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Pattern and Correlates of Prescribing Antipsychotics in a Leading Mental Hospital in Kenya

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ABSTRACT: ***Objectives:*** *To describe the prescribing patterns and identify correlates of prescribing antipsychotic.* ***Design:*** *A hospital-based cross-sectional study.* ***Setting:*** *A leading mental hospital in Kenya. Subjects: Adult patients receiving care for psychiatric illnesses* ***Outcome Measures:*** *The patients' socio-demographic profile and antipsychotic prescribing data were recorded and associations between the two were computed at P≤ 0.05. Results: The mean age of the participants was 36.7 (SD 13.4) years and a majority were males (64.7%). Most prescriptions contained first-generation antipsychotics (FGAs) (79.2%), and almost half (45.2%) had second-generation antipsychotics. Most patients (53.7%) used supramaximal doses, which was significantly associated with polypharmacy of FGAs (P<0.001). Prescribing more than one FGA significantly increased the odds of having a supramaximal dose by 18 times (P<0.001).* ***Conclusion:*** *Polypharmacy especially with FGAs and use of supramaximal doses was prevalent. Future studies should develop a scaled guideline that informs the clinical efficacy of various doses of chlorpromazine equivalents.*

Keywords: *Antipsychotics; Polypharmacy; FGAs; SGAs; CPZeq; Supramaximal.*

INTRODUCTION

An estimated 971 million persons globally were affected by mental disorders, according to a survey done in 2017, marking a 13.5% increase in number compared to 2007 (James et al., 2018). Mental illnesses have consistently formed more than 14% of the years lived with disability across the globe since 1990, with a prevalence greater than 14% 1 (James et al., 2018). Psychiatric disorders are among four of the top ten health conditions that contribute to the highest Disability Adjusted Life Years, hence a significant public health priority (Alam et al., 2015).

Prescribing practices of antipsychotics vary greatly across the globe. Prevalent practices include prolonged use of high dose treatment, polypharmacy, and the use of non-evidential treatment options that may augment the adverse effects for the patients, reduce patient's adherence, causes unnecessary health care costs, increases morbidity and mortality, and reduces the quality of care (Van Der Meer (1981); Summoro et al., 2015)

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Inappropriate prescribing is mainly attributed to lack of localized treatment algorithms for mental illnesses, lack of knowledge, skills, or information, overworking of health professionals, and the unrestricted availability of medications, especially in the low-and-middle-income countries (Abebaw et al. (2016). The mental healthcare system in Kenya further faces particular challenges, which include insufficient drug supply and low affordability, which influences the choice of antipsychotics prescribed. Additionally, inadequate human resources, lack of prioritization of mental health, stigma, traditional and religious beliefs, and insufficient training, especially in rural settings, (Ambikile & Iseselo (2017); Musyimi et al., 2017; Ndetei et al., 2008) affects the management practices.

Studies across the globe reveal a high rate of polypharmacy, with the UK having a prevalence of 48%, Europe 23%, Japan 90%, Oceania 16.4%, North America 16%, and 67.3% in Wales (Rajan & Clarke, 2013; Armstrong & Temmingh, 2017). In Sudan, most patients (94.8%) received a combination of first-generation antipsychotics (FGAs), second-generation antipsychotics (SGAs) and adjunctive medications. In a few countries like Oman, the rate of

monotherapy was 93% (Al Za'abi et al., 2014). A study in India showed that polypharmacy was closely associated with supramaximal doses (Ramadas et al., 2010).

The rate of SGA use in some developed countries is relatively high ranging between 87% to 90%, and usage of FGAs in these countries is much lower, ranging from 7% to 23% (Van Kammen, 2001). In most African countries, the use of FGAs is relatively high, being 74% in South Africa and 93.9% in Sudan (Eloff et al., 2017). The usage of SGAs was low in South Africa (26%) but much higher in Sudan (83.7%) (Eloff et al., 2017).

In Canada use of polypharmacy was significantly associated with the duration of hospitalization and having a comorbid personality disorder (Farrell & Brink, 2020). However, similar to other studies, the age, the primary diagnosis, employment status, level of education, religion, the number of previous psychiatric admissions, and ethnicity were not associated with polypharmacy (Farrell & Brink, 2020).

