traits

Study participants stated that psychiatrist personality traits are also effective in prescribing clozapine. One participant says:

”Well, the personality traits of a doctor who has a very high harm avoidance can be effective. He says, ’Well, my patient is resistant to treatment. At most, I say he did not respond. It is not my fault, it is the nature of the disease. I do not accept the risk of clozapine. “(Participant 10).

Psychiatrist’s Workplace

According to the interviews, a psychiatrist’s workplace is one of the things that can affect whether or not to prescribe clozapine. A participant in this regard says:

”It is essential that the psychiatrist work in a hospital. If I want to start clozapine, the patient must be hospitalized in my service to control all his problems. The patient who is hospitalized would be carefully controlled in all cases.“ (p 8).

Psychiatrist’s Work Experience

Based on the interviews, the psychiatrist’s work experience, and the feedback he has on his treatment

with clozapine can be effective in prescribing clozapine. A participant says:

“When I was a resident, I found it easier for the senior professors to start clozapine for patients, unlike younger professors, who were very cautious about prescribing. Perhaps patients and their families have more acceptance for senior professor decision.” (p 7).

Fear of Legal and Ethical Challenges

The majority of study participants believed that the serious side effects of clozapine in the patient and adverse events could cause legal and moral problems for the psychiatrist and it is one of the main reasons for not prescribing clozapine. A participant says:

“According to the guidelines, agranulocytosis may occur for the patient. However, the family considers this as a medical malpractice and sue the psychiatrist, and the psychiatrist’s professional reputation may be endangered. Therefore, the psychiatrist prefers not to impose himself to the risk. Even if the family does not sue, the psychiatrist may have an ethical challenge with himself” (p 11).

Lack of Support and Follow-Up Team

Participants in this study believed that there is no strong support and follow-up team in the health system for patients with schizophrenia to follow for whom clozapine is prescribed, making them less intended to prescribe clozapine. A participant says:

“The fact is that the psychiatrist in our system is alone and without support. We do not have a help system to follow the patients to act when there is a problem. On the other hand, there is no legal support system to support the psychiatrist in case of any problem. ”There is no way. Well, the risk goes up for the psychiatrist, and he is careful to prescribe.“ (p 2).

Family and Patients Related Barriers

The last extracted category was barriers related to family and patient, which had three subcategories, which we would describe below.

The Low Level of Economic and Educational Status and Poor Awareness of Families in Regard to the Illness

According to the interviews, the level of education, economic status, and awareness of families in regards to that can support the patient in treatment with clozapine are one of the most critical factors in prescribing clozapine. A participant says:

”There were cases in which I think there was an excellent indication to start clozapine, however, I felt that his family was not very supportive, and periodic lab tests may not be performed. Despite my desire to start clozapine for him, I gave up.“ (p 8).

Lack of Access to Medical Systems

According to interviews, the patient’s limited access to medical and laboratory centers for recommended follow-up to start clozapine use is one of the barriers that can affect the use of clozapine by a psychiatrist. A participant says:

”Certainly, if I see the patient lives in a small city or a village and cannot follow lab test, I prefer not to use clozapine. I usually use another drug in such cases.“ (p 4).

Lack of Patient Cooperation

Participants in their interviews cited patient non-cooperation as one of the barriers to clozapine administration. A participant says:

“Some of our patients are poor compliance. They usually do not want to use drugs regularly. Also, they may discontinue clozapine due to some unpleasant side effects such as drooling and may start it again without a consultant with a physician. I think it is a concern for a psychiatrist to use clozapine “ (p 9).

Discussion

The results of the present study, which is the first in Iran, classify barriers to clozapine use in three main categories: drug-related barriers, psychiatrists and health system-related barriers, and family and patients related barriers. The results are consistent with the results of previous studies (Gee et al. 2014; Tungaraza et al. 2015). We would discuss the results in detail below.

Drug-related barriers addressed psychiatrists’ concerns about dangerous and potentially life-threatening complications, as well as the difficulties of lab tests, and to satisfy the family and patient and educate them to starting the drug, which are the barriers to start clozapine use. This part of the results was similar to a qualitative study conducted by Ismail et al. (2019) in the Arab countries of the Persian Gulf. Concerns about the side effects of clozapine, patient, and family adherence to treatment have also been reported in similar studies, including the study by Essam Daod et al. (Baig 2021). Therefore, it seems that providing psychiatrists with information on how to properly manage medication, based on up-to-date guidelines in both residency course and continuing education program can be helpful to reduce the concern.

