

A Descriptive Retrospective Study of The Prevalence Of Antipsychotic Polypharmacy (APP) Among Schizophrenia Patients In Malaysia

Fares M.S Muthanna (✉ farismuthanna2020@gmail.com)

Walailak University

Hamza Khaliha Ibrahim

Higher Institute of Medical Technology

Research Article

Keywords: antipsychotic polypharmacy (APP), schizophrenia, Prevalence

Posted Date: March 31st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1507228/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

The study aimed to investigate the prevalence of APP among Malaysian patients diagnosed with schizophrenia.

Methods

A descriptive retrospective study was conducted to gather clinical and demographic information on adult individuals diagnosed with psychiatric disorders e.g schizophrenia who had been prescribed with antipsychotic drugs (Antipsychotic combination or Monotherapy) and had been admitted to Hospital Kajang in Malaysia between March 2016 and November 2016. Prevalence of antipsychotic polypharmacy (APP) is determined by determining whether the patient is given one or more antipsychotic medications or not. A descriptive analysis was carried out to evaluate the prevalence of APP among clinical and demographic variables.

Results

The study included 113 people suffering from schizophrenia. The prevalence of APP was 56.7% (n = 64). According to our results, the prevalence of APP among demographic and clinical variables were 48.4% (n = 31) among elderly patients, 61.8% (n = 40) among males, 70.3% (n = 19) among single, and 67.2% (n = 43) among unemployed schizophrenia patients.

Conclusion

According to this setting, the proportion of APP in schizophrenia patients is quite high. Being male, single and younger than 50 years of age was linked to a significant rise in APP prevalence; thus, protocols are required to recognize subgroups of psychiatric patients who are most likely benefit from novel management strategies and kidney functions.

Introduction

The use of more than one antipsychotic agent is referred to as "antipsychotic polypharmacy" (APP) during a covered period (weeks, months or years) (Pae C. U. (2020). It is often used to treat a wide range of psychiatric issues, including schizophrenia and cognitive impairment. Antipsychotics are medications that are primarily used to treat schizophrenia and other psychiatric issues such as dementia, delusion, bipolar disorder, and schizoaffective disorder. There are two kinds of APPs: typical (first-generation) antipsychotics and atypical antipsychotics, also known as (second-generation) (Ginovart, N., & Kapur, S. (2012) (Muthanna, Fares Mohammed Saeed, 2021). Antipsychotic polypharmacy (APP) was found to be

prevalent in 28.2% of people (Tesfaye, S *et al.*2016). According to recent reports, the following countries have a high prevalence of APP: Nigeria (70.4%) (Igbinomwanhia, N. G *et al.*2017); Vietnam (59.1%) (Yang, S. Y *et al.*2018); Malaysia (48%) (Fares M.S Muthanna *et al.*2018, Muthanna FMS) *et al.*2018; and United States (27.1%) (Boskailo, E. *et al.*2018). Prescribing a combination of antipsychotics is still a frequent practice advice to prevent and minimize multiple agents unless it has been tested in multiple trials (Crabtree, B. L *et al.*2011). Moreover, patients who are prescribed with multiple antipsychotics frequently require higher-than-recommended doses (Koen, L *et al.*2008). Polypharmacy is becoming more common, which has raised concerns about safety and risk issues which include the intensity of negative effects, patient costs, decreased pharmacokinetics, and decreased adherence to complicated drug regimens. Treatment for long time and adjustments of the dose should also be considered (Waddington, J. L *et al.*1995). Lack of available data and information on the advantages and disadvantages of multiple antipsychotics, as well as proper medication administration, determining the current prevalence of antipsychotic polypharmacy in Malaysia is difficult. As a result, the goal of this setting is to ascertain to find out how common antipsychotic polypharmacy among Malaysian schizophrenia patients.