Clinicians globally often prescribe high doses when patients show poor response to standard doses. Studies have attributed the use of high dose treatments to resistance, using antipsychotics for a longer duration of time, being diagnosed with bipolar disorder, having an anticholinergic prescribed, and polypharmacy (Adesola et al., 2013); (Lelliott et al., 2002); (Wilkie et al., 2001). A history of aggression and violence, the level of compliance to medication, the amount of social support by the caregiver, and other psychosocial factors could also influence the dose prescribed (Wilkie et al., 2001); Royal College of Psychiatrists (2006). A study from India determined that receiving a supramaximal dose was significantly associated with receiving a combination of a FGAs and SGAs. Contrary to other studies, a study done in Indian showed that the duration of illness does not influence the prescription of a high dose (Ramadas et al., 2010).

Studying the prescribing patterns provides an overview of the gaps in therapeutic trends and suggests modifications to make medical care rational, safe, and cost-effective. This study sought to describe the antipsychotic prescribing patterns in a leading tertiary psychiatric hospital. The study also endeavoured to determine the correlates of polypharmacy and the prescribing of supramaximal antipsychotic doses by clinicians.

METHODS

STUDY DESIGN AND SITE

A cross-sectional study was undertaken between August 2020 to October 2020 among adult psychiatric patients seeking treatment for various mental illnesses at Mathari National Teaching and Referral Hospital (MNTRH). This is the largest teaching and referral psychiatric facility in Kenya, with a bed capacity of 700. Study participants were recruited from the wards and the psychiatric outpatient clinics.

ETHICAL APPROVAL

The study was approved by the Kenyatta National Hospital/ University of Nairobi-Ethics and Research Committee (protocol number P185/03/2020). Permission was then granted by the Continuous Medical Education Director at MNTRH

All the potential participants underwent the entire consenting process before being voluntarily requested to sign the consent form.

STUDY POPULATION

The study population consisted of both adult males and females who were mentally ill and seeking treatment at the hospital. The exclusion criteria were failure to consent to the study, having acute mental disturbance, and having incomplete sociodemographic or medical records.

SAMPLE SIZE AND SAMPLING METHOD

Cochran's formula (13) was used to calculate a sample size of 151 based on the 10.8% estimated prevalence of mental illnesses in Kenya (Jenkins et al., 2012). An additional 10% of participants were added to address cases of non-responders, giving a target sample size of 167 participants that were sampled proportionally among the inpatients and outpatient units. A systematic random sampling method was used to recruit study participants in the study units.

DATA COLLECTION, ENTRY AND STATISTICAL ANALYSIS

A predesigned questionnaire was used to collect raw data from the participants and medical files such as sociodemographic details, diagnosis, duration of mental illness, history of previous psychiatric admissions and antipsychotics prescribed at the time of the study.

The primary outcome variable was the dose of antipsychotics prescribed. According to the documented international consensus, each dose of antipsychotic can be converted into an equivalent dose of chlorpromazine. Therefore, each antipsychotic prescribed was converted into its recommended equivalent dose of chlorpromazine. For patients receiving more than one antipsychotic, each drug prescribed was converted into its chlorpromazine equivalents (CPZeq), and the total dose was summed up. All the raw data was fed into a worksheet in Microsoft Excel 2016 and exported to STATA version 14 for statistical analyses.

Chi-square tests were done to assess the association between the sociodemographic factors and patterns of antipsychotic prescriptions, such as the number of FGAs and SGAs

prescribed as well as their doses. Logistic analysis was done using a backward elimination model to assess the independent correlates of prescribing a certain number of antipsychotics.

RESULTS

Two hundred and forty-three participants were recruited, but only 167 participants met the inclusion criteria. The respondents' sociodemographic and clinical characteristics are presented in Table I.

The majority of the participants were males (n =108, 64.7%). The mean age was 36.7±13.4 years, with a majority being within the 18 to 45 years age bracket (n=128, 76.6%). The mean body mass index (BMI) was 24.9 ± 4.5 kg/m^2, with slightly less than half of the participants exceeding the ideal body weight (n=71, 42.5%). Majority of the participants (n=103, 61.6%) had a history of previous psychiatric admission, they were single (n=93, 55.7%), affiliated to Christianity (n=142, 85.0%), and unemployed (n= 108, 64.7%).

The rate of use of FGAs was 79.2%, and that of SGAs was 45.2%. Antipsychotics were commonly prescribed, with 37.7% (n=63) of the patients being on monotherapy, 53.3% (n=89) dual therapy, 6.0% (n=10) triple therapy and one patient used four antipsychotics concurrently.