The second category extracted was the barriers related to the psychiatrist and the health system, which referred to issues such as psychiatrists’ attitudes toward clozapine, which were usually the result of their residency experiences. This finding is consistent with the findings of a systematic review by Verdoux et al. (2018) that indicated a lack of personal experience with clozapine, and a ”local culture“ of clozapine can influence the clozapine use by the psychiatrists. Given the importance of a positive attitude toward the drug, which is mainly formed during the residency and by modeling experienced professors, evidence-based approach to clozapine use by psychiatry professors is recommended. As reported in the Cohen study (2014), Bogers et al. (2016) and Carruthers et al. (2016) theoretical training alone are not sufficient, and the key role of a ”leader“ in the health care system can facilitate clozapine administration.

Furthermore, the personality traits of the psychiatrist, such as low risk-taking and fear of legal action, and the lack of a support system for them, were other issues that were mentioned in the category of the

psychiatrist and health system-related barriers. There is a lack of literature related to these results and the effect of Iranian psychiatrists' working conditions on these result. Further research in this area is recommended.

Psychiatrists' workplaces and access to hospital beds were other findings related to this category. They pointed out that physicians who have access to hospital beds are more comfortable than psychiatrists who do not have access to hospital beds to start clozapine for their patients. This finding was consistent with the study results of Ismail et al. (2019). They have reported that health system related barriers including the lack of a nation-wide monitoring program and shortage of in-patient beds are among the barriers of clozapine prescription. Isolated facilities and wards for patients who are admitted to receive clozapine can reduce psychiatrists' concerns about prescribing clozapine.

Previous studies have considered the lack of a follow-up and support team for patients treated with clozapine as another part of the barriers related to psychiatry and the health system, such as Gee et al. (2014) and Gören et al. (2016). They have emphasized the need for follow-up teams for patients treated with clozapine and for improving treatment systems providing services to these patients. It should be noted that the lack of follow-up teams in Iran is not limited to patients treated with clozapine, and many other psychiatric patients who require follow-up teams may not receive these services (Khazaie et al. 2013). Therefore, having follow-up and support teams for psychiatric patients, especially patients with TRS, should be considered in program planning in this area (Khazaie et al. 2016).

The last category extracted in this study was related to patients and families problems, which were mainly due to the lack of cooperation between patients and families in the necessary follow-up for this drug, especially periodic lab tests, and problems such as lack of easy access to medical systems. These problems have been repeatedly emphasized in previous studies, such as patients' lack of access to the laboratory, the need to go to other cities for this purpose, the congestion of medical centers as barriers to treatment with clozapine, and changes in the delivery system offered for easier access to these patients (Kelly et al. 2018; Rezaie et al. 2017; Muralidharan et al. 2019). It also seems as Rezaie and Phillips (2020) have stated

that providing information about the drug and its possible side effects can be effective in attracting the patient to cooperate in the regular use of the drug. On the other hand, considering the importance of the role of families in the treatment process of psychiatric patients, paying attention to their needs in receiving information and other mental health services can reduce burden of care for them and reduce their concerns and cooperation in the treatment process (Reupert et al. 2015; Rezaie et al. 2019).

Conclusion and Implications

This study classified the barriers to clozapine prescription from Iranian psychiatrists perspective into three categories of drug-related barriers, psychiatrist and health care system-related barriers, and patients and family-related barriers. These barriers can result in a delay in treatment with clozapine. Although the results cannot be extended to other countries, there are several useful conclusions and implications for this study. First, the study showed that there may be different-layers of barriers against clozapine prescription. In line with previous studies (Baig 2021; Farooq et al. 2019), we believe in the importance of considering all types of barriers in planning related to clozapine treatment. Second, the barriers are classified into three different groups. Considering appropriate strategies for every group of barriers is important, but this study shows psychiatrists and healthcare are the key barriers to overcome. Accordingly, strategies to increase psychiatrists-knowledge and experience as the main clozapine prescribers need to be implemented. Namely, continuous education programs on updated guidelines and regular participation in healthcare service for patients who are treated with clozapine can improve the psychiatrist's tendency towards clozapine prescription among patients with TRS. Consequently, this tendency will improve the psychiatrist's motivation for prescribing clozapine and managing patients who are treated with clozapine. Furthermore, the strategies to overcome healthcare system-related barriers such as the addition of a follow-up team, and providing easy access to lab tests can improve patients' and their families' commitment to treatment. Finally, these different types of barriers should be considered in the context of Iran including psychiatry residency education programs, and mental

health care system delivery. Therefore, programs to overcome the barriers should be tailored and assessed specifically for Iran.

Limitation

This is the first qualitative study to explore barriers to clozapine prescription in Iran. While the study provides in-depth data about the barriers, it faced some limitations that need to be mentioned. This study did not include other parts of health care workers' perspectives, especially nurses, patients, and their families. Further qualitative and quantitative studies to investigate the barriers from those mentioned groups are recommended.

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Declarations

Conflict of interest The authors have not disclosed any conflict of interests.