Methods

A retrospective cross-sectional setting was performed at Kajang Hospital -Malaysia. Patients with schizophrenia were identified from medical records over a 9-month period between March 2016 and November 2016. A range of clinical data was extracted from medical records, including demographic and clinical data. Patients between the ages of 18 and 65 (during the period of the study) or diagnosed with schizophrenia and receiving antipsychotic treatment were included, whereas patients prescribing with other psychotic management, such as a combination of antidepressants and antipsychotics, and those with missing data were excluded.

SAMPLE SIZE DETERMINATION

For a single population proportion estimation at the 95 % confidence interval (CI) ($Z / 2 = 1.96$) and margin of error of 5%, we calculated the sample size using the following formula ($n = Z_2 \times P (1 - P) / d_2^2$). Due to a data shortage in Malaysia, antipsychotic prescription was found to be 50% among psychiatric patients, and the total study population of 113 was linked to a 10% increase in the likelihood of emergency treatment for rates of non-response.

SAMPLING TECHNIQUES

Data was gathered from the medical records of patients admitted to the psychiatric department at Kajang Hospital, a government hospital in Selangor, Malaysia, located in the province of Hulu Langat in the eastern part of Kajang town. With the establishment of the town in 1889, Kajang Hospital was established. In the 1970s, the hospital had 250 beds, which have now been increased to 306 beds.

STATISTICAL ANALYSIS

The data was analyzed using descriptive statistics to explain the clinical and demographic information of the psychiatric participants using SPSS version 20. We measured the mean and standard deviation for continuous data, and the proportion and frequency for categorical variables

ETHICS APPROVAL

The Medical Research Ethical Centre (MREC) (5) KKMNIHSEC/P17-1198) and NMRR-17-987-35495 (IIR) reviewed and approved all aspects and protocols of this setting. The researcher adhered to the principles of the Helsinki Declaration and Malaysian Good Clinical Practice Guidelines.

Results

Data was collected from schizophrenia patients at Kajang Hospital between the ages of 18 and 65. A total of 202 cases were screened, 89 were removed due to antidepressant use or missing data, and only 113 met the criteria of inclusion. Table 1 describes clinical and demographic information for the 113 participants who enrolled in this setting. As shown, the proportion of APP was 56.7% (64/113). Out of the overall number of participants in the study, 52.2% (59/113) were males and 47.8% (54/113) were females. Majority of patients were young with age category less than 50 years old (54%) and the average age of the participants was 52.77 year. Furthermore, according to Table 1, approximately 45.1 % (51/113) of the participants were Malay, followed by 29.2% (33/113) Indians, and 22.1% (25/113) Chinese. In terms of marital status, 43.3% (49/113) of the patients were married, 33.6% (38/113) were single, and 23% (26/113) were divorced. The majority of the patients, 47% (47/113) were normal BMI, (24.8%) (28/113) were underweight and 23% (26/113) were overweight. Moreover, approximately 56.6 % (64/113) of total patients were unemployed and 30.1% (35/113) were smokers.

In this study, 70.1% (80/113) of the patients were receiving APP medications more than three months and only 29.2% (33/113) were treated with APP less than 3 months. Additionally, nearly half of patients prescribed with APP developed EPS 51.7% (58/113), and 48.7 % (55/113) did not.. Finally, in terms of

APP medication type, approximately 18.96% (21/113) received First generation antipsychotics (FGAs), 24.8% (28/113) received second generation antipsychotics (SGAs) and 56.7% (64/113) received a mixture of typical (FGAs) and atypical (SGAs) (Table 1).

The proportion of antipsychotic polypharmacy (APP) among individuals was 56.7%. Majority of patients 51.6% aged less than 50 prescribed with APP and 61.8% were males, (70.3%) were single, and 45.3% were Malay.

Sixty-seven (67.2%) of APP prevalence was observed among unemployed schizophrenia patients ,34.5% among normal BMI patients, and 64% among non-smokers. In terms of patient admission, approximately 82.8 % (n = 53) of schizophrenia patients were admitted to the hospital for more than three months and only 17.2 % for less than three months. With regards to the side effects, about 59.4% (n=38) of patients receiving multiple APP developed EPS whereas only 40.8 % developed EPS after receiving AP monotherapy. (Table 2).