The average dose of antipsychotics prescribed was 1021.0mg of CPZeq per person. Patients who used standard doses (≤1000 mg of CPZeq) were 46.3% (n=76), while those who used supramaximal doses were 53.7% (n=88). Patients with bipolar disorder received the lowest dose of antipsychotics, 829.5 mg ± 548.8 mg of CPZeq.

Patients with schizoaffective disorders received the highest number of mood stabilizers (0.8 per person) as well as the highest number of FGAs (1.4 per person), as shown in Table I. Patients with schizophrenia were the least likely to receive SGAs, having the lowest average of 0.3 SGAs per person. However, they were more likely to receive FGAs, having the highest average of 1.4 FGAs per person. Patients diagnosed with a bipolar mood disorder, schizoaffective disorders, and acute psychosis received the highest number of SGAs (0.6 drugs per person).

Patients diagnosed with SZA/DIP received a relatively low dose of antipsychotics (900.0 ± 673.9mg CPZeq), but paradoxically this was accompanied by having the highest number of anticholinergics prescribed (0.3 per person). Those diagnosed with acute psychosis (n=9) received the highest number of antipsychotics (1.9 per person), which corresponded to having the highest average dose of antipsychotics per person (1038.9 ± 739.8mg of CPZeq). Unexpectedly, these participants received the lowest of anticholinergics (0.2 per person).

Among the 163 patients on antipsychotics, 77 (47.2%) received oral haloperidol, representing the most commonly used FGA. Fluphenazine decanoate injection was the most preferred intramuscular depot, administered to 42.3% (n=69) of the participants. The most preferred anticholinergic was trihexyphenidyl (benzhexol) oral formulation used on a *pro re nata* (as needed) basis. The most prescribed SGA was the oral formulation of olanzapine, which was issued to 25.2% of the patients (n=41). Risperidone was the second most preferred SGA, which was prescribed to 33 participants (20.2%). Some of the other injectable depots that were used included zuclopenthixol decanoate injection (n=15, 9.2%) and flupentixol decanoate (n=12, 7.4%).

There was a significantly higher chance of participants using a mood stabilizer to receive a relatively high dose of CPZeq (P = 0.001), as shown in Table I. Similarly, participants receiving a high dose of antipsychotics had a higher chance of being on an anticholinergic drug (P = 0.004). Those participants who had no comorbidity had a significantly higher chance of receiving a high dose of antipsychotics (P = 0.002).

Having at least a secondary education was associated with the probability of receiving fewer SGAs (OR = 0.28, P=0.010). Having a higher number of FGAs prescribed significantly increased the odds of a patient receiving a supramaximal dose by up to 18 times (P <0.001).

Table 1.

Average Number of Drugs Prescribed per Person

Diagnosis	SZA	BMD	DIP	SAD	SZA/DIP	APY
Number of Patients	56	28	27	16	12	9
Average Number of Antipsychotics	1.7	1.6	1.8	1.6	1.7	1.9
Average Number of FGAs	1.4	1	1.3	0.9	1.4	1.3
Average Number of SGAs	0.3	0.6	0.4	0.6	0.3	0.6
Average Dose (CPZeqs) mg	1021.0 ± 608.0	829.5 ± 548.8	965.7 ± 647.8	910.9 ± 702.4	900.0 ± 673.9	1038.9 ± 739.8
Average Number of Anticholinergics	0.3	0.3	0.3	0.3	0.6	0.2
Average Number of Mood Stabilizers	0.8	0.7	0.6	0.6	0.7	0.6

DISCUSSION

There was male predominance (64.7%) among the participants, showing that mental illnesses mostly affected males more than females. This was similar to other study done in Kenya (55.49%) and Sudan (57%), where the majority were male (Ndetei et al., 2008); Mohamed & Yousef, (2020); Katayi (2014). The rate of polypharmacy in this study was at 60%, almost similar to that in Qatar at 58.8% and Asia, where 45.7% had more than one antipsychotic Ouanes et al. (2020). A study in the USA had a polypharmacy rate of 57% (Faries et al., 2005), Japan 69% (Ito et al., 2005), while Korea had the lowest rate at 9.0% (James et al., 2018). Some studies support the use of polypharmacy, suggesting that combining drugs could reduce rehospitalisation (Maenner et al., 2014). Polypharmacy is applicable in exceptional instances such as during cross-titration of antipsychotics, augmenting the efficacy of clozapine, and when managing particular side-effects, and when rapid tranquilization is needed (Connolly & Taylor et al., 2014). However, there is no conclusive evidence for this practice, and clinical guidelines primarily emphasize monotherapy.

