ORIGINAL RESEARCH



Antipsychotic medication non-adherence and its determinants among out-patients with schizophrenia

Paul Erohubie¹, Sunday Oriji^{2*}, Sunday Olotu³, Imafidon Agbonile⁴, Ihechiluru Anozie⁵, Omigie Erohubie⁶, Anthony Enebe⁷, Justus Onu⁸

- 1. Irrua Specialist Teaching Hospital Ringgold standard institution Department of Psychiatry Irrua, Edo State, Nigeria
- 2. Nnamdi Azikiwe University Ringgold standard institution Department of Mental Health, Nnewi campus, Nnewi, Anambra, Nigeria
- 3. Federal Neuro Psychiatric Hospital Ringgold standard institution Clinical services, Benin City, Edo State, Nigeria
- 4. Federal Neuro Psychiatric Hospital Ringgold standard institution clinical services Benin City, Edo State, Nigeria
- 5. Federal Neuro Psychiatric Hospital Ringgold standard institution clinical services, Benin City, Edo State, Nigeria
- 6. Edo State University Uzairue Ringgold standard institution Department of Radiology, Iyamho, Edo State, Nigeria
- 7. Federal Medical Centre Asaba Ringgold standard institution psychiatry, Asaba, Delta State, Nigeria
- 8. Nnamdi Azikiwe University Ringgold standard institution Department of Mental Health, Nnewi Campus, Nnewi, Anambra, Nigeria

*Corresponding Author: Sunday Oriji; E-mail: orijisunday@gmail.com

Abstract

Introduction

While antipsychotics are key requirement in acute and long-term management of schizophrenia, medication adherence remains a major unmet need in its care. This paper assessed the prevalence of oral antipsychotic non-adherence among outpatients with schizophrenia and its associated clinico-demographic factors.

Mathad

Three hundred and ten adult outpatients (18-64 years of age) were cross-sectionally interviewed after being diagnosed of schizophrenia using ICD-10 criteria, and the diagnosis confirmed with the Mini International Neuropsychiatric Interview (MINI). The socio-demographic questionnaire, Morisky Medication Adherence scale (MMAS-8), Brief Psychiatric Rating Scale (BPRS), Liverpool University Neuroleptic Side Effects Scale (LUNSERS), Drug Attitude Inventory (DAI-10), Scale to Assess Unawareness of Mental Disorders (SUMD) were used to obtain participants' demographic profile, level of medication adherence, illness severity, attitude towards antipsychotics, and level of insight respectively.

Results

At least one in every two outpatients with schizophrenia (n=158; 51.0%) did not adhere to their antipsychotics as prescribed. The independent risk factors for poor oral antipsychotic adherence were illness severity (p= 0.001; AOR 1.13), psychoactive substance use (p= 0.009; AOR 1.87), young age (p= 0.014; AOR 2.09), perceived poor social support (p= 0.025; AOR 3.58), use of first generation antipsychotics alone (p= 0.006; AOR 17.99), use of second generation antipsychotics alone (p= 0.02; AOR 29.36), and awareness of symptoms (p= 0.025; AOR 1.18).

Conclusion

The high rate of poor medication adherence should necessitate much emphasis on the highlighted modifiable risk factors and the need for continuous adherence assessments and education in clinical practice.

Keywords: Antipsychotics, adherence, determinants, schizophrenia, Nigeria.

Introduction

Schizophrenia is a chronic deteriorating mental disorder that is usually associated with disruption in cognition, emotion, behaviour, psychosocial and occupational functioning. The World Health Organisation (WHO) lists schizophrenia as one of the top six leading cause of disability and affects about 24 million persons worldwide¹.

The disabilities result from the early onset and contribute to chronicity of schizophrenia across the life span. Schizophrenia impact negatively on the patient's ability to engage in productive work and social relationships, and sufferers are more likely to die from potentially preventable medical conditions². The higher mortality is attributed to poor adherence to medical treatments, economic disadvantages and negative health behaviours².

Antipsychotic medications play an important role in schizophrenia treatment and symptom control. Effective management of schizophrenia however requires continuous

long term treatment with medications². Several antipsychotic medications are available with proven efficacy in reducing the symptoms of schizophrenia and other psychotic disorders, improving the wellbeing of patients and enabling them to live meaningful lives. However, poor medication adherence is common^{3,4} and leads to poor clinical outcomes, personal suffering and increased burden of care for relatives and significant others.