Discussion

The prevalence of APP in Malaysian individuals diagnosed with schizophrenia was successfully identified in this study. The current study's findings were higher than those of previous studies conducted in the United States, and France, which were 27.1%, 28.6% respectively (Sim, K et al.2004; Millier, A *et al.*2011), but lower than the results in Singapore, which was 71.7%, (Sim, K et al.2004). Differences in sociodemographic characteristics, individual differences, and the tools used, which involved clinical judgments, may explain disparities in rates of antipsychotic polypharmacy between studies (Adeponle, A. B *et al.*2007). Apart from that, different settings used different inclusion criteria; for example, in the United States, individuals had to be on treatment for at least 2 months (Faries, D *et al.*2005).

In this setting, 43.4% of patients were receiving only one depot antipsychotic medication, and 56.7% were prescribed depot APP which is in consistent with the outcomes of a French study that found that the vast majority of schizophrenia individuals were given antipsychotics orally with depots.. (Millier, A., *et al.*2011).

Our findings also indicated that the prevalence of APP is much higher in young patients than in elderly patients. This finding is similar to that of Constantine RJ's (Constantine, R. J.*et al.*2010) study, which found that antipsychotic polypharmacy is more common in adolescents than in older patients. According to one previous study, the increased prevalence of APP among adult patients may be due to adults at onset is linked to severe illness and worse outcomes. (Kumra, S *et al.*2008).

In his setting, Steinberg L *et al.*(2008) explained that the neurobiological system responsible for self-regulation and control undergoes a complex maturation process during late adolescence and early adulthood. This maturation is accompanied by a decline in prefrontal gray matter due to synaptic pruning, an increase in myelination within the prefrontal cortex, and a proliferation of white matter tracts between cortical and subcortical areas, particularly the prefrontal regions, amygdala, nucleus accumbens,

and hippocampus. The decrease in the prevalence of management of App during late adolescence among adults who do not have long-term severe behavioral disorders or enduring cognitive impairments could be explained by this normal growth and development of neurobiological systems.

Our findings also revealed an increased prevalence of APP in single Malay patients with schizophrenia. This finding is similar to a recent research suggesting that prevalence of APP is more common in single patients (Santone, G *et al.*2011). Unmarried patients are more likely than married patients to have APP, because their illnesses are more severe, chronic, or dangerous.

Furthermore, the high proportion of APP in unemployed individuals found in this study was supported by a study conducted in Turkey by Tesfaye et al. (2016) who found that occupational status was significantly correlated with multiple optimal psychiatric management for these groups.

antipsychotic medications. Patients who receive one or combination of antipsychotics spent the same amount of time in the hospital,. Our findings differed from those of Lerma-Carrillo et al. (2008), who discovered no variation in hospitalization time between individuals receiving APP and those receiving monotherapy, despite the fact that their sample had a longer mean hospitalization time (25.7 and 23.8 days for the monotherapy and APP group, respectively).Mismanagement can result in adverse effects, and mismanaged individulas were more susceptible to be hospitalized than compliant patients due to an increase adverse effects, implying antipsychotic interactions. Long duration of treatment or longer illness correlated significantly with APP, because such individuals had little adequate and insufficient follow-up and were given poor prognoses. Psychiatric patients were also more likely to experience side effects due to repeated antipsychotic drug administration to treat aggravated psychotic symptoms..

In this setting, EPS was found to be higher in individuals prescribed multiple antipsychotics than in patients prescribed with one antipsychotic medication. This outcome was consistent with various settings conducted in the United States, which discovered a high prevalence of APP among EPS patients (Centorrino, F *et al.*2004). This could be because people who have been diagnosed with schizophrenia are taking antipsychotic medications in higher doses than what is required on a daily basis, and they have limited access to SGA.