One patient was on a drug holiday. This practice is thought to "re-sensitize" neurons to the acute pharmacological activities of antipsychotics. It is also helpful in treating tardive dyskinesia (Bergman et al., 2018) and neuroleptic malignant syndrome (Taylor et al., 2021). However, this comes with the risk of poor compliance to therapy, thus destabilizing a patient and presenting a difficulty in distinguishing discontinuation and rebound effects (Bergman et al., 2018).

Despite the fact that SGAs are perceived to be much safer than the FGAs because they have a reduced risk of causing extrapyramidal side effects and adverse neurological effects, the rate of their use was relatively low at 45.2% compared to other countries such as Arab countries (95.6%), China (86.6%), Turkey (96.9%), Korea (93%), India (93.5%) and New Zealand (87.0%) (Van Kammen, 2001). The same difference was noticeable in the higher use of FGAs (79.2%) compared to other countries such as Arabian countries (23.4%), Turkey (17.2%), New Zealand (13.0%), India (33.81%) and Korea (7%) (Van Kammen, 2001). This may be explained by the exorbitant cost of and hence unavailability of SGAs in resource-limited settings such as Kenya.

Haloperidol was the most commonly used FGA, while fluphenazine was the most frequently used injectable formulation as observed in Sudan, Mohamed & Yousef, (2020) and Korea (James et al., 2018). Olanzapine was the most preferred SGA issued to 25% of the participants, followed by risperidone at 20%. Although both olanzapine and risperidone are well tolerated and efficacious, olanzapine has been consistently associated with a greater reduction in the severity of psychiatric illnesses, improvement of negative symptoms (James et al., 2018), and less extrapyramidal effects (Shoja Shafti & Gilanipoor, 2014) and perhaps the most preferred SGA among the participants.

The dose of CPZeq is a measure of whether a patient received a standard dose of antipsychotics (≤1000mg of CPZeq) or a higher than the recommended dose of antipsychotics (>1000mg of CPZeq, also known as a supramaximal dose). In most cases, the maximum effective dose of an individual drug was within the allowed limit; however, the cumulative dose, which was calculated by adding up all the antipsychotics prescribed per patient, was higher than the standard dose. The high prevalence of supramaximal doses could be attributed to the high rate of polypharmacy, especially with FGAs. Furthermore, the addition of an FGA to a prescription increased the odds of a patient receiving a supramaximal dose by 18 times ($P < 0.001$).

The high use of FGAs contributed to patients receiving a relatively high mean dose CPZeq of 930.4 ± 617.5mg. This is in contrast to other countries that had a much lower mean dose, such as Qatar with a mean CPZeq of 577.8mg, Korea 732.1mg (Kim et al., 2014), and Turkey 684.1mg (Yaziciet al., 2017). The plausible explanation would be that the high-income countries frequently use SGAs resulting in lower doses of CPZeq. Patients on higher doses of CPZeq were most likely to use anticholinergics such as benzhexol ($P=0.004$) to counter the extrapyramidal side effects.

A high dose of CPZeq was associated with the use of a mood stabilizer ($P = 0.001$). Studies have indicated that a combination of a mood stabilizer and an antipsychotic is commonly indicated for relapsing cases of mental illnesses. In addition, a positive history of prior admission was significantly associated with the use of a mood stabilizer ($P = 0.003$), pointing towards the high likelihood of relapsing patients receiving a mood stabilizer. These findings are intertwined in that patients who relapse are likely to receive a higher dose of antipsychotics to stabilize them, in combination with a mood stabilizer.

Though this study gives important data on trends and covariates of antipsychotics prescribing in limited-resource settings, it is important to appreciate some limitations. Firstly, this study was largely dependent on the medical records entered in patient's files by the healthcare team, and any erroneous entries or omissions could not be verified. Additionally, there was insufficient documentation on clinical decisions that informed switching among antipsychotics or prescribing specific doses, making it difficult to assess whether the choice of drug and the dose was rational.

CONCLUSION

Psychiatric disorders were mainly managed using FGAs at a much higher frequency than in developed countries. Polypharmacy of antipsychotics was evident, which contributed to most of the patients receiving supramaximal chlorpromazine dose equivalents and adjunct therapy with anticholinergics.

We recommend the use of SGAs as opposed to prescribing two or more FGA concurrently to ensure that patients benefit from lower doses of CPZeq, which are associated with a lower risk of extrapyramidal side effects. Future studies should develop a scaled guideline that informs the clinical efficacy of various doses of CPZeq, particularly for the FGAs.