Adherence is defined as the extent to which the patient's behaviour (in terms of taking medications, following diets, or executing other lifestyle changes) matches medical recommendations jointly agreed between patient and prescriber⁵. Poor adherence to antipsychotic medication is associated with relapse, re-hospitalization, poor mental functioning, increased suicidal behaviours, simultaneous poor adherence to medications for co-morbid conditions, increased mortality and higher healthcare costs^{2,5}. A recent systematic review and meta-analysis reported that 56.0% of patients with schizophrenia do not take their

© 2024 Kamuzu University of Health Sciences and the Medical Association of Malawi. This work is licensed under the Creative Commons Attribution 4.0 International License. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

medications as prescribed⁶. In order to reduce this high rate and aforementioned negative consequences associated with medication non-adherence, clinicians are increasingly interested in its evaluation.

In Nigeria, very few studies⁷⁻⁹ have looked at factors associated with poor medication adherence in psychiatric settings, and only one recent study 10 worked exclusively on schizophrenia. Hence, this study aimed to focus on this less studied diagnostic entity with respect to evaluating the determinants of poor antipsychotics adherence among outpatients with schizophrenia.

Method

Study design

This was a cross-sectional study.

Study setting

The study was carried out at the out-patients department (OPD) of the Federal Neuropsychiatry Hospital (FNPH), Benin City, Nigeria. The hospital is a 230 bed facility and provides in-patient and out-patient care as well as emergency services to walk-in and referral cases.

Study Population

This comprised 310 adult patients attending the outpatient clinic of the FNPH. The consented individuals aged between 18 and 64 years, who were diagnosed of schizophrenia using International Classification of Diseases (ICD-10) criteria, and the diagnosis confirmed with the Mini International Neuropsychiatric Interview (MINI) were recruited. The participants must have been on antipsychotic medications for at least two months prior to enrolment in the study. Participants with co-morbid physical and psychiatric disorders, those on depot antipsychotic medications only, and those receiving anticholinergic medications were excluded.

Ethical Consideration

Ethical approval was obtained from the Ethics and Research Committee of the Federal Neuro-Psychiatric Hospital, Benin City, Nigeria with protocol number PH/A,864/Vol, IV/38.

Study instruments

Socio-demographic Questionnaire

A socio-demographic questionnaire was developed by the researchers which comprised of two sections. Section A consisted of socio-demographic characteristics of patients including age, gender, religion, marital status, education, employment, monthly household income and cost of medications per month. Section B consisted of characteristics such as psychoactive substance use (lifetime and 12- months use), number of previous hospital admissions, class of antipsychotics currently on (typical or atypical antipsychotics and mixed), number of antipsychotic medications taken per day, dosage regimen, frequency of out-patient visits, living circumstance (living alone, living with spouse, with relatives or with friends) and perceived levels of social support (the options include 'good', 'fair', 'poor').

Morisky 8-item Medication Adherence scale (MMAS-8)

The level of medication adherence in this study was defined by the application of MMAS-8. It is a reliable and validated 8-item self-reported measure of medication use patterns in psychiatric patients¹¹. Scores obtained from this scale ranged from 0 to 8, where higher scores indicated poorer adherence. For the purpose of this study, poor medication adherence was defined as MMAS-8 score of greater than 0 (sum of low and medium adherence) while score of 0 was considered adherent.

Mini International Neuropsychiatric Interview (M.I.N.I) English version 6.0.0

The MINI, a short structured diagnostic interview was used to confirm the diagnosis of schizophrenia in patients who were selected for the study. The reliability and validity of the MINI is similar to the Composite International Diagnostic Interview (CIDI), a widely accepted standardized tool¹². The psychosis module of the MINI was used in this study.

Brief Psychiatric Rating Scale (BPRS)

The BPRS 13 was used to assess the severity of symptoms of participants in this study.

It contains 18 ordered categories of symptoms of mental illnesses. A 7-point rating scale is used ranging from 1-'not present', to 7- 'extremely severe'. Scores of each item on the scale are summed up to give a total score which is an index of severity.

Liverpool University Neuroleptic Side Effects Scale (LUNSERS)

The LUNSERS was used to assess the presence or otherwise of side effects of participants in this study. The scale consists of 41 known side effects of neuroleptics, plus 10 "red herring" items (referring to symptoms which are not known side effects) scored on a five point rating scale of 0-4 (0 = "not at all",4 = "very much"). The scores for each group of side effects were summed up to give a total score. It has good reliability and validity (Cronbach alpha of 0.89)¹⁴.