Conclusion

This study sheds light on the prevalence of APP among Malaysian schizophrenia patients. The results can help healthcare professionals strategize medication treatment to achieve the best clinical outcomes. Future research about the risks and benefits of APP should be prescribed to patients to prevent medication mismanagement. Some studies are required to detect the best way to treat schizophrenia and other psychiatric patients, as well as whether or not it has an impact on the patient's health. Our research makes a contribution to this endeavor by giving information which can be used to recognize patient groups at higher risk of developing APP. Effective schizophrenia treatment should be included in Finally, our results showed that patients who had been sick for longer periods of time were more likely to have

APP. Suokas et al (2013) discovered similar results, indicating that patients who have been in the hospital for an extended period of time have a partial response to various management regimens.

Declarations

FUNDING

The authors state that they received no funding for this research.

CONFLICTS OF INTEREST

No conflict

References

Adeponle, A. B., Obembe, A. O., Adeyemi, S. O., & Suleiman, G. T. (2007). Polypharmacy in psychiatric out-patient practice in northern Nigeria. *African journal of psychiatry*, *10*(4), 215–218. <https://pubmed.ncbi.nlm.nih.gov/19588029/>

Boskailo, E., Malkoc, A., McCurry, D. B., Venter, J., Drachman, D., & Ramos, G. M. (2017). Assessment of inpatient psychiatric readmission risk among patients discharged on an antipsychotic polypharmacy regimen: A retrospective cohort study. *Acta medica academica*, *46*(2), 133–144. <https://doi.org/10.5644/ama2006-124.198>

Centorrino, F., Goren, J. L., Hennen, J., Salvatore, P., Kelleher, J. P., & Baldessarini, R. J. (2004). Multiple versus single antipsychotic agents for hospitalized psychiatric patients: case-control study of risks versus benefits. *The American journal of psychiatry*, *161*(4), 700–706. <https://doi.org/10.1176/appi.ajp.161.4.700>

Constantine, R. J., Boaz, T., & Tandon, R. (2010). Antipsychotic polypharmacy in the treatment of children and adolescents in the fee-for-service component of a large state Medicaid program. *Clinical therapeutics*, *32*(5), 949–959. <https://doi.org/10.1016/j.clinthera.2010.04.021>

Crabtree, B. L., Dostrow, V. G., Evans, C. J., Cuffel, B. J., Alvir, J. M., & Sanders, K. N. (2011). Outcome assessment of an antipsychotic drug algorithm: effects of the Mississippi State Hospital algorithm project. *Psychiatric services (Washington, D.C.)*, *62*(8), 963–965. https://doi.org/10.1176/ps.62.8.pss6208_0963