References

- Baig AI, Bazargan-Hejazi S, Ebrahim G, Rodriguez-Lara J. Clozapine prescribing barriers in the management of treatment-resistant schizophrenia: A systematic review. *Medicine*. 2021;100(45):e27694-.
- Bogers JP, Schulte PF, Van Dijk D, Bakker B, Cohen D. Clozapine underutilization in the treatment of schizophrenia: how can clozapine prescription rates be improved? *J Clin Psychopharmacol*. 2016;36(2):109–11.
- Carruthers J, Radigan M, Erlich MD, Gu G, Wang R, Frimpong EY, et al. An initiative to improve clozapine prescribing in New York State. *Psychiatr Serv*. 2016;67(4):369–71.
- Cohen D. Prescribers fear as a major side-effect of clozapine. *Acta Psychiatr Scand*. 2014;130(2):154–5.
- Dworkin SL. Sample size policy for qualitative studies using in-depth interviews. *Arch Sex Behav*. 2012;41:1319–20.
- Farooq S, Choudry A, Cohen D, Naeem F, Ayub M. Barriers to using clozapine in treatment-resistant schizophrenia: systematic review. *Bjpsych Bull*. 2019;43(1):8–16.
- Gee S, Vergunst F, Howes O, Taylor D. Practitioner attitudes to clozapine initiation. *Acta Psychiatr Scand*. 2014;130(1):16–24.
- Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today*. 2004;24(2):105–12.
- Gören JL, Rose AJ, Engle RL, Smith EG, Christopher ML, Rickles NM, Semla TP, McCullough MB. Organizational characteristics of Veterans Affairs clinics with high and low utilization of clozapine. *Psychiatr Serv*. 2016;67(11):1189–96.
- Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277–88.
- Ismail D, Tounsi K, Zolezzi M, Eltorki Y. A qualitative exploration of clozapine prescribing and monitoring practices in the Arabian Gulf countries. *Asian J Psychiatr*. 2019;39:93–7.
- Kane JM, Correll CU. Past and present progress in the pharmacologic treatment of schizophrenia. *J Clin Psychiatry*. 2010;71(9):13909.
- Kane JM, Correll CU. Pharmacologic treatment of schizophrenia. *Dialogues Clin Neurosci*. 2010;12(3):345.
- Kelly DL, Freudenreich O, Sayer MA, Love RC. Addressing barriers to clozapine underutilization: a national effort. *Am Psychiatric Assoc*. 2018. <https://doi.org/10.1176/appi.ps.201700162>.
- Khazaie H, Rezaie L, de Jong DM. Dropping out of outpatient psychiatric treatment: a preliminary report of a 2-year follow-up of 1500 psychiatric outpatients in Kermanshah, Iran. *Gen Hosp Psychiatr*. 2013;35(3):314–9.
- Khazaie H, Rezaie L, Shahdipour N, Weaver P. Exploration of the reasons for dropping out of psychotherapy: a qualitative study. *Eval Program Plann*. 2016;56:23–30.
- Lincoln YS. Emerging criteria for quality in qualitative and interpretive research. *Qual Inq*. 1995;1(3):275–89.
- Lobos CA, Komossa K, Rummel-Kluge C, Hunger H, Schmid F, Schwarz S, Leucht S. Clozapine versus other atypical antipsychotics for schizophrenia. *Cochrane Database Syst Rev*. 2010(11).
- McGrath J, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidem Rev*. 2008;30:67–767.
- Muralidharan A, Mills WL, Evans DR, Fujii D, Molinari V. Preparing long-term care staff to meet the needs of aging persons with serious mental illness. *J Am Med Dir Assoc*. 2019;20(6):683–8.
- Reupert A, Maybery D, Cox M, Scott SE. Place of family in recovery models for those with a mental illness. *Int J Ment Health Nurs*. 2015;24(6):495–506.
- Rezaie L, Phillips D. Post-discharge needs of Iranian women diagnosed with severe mental illness: a qualitative study. *J Psychiatr Ment Health Nurs*. 2020;27(6):752–62.
- Rezaie L, Schwebel DC. Psychological needs of the families of patients who attempted suicide by self-immolation: an overlooked issue. *Burns*. 2019;45(8):1938–9.
- Rezaie L, Shafaroodi N, Philips D. The barriers to participation in leisure time physical activities among Iranian women with severe mental illness: A qualitative study. *Mental Health Phys Activity*. 2017;13:171–7.
- Tungaraza TE, Farooq S. Clozapine prescribing in the UK: views and experience of consultant psychiatrists. *Ther Adv Psychopharmacol*. 2015;5(2):88–96.
- Verdoux H, Quiles C, Bachmann CJ, Siskind D. Prescriber and institutional barriers and facilitators of clozapine use: a systematic review. *Schizophr Res*. 2018;201:10–9.
- Yoshimura B, Sato K, Takaki M, Yamada N. Algorithm-based pharmacotherapy for first-episode schizophrenia

involuntarily hospitalized: a retrospective analysis of real-world practice. *Early Interv Psychiatr.* 2019;13(1):39–46.

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