Drug Attitude Inventory (DAI-10)

The 10-item version of DAI-10 was used to assess the attitudes of participants towards antipsychotic medications. It assesses attitudes, experience, and belief about antipsychotics medications, and it has been validated among patients with schizophrenia in Nigeria with Cronbach's alpha of 0.56¹⁵. Positive scores indicated positive attitude towards antipsychotic medications while negative scores indicated negative attitude towards antipsychotic medications. A score of zero indicated neutral attitude towards medications.

Scale to Assess Unawareness of Mental Disorders (SUMD)

The insight of participants was assessed using this scale. It consisted of a total of eleven domains and six items which describe 3 dimensions: awareness of the mental disorder and response to medications (items 1–2), level of awareness of positive symptoms (items 3–4) and level of awareness of negative symptoms (items 5–6). Each of these domains is rated on a Likert scale. Thus 1-2 is scored as being insightful, while 3-6 is scored as poor insight for each domain.

Procedure

Systematic random sampling method was employed in this study. The first participant for each clinic day was selected by simple random sampling using a table of random numbers. Subsequent participants for each day were selected according to the calculated sampling interval of 2. A written informed consent was obtained from the participants and the instruments were researcher-administered. This process continued per clinic day until the desired sample size was obtained.

Table 1: Socio-demographic Characteristics of Participants.

Variable	Parameters	Frequency	Percentage
Age (years)	18-30	78	25.1
	31-36	91	29.4
	37-42	61	19.7
	43-64	80	25.8
Gender	Male	166	53.5
	Female	144	46.5
Marital Status	Married	90	29.0
	Never married	217	70.0
	Separated	3	1.0
Educational status	No Formal Education	5	1.6
	Primary	68	21.9
	Secondary	133	42.9
	Post-secondary	104	33.6
Employment status	Unemployed	177	57.1
	Employed	133	42.9
Monthly Income (₦)	2,000 – 13,000	78	25.2
	13,001 – 28,500	77	24.8
	28,501 – 60,000	81	26.1
	60,001 – 310,000	74	23.9
Medications cost/month (₦)	250 – 1,000	93	30.0
	1,001 – 2,510	62	20.0
	2,511 – 4,000	90	29.0
	4,001 – 50,000	65	21.0

The case note of patients sampled each day was tagged to prevent being sampled more than once in the course of the study.

Data analysis

Data was captured using a paper questionnaire and entered into an electronic spread sheet (SPSS version 23). Descriptive statistics were used to summarise the data and presented in tables. Comparison of categorical variables with outcome variable was performed using the Chi-squared test. The outcome variable was dichotomized into poor/good adherence. Low/medium adherence on the MMAS (Score1-8) was classed as "poor adherence" while high adherence on the MMAS (Score 0) was classed as "good adherence".

The following categorical variables were dichotomized for the purpose of cross tabulations; age was dichotomized using the median age, marital status was dichotomized into married/others, educational status was dichotomized into <12 years (no formal education, primary and secondary) and >12years (post-secondary), living status (living alone/living with relatives, spouse, parents, others).

The continuous variables including age, number of previous admissions, medications taken, dosage, BPRS scores, DAI-10 scores, LUNSERS scores, SUM-D scores, monthly income, cost of medications/month, and frequency of outpatient visits were tested for normality of data using the one-sample Kolmogorov-Smirnov tests and were all found to be non-normally distributed. Continuous data were then compared with the outcome variable poor/good adherence using the Mann-Whitney U test.

Significant associations with poor medication adherence on bivariate analysis were entered into a binary logistic regression model using poor/good medication adherence as the outcome variable to ascertain predictors of poor medication adherence. The model fit well into the data (Hosmer and Lemeshow: p=0.55) and explained 40.9% in data variance. All comparisons were two-tailed and level of significance was set apriori at p<0.05.