- Fares M.S Muthanna, Zainal ZA, Che Mi N, & Paneerselvam GS. (2018). The usage of antipsychotic polypharmacy to treat patients with schizo-phrenia and other psychiatric disorders in Hospital Kajang. *International Journal of Research in Pharmaceutical Sciences*, 9(4), 1497-1503. <https://doi.org/10.26452/ijrps.v9i4.1709>
- 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, 26. <https://doi.org/10.1186/1471-244X-5-26>
- Ginovart, N., & Kapur, S. (2012). Role of dopamine D(2) receptors for antipsychotic activity. *Handbook of experimental pharmacology*, (212), 27–52. https://doi.org/10.1007/978-3-642-25761-2_2
- Igbinomwanhia, N. G., Olotu, S. O., & James, B. O. (2017). Prevalence and correlates of antipsychotic polypharmacy among outpatients with schizophrenia attending a tertiary psychiatric facility in Nigeria. *Therapeutic advances in psychopharmacology*, 7(1), 3–10. <https://doi.org/10.1177/2045125316672134>
- Kelleher, J. P., & Baldessarini, R. J. (2004). Multiple versus single antipsychotic agents for hospitalized psychiatric patients: case-control study of risks versus benefits. *The American journal of psychiatry*, 161(4), 700–706. <https://doi.org/10.1176/appi.ajp.161.4.700>
- Koen, L., Magni, P., Niehaus, D. J., & le Roux, A. (2008). Antipsychotic prescription patterns in Xhosa patients with schizophrenia or schizoaffective disorder. *African journal of psychiatry*, 11(4), 287–290.
- Kumra, S., Kranzler, H., Gerbino-Rosen, G., Kester, H. M., DeThomas, C., Cullen, K., Regan, J., & Kane, J. M. (2008). Clozapine versus "high-dose" olanzapine in refractory early-onset schizophrenia: an open-label extension study. *Journal of child and adolescent psychopharmacology*, 18(4), 307–316. <https://doi.org/10.1089/cap.2007.0089>
- Muthanna, Fares Mohammed Saeed. ANTIPSYCHOTIC POLYPHARMACY (INCIDENCE, IMPORTANCE AND SIDE EFFECTS), vol. 2, no. 7, 2021.
- Lerma-Carrillo, I., de Pablo Brühlmann, S., del Pozo, M. L., Pascual-Pinazo, F., Molina, J. D., & Baca-García, E. (2008). Antipsychotic polypharmacy in patients with schizophrenia in a brief hospitalization unit. *Clinical Neuropharmacology*, 31(6), 319–332. <https://doi.org/10.1097/WNF.0b013e31815cba78>
- Millier, A., Sarlou, E., Azorin, J. M., Boyer, L., Aballea, S., Auquier, P., & Toumi, M. (2011). Relapse according to antipsychotic treatment in schizophrenic patients: a propensity-adjusted analysis. *BMC psychiatry*, 11, 24. <https://doi.org/10.1186/1471-244X-11-24>
- Muthanna FMS, Zainal ZA, Che Mi N, Paneerselvam GS (2018) Antipsychotic Polypharmacy among Psychiatric Patients in Hospital Kajang, Malaysia. *J Neurol Disord*

6: 374 . <https://www.hilarispublisher.com/abstract/antipsychotic-polypharmacy-among-psychiatric-patients-in-hospital-kajang-malaysia-37604.html>

Pae C. U. (2020). Antipsychotic Polypharmacy in Treatment of Schizophrenia; Should or Should Not?. *Chonnam medical journal*, 56(3), 157–165. <https://doi.org/10.4068/cmj.2020.56.3.157>

Santone, G., Bellantuono, C., Rucci, P., Picardi, A., Preti, A., & de Girolamo, G. (2011). Patient characteristics and process factors associated with antipsychotic polypharmacy in a nationwide sample of psychiatric inpatients in Italy. *Pharmacoepidemiology and drug safety*, 20(5), 441–449. <https://doi.org/10.1002/pds.2083>

Sim, K., Su, A., Fujii, S., Yang, S. Y., Chong, M. Y., Ungvari, G. S., Si, T., Chung, E. K., Tsang, H. Y., Chan, Y. H., Heckers, S., Shinfuku, N., & Tan, C. H. (2004). Antipsychotic polypharmacy in patients with schizophrenia: a multicentre comparative study in East Asia. *British journal of clinical pharmacology*, 58(2), 178–183. <https://doi.org/10.1111/j.1365-2125.2004.02102.x>

Steinberg L. (2008). A Social Neuroscience Perspective on Adolescent Risk-Taking. *Developmental review : DR*, 28(1), 78–106. <https://doi.org/10.1016/j.dr.2007.08.002>

Suokas, J. T., Suvisaari, J. M., Haukka, J., Korhonen, P., & Tiihonen, J. (2013). Description of long-term polypharmacy among schizophrenia outpatients. *Social psychiatry and psychiatric epidemiology*, 48(4), 631–638. <https://doi.org/10.1007/s00127-012-0586-6>