KEY POINTS

- First-generation antipsychotics are still mainstay pharmacological approaches in the management of psychiatric illnesses in Kenya.
- Polypharmacy, though not recommended by clinical guidelines, is highly preferred by psychiatrists in treating mental illnesses.
- Patients having polypharmacy using first-generation antipsychotics are more likely to receive supramaximal doses and thus require concurrent use of benzhexol and mood stabilizers.

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CONFLICT OF INTEREST

The author declares no conflict of interest

AUTHORS' CONTRIBUTIONS

KM conceived the topic, developed the idea, collected and analysed the data and drafted the manuscript. DN and BA assisted in developing the idea, developing the proposal, analysing the data and interpreting it, and developing the manual.

DATA AVAILABILITY

Datasets used are available on request via email kinyanjuh@gmail.com

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REFERENCES

James SL, Abate D, Hassen Abate K, Abay SM, Abbafati C, Abbasi. (2018). 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. *Lancet, 392*:1789–1858.

Alam, M. T., Maruf, M. M., Sarkar, M., Ahmed, H. U., & Akhter, M. (2015). Pattern of prescribing psychotropics in the outpatient department of a tertiary psychiatric hospital. *Bangladesh Journal of Psychiatry*, *29*(1), 10-13.

Van Der Meer J. (1981).Rational medicine. *Ned Tijdschr Geneeskd, 125*:626–627.

Summoro, T. S., Gidebo, K. D., Kanche, Z. Z., & Woticha, E. W. (2015). Evaluation of trends of drug-prescribing patterns based on WHO prescribing indicators at outpatient departments of four hospitals in southern Ethiopia. *Drug design, development and therapy*, *9*, 4551.

Abebaw, D., Haile, K., Kassaw, C., Belete, A., Fanta, T., & Azale, T. (2016). Pattern of Rational use of Psychotropic Drugs for People with Severe Mental Illness in a Mental Specialized Hospital in Addis Ababa, Ethiopia: A Mixed Method Study. *Journal of Family Medicine*, *3*(11), 1099.

Ambikile, J. S., & Iseselo, M. K. (2017). Mental health care and delivery system at Temeke hospital in Dar es Salaam, Tanzania. *BMC psychiatry*, *17*(1), 1-13.

Musyimi, C. W., Mutiso, V. N., Ndetei, D. M., Unanue, I., Desai, D., Patel, S. G. & Bunders, J. (2017). Mental health treatment in Kenya: task-sharing challenges and opportunities among informal health providers. *International journal of mental health systems*, *11*(1), 1-10.

Ndetei, D. M., Khasakhala, L., Maru, H., Pizzo, M., Mutiso, V., Ongecha-Owuor, F. A., & Kokonya, D. A. (2008). Clinical epidemiology in patients admitted at Mathari psychiatric hospital, Nairobi, Kenya. *Soc Psychiatry Psychiatr Epidemiol*, *43*(9), 736-742.

Rajan, L., & Clarke, I. (2013). Audit of combination and high-dose antipsychotic treatment in the community. *Psychiatrist*, *37*(9), 302-307.

Armstrong, K. S., & Temmingh, H. (2017). Prevalence of and factors associated with antipsychotic polypharmacy in patients with serious mental illness: Findings from a cross-sectional study in an upper-middle-income country. *Rev Bras Psiquiatr*, *39*, 293-301.

Al Za'abi, M., Al-Hinai, A. S., & Al-Busaidi, S. A. (2014). Utilization pattern of antipsychotics at a tertiary care hospital in Oman. *Afr J Psychiatry (South Africa)*, *17*(6), 1000171.

Ramadas, S., Kuttichira, P., TP, S., & Ummer, S. A. (2010). A study of an antipsychotic prescription pattern of patients with schizophrenia in a developing country. *Indian J Psychol Med*, *32*(1), 13-16.

Van Kammen DP. (2001). Essential Psychopharmacology: Neuroscientific Basis and Practical Applications, 2nd ed. • Essential Psychopharmacology of Depression and Bipolar Disorder. *Am J Psychiatry,158*:1538-1539.

Eloff I, Esterhuysen W, Odayar K. (2017). Antipsychotic use in a resource-limited setting: Findings in an Eastern Cape psychiatric hospital. *South African J Psychiatry, 20;*23.