Table 2: Clinical-related characteristics of participants

Variable	Parameter	Frequency	Percentage
12-month psychoactive substance use	Yes	91	29.4
	No	219	70.6
Lifetime psychoactive substance use	Yes	186	60.0
	No	124	40.0
Pattern of psychoactive substance use	No use	124	40.0
	Alcohol alone	114	36.8
	Cannabis alone	2	0.6
	Tobacco alone	11	3.5
	Alcohol+Cannabis	9	2.9
	Alcohol+Tobacco	24	7.8
	Cannabis+Tobacco	14	4.5
	Alcohol+Cannabis+Tobacco	12	3.9
Number of previous admissions	None	260	83.9
	One	30	9.7
	Two	15	4.8
	Three or more	5	1.6
Frequency of outpatient visits/year	Twelve	226	72.9
	Eight	30	9.7
	Six	42	13.5
	Four	8	2.6
	Less than four	4	1.3
Duration since last admission	Less than one year	5	10.0
	One to five years	20	40.0
	Six to ten years	13	26.0
	Over ten years	12	24.0
Class of antipsychotics used	Typicals	126	40.6
	Atypicals	168	54.2
Attitude to medication (DAI-10)	Mixed Negative	16	5.2 3.55
nulude to medication (DAI-10)	Neutral	11	3.55
	Positive	288	92.9
Medication adherence (MMAS-8)	Poor/Low	116	37.4
	Fair/Medium	42	13.6
	Good	152	49.0

Results

Table 1 shows the socio-demographic characteristics of participants. The female to male ratio was 0.87 to 1. Majority (n=91; 29.4%) were in the range of 31-36 years. Majority of the participants (97%) were Christians and 186 (60%) were never married. At least one in four (n=237; 76.5%) had a minimum of secondary education while more than half (n=177; 57.1%) were unemployed. One-hundred and fifty-five (50%) of the participants and/or their relatives earned less than N28, 500 (\$79.0) per month. Half of the participants (50%) spent less than N2\$, 510 (\$7.0) on medications monthly. One in every ten (n=32; 10.3%) perceived they had poor social support (Table 1).

At least one in two participants had poor antipsychotic medication adherence (n=158; 51.0%). Ninety-one participants (29.4%) had used psychoactive substance in the twelve month preceding the study. The commonest psychoactive substance used was alcohol (51.3%). Nearly one-fifth (n=59; 19.1%) of the participants used more than one psychoactive substances. Within the year preceding the study, majority of the participants (n=226; 72.9%) had attended the clinic 12 times (Table 2). Majority received atypical antipsychotic medication (n=168; 54.2%), and excellent number of them had good attitude to antipsychotic medications (n=288; 92.9%) (Table 2). The mean BPRS score was 24.43 (S.D= 9.28), mean SUMD score was 21.29 (S.D=9.49) while the mean LUNSERS score was 4.89 (S.D=6.34) (Table 3).

Age less than 36 years (p<0.02), perceived poor social support (p<0.001), and lower cost of medications (p<0.001) were significantly associated with poor medication adherence (Table 4). The clinical parameters significantly associated with poor medication adherence in this study included: 12-month psychoactive substance use (p<0.04), use of first generation antipsychotics alone (p<0.001), more severe illness (p<0.001), awareness of symptoms (p<0.001), awareness of positive symptoms (p<0.001) (Table 6). The participants with psychic side effects (p<0.003) and poor attitude to medication (p<0.001) were significantly associated with poor medication adherence (Table 6).

On regression analysis, there is thirteen per cent likelihood of poor medication adherence in a unit rise in illness severity (p<0.001, AOR 1.13). The use of psychoactive substance at least 12 months prior to the study, predicts poor medication adherence (p<0.009, AOR 1.87). The participants were at least twice and thrice more likely to ignore their antipsychotics if they were younger in age (p=0.014; AOR 2.09) and had perceived poor social support (p<0.025, AOR 3.58), respectively. The use of first generation antipsychotics alone (p<0.006, AOR 17.99), use of second generation antipsychotics alone (p<0.025, AOR 29.36) and being aware of their symptoms (p<0.025, AOR 1.18) were independent predictors of poor medication adherence (Table 7).

Discussion

The observed poor medication adherence rate of 51% in this study appears to be well within the previously reported range of 15.8% to 77.7% for patients with schizophrenia^{4,7,10,16–19}. While several studies reported lesser poor adherence rates^{4,10,17,18,20} than ours, some had higher poor adherence rates^{7,16,21–23}. Possible reasons for the inconsistent rates may be due to differences in methodology- the study instruments, heterogeneity in the definition of adherence and population

studied.