Tesfaye, S., Debencho, N., Kisi, T., & Tareke, M. (2016). Prevalence of Antipsychotic Polypharmacy and Associated Factors among Outpatients with Schizophrenia Attending Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia. *Psychiatry journal*, 2016, 6191074. <https://doi.org/10.1155/2016/6191074>

Waddington, J. L., Youssef, H. A., & Kinsella, A. (1995). Sequential cross-sectional and 10-year prospective study of severe negative symptoms in relation to duration of initially untreated psychosis in chronic schizophrenia. *Psychological medicine*, 25(4), 849–857. <https://doi.org/10.1017/s0033291700035108>

Yang, S. Y., Chen, L. Y., Najoan, E., Kallivayalil, R. A., Viboonma, K., Jamaluddin, R., Lin, S. K., et al (2018). Polypharmacy and psychotropic drug loading in patients with schizophrenia in Asian countries: Fourth survey of Research on Asian Prescription Patterns on antipsychotics. *Psychiatry and clinical neurosciences*, 72(8), 572–579. <https://doi.org/10.1111/pcn.12676>

Tables

Table 1: Demographic and clinical data for the 113 patients included in the study

Variable		N (%)
Mean age / years (SD)	42.77 (SD 10.25)	
Age / years	≥ 50	52 (46%)
	< 50	61 (54%)
Gender	Males	59 (52.2%)
	Females	54 (47.8%)
Race	Malay	51 (45.1%)
	Indian	33 (29.2%)
	Chinese	25 (22.1%)
	Others	4 (3.5%)
Marital status	Married	49 (43.3%)
	Single	38 (33.6%)
	Divorced	26 (23%)
Body Mass Index (BMI) kg/m ²	Underweight BM (≥ 25)	28 (24.8%)
	Normal	47 (42%)
	Overweight BMI (< 25)	26 (23%)
	Obese	12 (10.6%)
Employment Status	Employed	49 (43.4%)
	Non Employed	64 (56.6%)
Social Status	Smoking	35 (30.1%)
	Non-Smoking	78 (69%)
Duration of illness	< 3 months	33 (29.2%)
	≥ 3 months	80 (70.1%)
Type of APPs	FGA	21 (18.6%)
	SGA	28 (24.8%)
	FGA + SGA	64 (56.7%)
EPS ^a	Yes	58 (51.2%)
	No	55 (48.7%)

a

EPS = Extrapyramidal Symptoms , FGA = First generation antipsychotics, SGA= Second generation antipsychotics

Table 2: Prevalence of APPs among demographic and clinical factors.

Variable		Antipsychotics	
		Monopharmacy Frequency, n= 49	Polypharmacy Frequency, n = 64
Age / years	≥ 50	22 (44.9%)	31 (48.4%)
	< 50	27 (55.1%)	33 (51.6%)
Gender	Males	19 (38.8%)	40 (61.8%)
	Females	30 (61.2%)	24 (38.8%)
Marital status	Married	28 (57.2%)	21 (32.8%)
	Single	19 (29.7%)	19 (70.3%)
	Divorced	2 (4%)	24 (37.5%)
Race	Malay	22 (44.9%)	29 (45.3%)
	Indian	9 (18.4%)	24 (37.5%)
	Chinese	15 (30.6%)	10 (15.7%)
	Others	3 (6.1%)	1 (1.6%)
Employment Status	Employed	28 (57.1%)	21 (32.8%)
	Non Employed	21 (42.9%)	43 (67.2%)
Body Mass Index (BMI) kg/m ²	Underweight BM (≥ 25)	9 (18.4%)	19 (29.7%)
	Normal	25 (51%)	22 (34.5%)
	Overweight BMI (< 25)	8 (16.3%)	18 (28.1%)
	Obese	7 (14.3%)	5 (7.8%)
Social Status	Smoking	12 (24.5%)	23 (36%)
	Non-Smoking	37 (77.5%)	41 (64%)
Duration of illness	< 3 months	22 (44.9%)	11 (17.2%)
	≥ 3 months	27 (55.1%)	53 (82.8%)
EPS ^a	Yes	20 (40.8%)	38 (59.4%)
	No	29 (59.2%)	26 (40.6%)