Farrell C, Brink J. (2020). The prevalence and factors associated with antipsychotic polypharmacy in a forensic psychiatric sample. *Front Psychiatry, 17*;11:263.

Adesola AO, Anozie IG, Erohubie P, James BO. (2013). Prevalence and correlates of "high dose" antipsychotic prescribing: findings from a hospital audit. *Ann Med Health Sci Res, 3*(1):626-6.

Lelliott P, Paton C, Harrington M, Konsolaki M, Sensky T, Okocha C. (2002). The influence of patient variables on polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients. *Psychiatr Bull*, *26*(11):411-414.

Wilkie A, Preston N, Wesby R. (2001). High dose neuroleptics–who gives them and why?. *Psychiatr Bull, 25*(5):179-183.

Royal College of Psychiatrists. (2006). *Consensus statement on high-dose antipsychotic medication*. Royal College of Psychiatrists.

Jenkins R, Njenga F, Okonji M, Kigamwa P, Baraza M, Ayuyo J. (2012). Prevalence of common mental disorders in a rural district of Kenya, and socio-demographic risk factors. *Int J Environ Res Public Health.;9*(5):1810-1819.

Gardner D, Murphy A. O.'Donnell H, F. Centorrino, and R. Baldessarini, (2010)."International consensus study of antipsychotic dosing,". *Am J Psychiatry, 167*:686-693.

Atkins M, Burgess A, Bottomley C, Riccio M. (1997). Chlorpromazine equivalents: a consensus of opinion for both clinical and research applications. *Psychiatr Bull*, *21*(4):224-226.

Leucht S, Samara M, Heres S, Patel MX, Furukawa T, Cipriani A (2015). Dose equivalents for second-generation antipsychotic drugs: the classical mean dose method. *Schizophr Bull, 41*(6):1397-1402.

Mohamed MM, Yousef BA. (2020). Prescription patterns of antipsychotics in the management of first episode psychosis at three psychiatric hospitals in Khartoum, 2018: A descriptive cross-sectional study. *J Fam Med Prim Care, 9*(1):402.

Katayi, E. O. (2014). *Impact of side effects of antipsychotics on attitude and adherence to treatment among adult psychiatric outpatients at Mathari Hospital in Kenya* (Doctoral dissertation, University of Nairobi).

Ouanes S, Becetti I, Ghuloum S, Hammoudeh S, Shehata M, Ghabrash H (2020). Patterns of prescription of antipsychotics in Qatar. *Plos one, 15*(11):0241986.

Faries D, Ascher-Svanum H, Zhu B, Correll C, Kane J. (2005). Antipsychotic monotherapy and polypharmacy in the naturalistic treatment of schizophrenia with atypical antipsychotics. *BMC psychiatry, 5*(1):1-1.

Ito H, Koyama A, Higuchi T. (2005). Polypharmacy and excessive dosing: psychiatrists' perceptions of antipsychotic drug prescription. *Br J Psychiatry, 187*(3):243-247.

Maenner MJ, Rice CE, Arneson CL, Cunniff C, Schieve LA, Carpenter LA (2014). Potential impact of DSM-5 criteria on autism spectrum disorder prevalence estimates. *JAMA psychiatry, 71*(3):292-300.

Connolly A, Taylor D. (2014). Factors associated with non evidence-based prescribing of antipsychotics. *Ther Adv Psychopharmacol, 4*(6):247-256.

Bergman, H., Rathbone, J., Agarwal, V., & Soares-Weiser, K. (2018). Antipsychotic reduction and/or cessation and antipsychotics as specific treatments for tardive dyskinesia. *Cochrane Database of Systematic Reviews*, (2).

Taylor, D. M., Barnes, T. R., & Young, A. H. (2021). *The Maudsley prescribing guidelines in psychiatry*. John Wiley & Sons.

Shoja Shafti, S., & Gilanipoor, M. (2014). A comparative study between olanzapine and risperidone in the management of schizophrenia. *Schizophr Res Treatment*, *2014*.

Kim HY, Lee HW, Jung SH, Kang MH, Bae JN, Lee JS. (2014). Prescription patterns for patients with schizophrenia in Korea: a focus on antipsychotic polypharmacy. *Clin Psychopharmacol Neurosci, 12*(2):128.

Yazici E, S. Cilli A, Yazici AB, Baysan H, Ince M, Bosgelmez S. (2017). Antipsychotic Use Pattern in Schizophrenia Outpatients: Correlates of Polypharmacy. *Clin Pract Epidemiol Ment Heal, 13*:92–103.