Most of the participants in this study had positive attitude towards medication, similar to the finding of Adewuya et al¹⁹ and Nagai et al,²⁴ Although not statistically significant on multivariate analysis, the observed positive attitude towards medication adherence by a majority of participants may present a vista of opportunity that can be explored in the design of clinical interventions towards improving medication adherence. Adherence is hinged on positive attitudes towards prescribed medications^{24,25}. However, patients may be favourably disposed to taking medications (cognitive) but lack the affective and behavioural components of attitude and hence may not take the prescribed medications. This could explain our finding of poor medication adherence amidst good positive attitude towards medications (92.9%). Some other reasons could also be adduced for this finding. First, the strict definition of "adherence" in this study as MMAS score of zero may have accounted for this observation. If a patient failed to take his/her medications only once, he was considered to have poor adherence. Secondly, few participants preferred to be interviewed in company of their relatives. They may have expressed good attitude towards medications as a way of giving good impression about themselves before their relatives (social desirability bias) when in fact they were not taking their medication correctly as prescribed. This underscores the need for carers to monitor and supervise the medication-taking behaviours of their relatives with schizophrenia and encourage them to be adherent.

In this study, participants with psychic side effect (excessive sedation only) were significantly more likely to be poorly adherence to their medications compared with those who had no side effects, though the significance was not sustained on multivariate analysis. It is not merely the presence of side effects that is the problem but lack of knowledge about the danger or otherwise of each side effect experienced that makes patients not to continue their medications. It is important to acknowledge this, not only in the acute treatment of schizophrenia but also during maintenance treatment. Similar to the findings in this study, Eticha et al in Ethiopia found that unpleasant side effects of medications were significantly associated with poor medication adherence²⁰.

Available body of evidence suggests inconsistent relationship between patients' socio-demographic characteristics and medication non-adherence⁶. Unlike Eticha et al²⁰ in Ethiopia, who reported that older patients (60 years or above) were more likely to be non-adherent to prescribed antipsychotics, we found only age factor (younger age <36years) being a predictor of poor medication adherence among participants. This is similar to finding by Brodeur et al 21 among psychiatric patients in Quebec. The younger ones may skip doses or quit taking their medications for fear of being stigmatized that they have chronic illness like schizophrenia, especially when they get married or get a new job. This may not be unrelated to previously established evidence that stigma is a major barrier to medication adherence²⁶⁻²⁸. More so, having a challenging job, sedation at work, and studying for examinations are possible reasons why the young may be poorly adherent when compared to older persons with schizophrenia.

Consistent with our finding, Semahegn et al⁶, Osasona et al⁷ and Taru et al¹⁰ had reported significant relationship between poor social support and poor medication adherence among patients with psychiatric illnesses.

Table 3: Clinical related characteristics (continuous variables) of participants

Variable	Parameter	Range	Mean	Median	Standard deviation
Severity of psychopathology	of BPRS Scores	18 - 68	24.43	20.00	9.28
Insight (SUM-D)	Awareness of symptoms	2 – 15	5.75	5.00	2.93
	Awareness of positive symptoms				
	Awareness of negative symptoms	0 – 20	7.49	6.00	4.09
	Total Score	0 – 20	8.06	8.00	5.36
		4 – 50	21.29	20.00	9.49
Side-effect (LUNSERS)	Total Score	0 – 32	4.89	3.00	6.34
	Allergic	0 – 2	0.01	0.00	0.16
	Psychic	0 – 17	1.96	0.00	3.52
	Hormonal	0 – 8	0.78	0.00	2.21
	Anticholinergic	0 – 8	0.23	0.00	0.98
	Extrapyramidal	0 – 19	1.20	0.00	3.18
	Autonomic	0 – 7	0.12	0.00	0.67
	Miscellaneous	0 – 8	0.61	0.00	1.50

Table 4: Socio-demographic correlates of poor medication adherence

Variable	Poor adherence	Good	Statistics		
		adherence			
	N=156 (%)	N=154 (%)	[]2	df	Р
Age					
< 36 years	95 (56.2)	74 (43.8)	5.16	1	0.02
≥ 36 years	61 (43.3)	80 (56.7)			
Gender					
Male	82 (49.4)	84 (50.6)	0.12	1	0.73
Female	74 (51.4)	70 (48.6)			
Marital status					
Married	40 (36.4)	50 (63.6)	1.73	1	0.19
Not married	116 (52.7)	104 (47.3)			
Educational status					
< 12 years	40 (51.9)	33 (48.1)	0.76	1	0.38
≥ 12 years	116 (48.9)	121 (51.1)			
Employment					
Unemployed	91 (51.4)	86 (48.6)	0.19	1	0.66
Employed	65 (48.9)	68 (51.1)			

Living status					
Alone	16 (48.5)	17 (51.5)	0.05	1	0.82
With others Perceived social support	140 (50.5)	137 (49.5)			
Poor	26 (81.3)	6 (18.7)	16.82	2	0.001
Fair	50 (54.3)	42 (45.7)			
Good	80 (43.1)	106 (56.9)			

Key: \mathbb{P}^2 = Chi-square test. df = degree of freedom. p= P-value.