a

EPS = extrapyramidal Symptoms

Figures

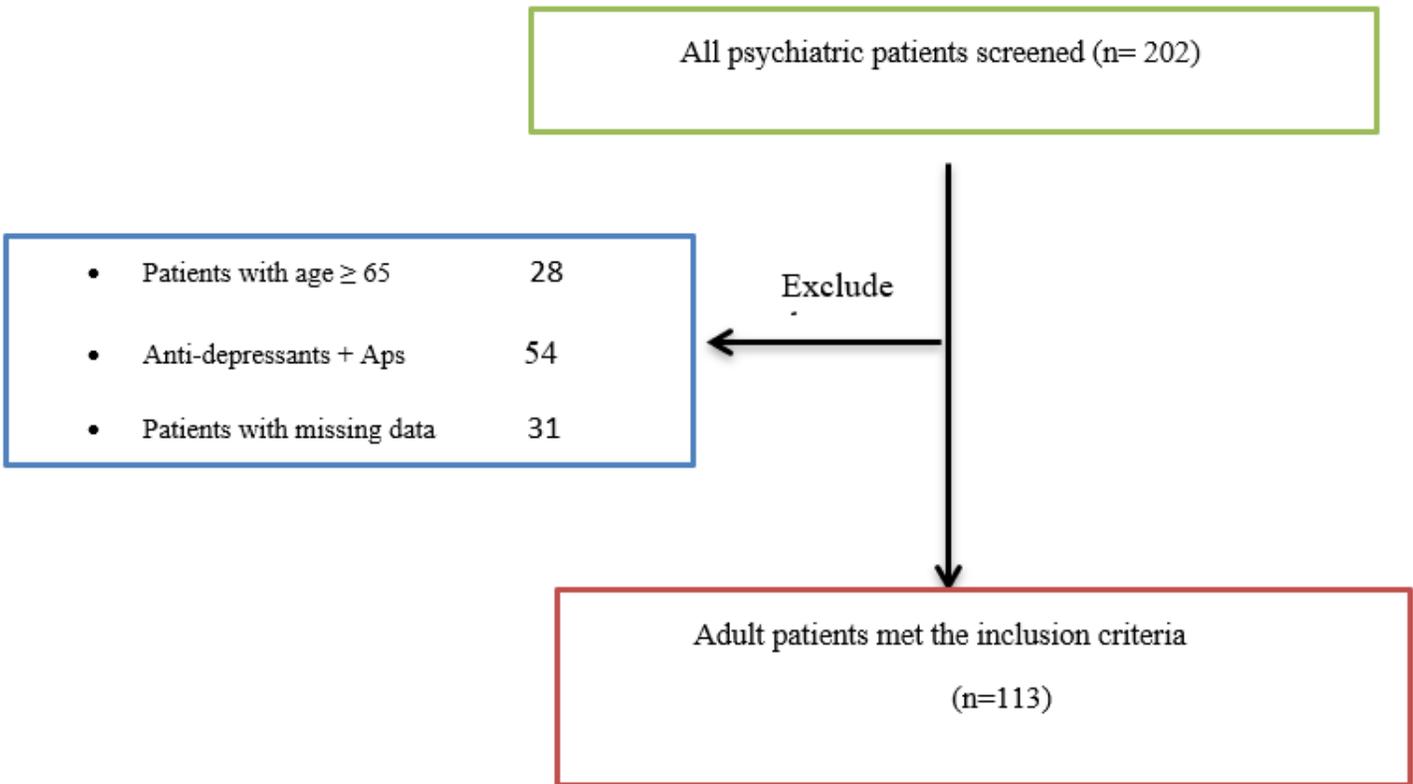


Figure 1

Adult patients with schizophrenia screened during study period