Table 5: Clinical correlates of poor medication adherence

Variable	Poor adherence	Good adherence	Statistics	
	N=156 (%)	N=154 (%)	<u></u> 2	Р
Lifetime psychoactive substance use				
Yes	97 (52.2)	89 (47.8)	0.62	0.43
No	59 (47.6)	65 (52.4)		
12-month psychoactive substance use				
Yes	54 (59.3)	37 (40.7)	4.19	0.04
No	102 (46.6)	117 (53.4)		
Class of antipsychotics				
FGAs	78 (61.9)	48 (38.1)	17.65	0.001
SGAs	76 (45.2)	92 (54.8)		
FGA+SGA	2 (12.5)	14 (87.5)		

Key

□² = Chi-square test

p= P-value

There are plausible reasons for this observation. First, absence of good social support in a family could lead to poor medication supervision. Family members and or carers often help to remind patients to take their medications and thus reinforce medication-taking behaviour in their relatives/clients with psychiatric illnesses.

Secondly, significant others often give practical support to patients in terms of purchasing their medications, helping with household chores, and providing transportation. This may help them cope better with their illness and possibly improve adherence to medications. Thirdly, lack of emotional support in particular (which is a subset of social support) may have contributed more to the scenario observed in this study. Emotional support involves meeting unmet needs and providing succor.

In this study, use of psychoactive substance and illness severity were independent predictors of poor medication adherence. This is in tandem with findings from previous studies^{20,21,23,29}. Some possible reasons for these results may be as follows: alcohol may induce liver enzymes which accelerate the degradation of antipsychotics, thus giving the impression that the medications are ineffective and may result in poor adherence. Psychoactive substance use

worsens illness symptoms, and patients who experience severe symptoms despite medication intake may view the medications as not working, hence may stop taking them. Also, patients with severe symptoms may lack insight, thus refuse to take medications believing they are not beneficial. Furthermore, the side effects of medications being taken may give subjective experience of worsening symptoms and as such patients may stop taking the medications. In view of the fact that psychotic state often comes with a burden of paranoid beliefs, it may therefore not be far-fetched to infer that a possible contributing factor to non-adherence may be the paranoid perception of actions undertaken by the attending physicians as well as caregivers as potentially harmful. A confounding observation in this study is that those on combination of typical and atypical antipsychotics had better adherence than those using either medication.

Although evidence from research had shown that there is controversy on greater efficacy in antipsychotic polypharmacy over antipsychotic monopharmacy³⁰. Some explanations could be suggested for the findings in this study. Low potency antipsychotic drugs such as chlorpromazine are often used in the study centre to manage complaints of insomnia in patients on less sedating atypical antipsychotic.

Table 6: Clinical correlates (continuous variables) of poor medication adherence

Variable		Poor adherence	Good adherence	U	Р
		Median	Median		
BPRS		23	19	7,516	0.001
SUM-D	Awareness of symptoms	7	4	20,386	0.001
	Awareness of positive symptoms	7	6	21,805	0.01
	A wareness of negative symptoms	9	7.5	22,716	0.12
	Total Scores	22	18	21,106	0.001
DAI-10		6	8	20,523	0.001
LUNSERS	Total Score	4	0	22,813	0.13
	Allergic	0	0	23,79	0.16
	Psychic	0	0	21,996	0.003
	Hormonal	0	0	23,664	0.42
	Anticholinergic	0	0	23,344	0.07
	Extrapyramidal	0	0	24,001	0.62
	Autonomic	0	0	23,564	0.25
	Miscellaneous	0	0	23,801	0.35
Duration since last admission (years)		4.5	7	220	0.11
Frequency of outpatient visits/		12	12	11,435	0.35
D o s a g e regimen		1	1	11,962	0.92
Number of medications aken/day		1	1	11,488	0.45

Key: U = Mann-Whitney-U test.

p = P-value.

This consequential sleep enhancing effect experienced by the patients may make them more adherent to all the prescribed medications. Also, participants who may have experienced troublesome side effects on a high dose of either type of antipsychotics may be given a combination of both typical and atypical antipsychotics at lower doses to resolve the problems of side effects. Because of the high illiteracy level in this clime, patients give more regards to multiples of drug types than a single medication type dispensed to them after consultation, hence are likely to ignore monotherapy in

favour of polypharmacy. The only part of insight that was an independent risk factor for poor medication adherence in this study was 'being aware of symptoms', in line with Buchman-Wildbaum et al²⁸ result where being aware of illness, and not need for treatment, had no prediction for adherence.

This means that though participants were aware they had symptoms of mental illness, they did not take their medications as prescribed. The causal attribution of the

Table 7: Predictors of poor medication adherence

Variable	В	SE	Wald	OR(95%CI)	Р
Constant	-4.67	1.34	12.20		
Use of psychoactive substance (12 months)	-0.87	0.33	6.82	1.87 (0.219-0.806)	0.009
Gender	-0.47	0.31	2.41	0.62 (0.342-1.132)	0.120
Perceived social support					
Good (ref.)				1	
Fair	0.31	0.31	0.98	1.36 (0.74-2.51)	0.32
Poor	1.28	0.57	5.01	3.58 (1.25-11.06)	0.025
Younger age (<36 years)	0.74	0.30	6.05	2.09 (1.16-3.78)	0.014
Psychic side effects (LUNSERS)	0.06	0.04	1.96	1.06 (0.98-1.16)	0.16
Type of antipsychotic					
FGA+SGA (ref.)				1	
SGA only	3.38	1.07	9.95	29.36 (3.59-239.72)	0.002
FGA only	2.89	1.06	7.49	17.99 (2.28-141.78)	0.006
BPRS	0.13	0.03	23.95	1.13 (1.08-1.20)	0.001
Insight (SUM-D)					
Aware of symptoms	0.17	0.07	5.04	1.18 (1.02-1.36)	0.025
Aware of positive symptoms	-0.02	0.06	0.16	0.98 (0.88-1.09)	0.68
Total insight score	-0.02	0.03	0.62	0.98 (0.92-1.04)	0.43
Cost of medication	0.00	0.00	2.52	1.00 (1.00-1.00)	0.112

Key: B= Regression coefficient. SE = Standard Error of Regression coefficient. Wald = Wald Chi-square. OR= Odd ratio. P= p-value.

symptoms experienced may be a reason for this finding. Participants may be aware of their unusual experiences such as hearing voices of unseen people, hearing their thoughts spoken aloud or seeing things invisible to others in their clear consciousness, but attribute these experiences to spiritual or traditional causes, as commonly seen in this part of the world. They may therefore seek healing/spiritual treatment and ignore prescribed orthodox medications. This is contrary to the findings by earlier studies^{22,29}, in which lower level of insight was a predictor of sub-optimal adherence. Differences in the methodology and population of patients studied could have accounted for this discrepancy. While we studied individuals with schizophrenia, El Abdellati et al²⁹ and Elowe et al²² populations were heterogeneous. Insight may vary with diagnoses.

Besides the relatively large sample size, the use of validated tools for case ascertainment and measurement of important outcomes, and focusing exclusively on patients with schizophrenia were the strengths of this study. Patients who had been on antipsychotic medication for at least two months were selected for this study. This lower limit of two months from commencement of antipsychotics is brief for long term side effects of antipsychotics to be detected, and that was also a shortcoming for this work. Lastly, adherence was evaluated by patients' self-report, which is prone to bias and inaccuracy.

In conclusion, this study demonstrated high prevalence of poor adherence to antipsychotic medications among persons with schizophrenia. Poor medication adherence was independently predicted by active use of psychoactive substances, perceived poor social support, younger age, use of first or second generation antipsychotics only, awareness of symptoms and more severe psychopathology. Because of the high rate of poor medication adherence there is a need for continuous adherence assessments in clinical practice and emphasis on the importance of medication adherence.

Authors' contribution statements

E.P.O, A.I.O, O.S.O* conceptualized and designed the study. E.P.O, A.I.G, E.O.A and O.S.O collected and analysed the data. O.S.O, and O.J.U drafted the initial manuscript, and all authors perused, made input in the final manuscript.

Conflicting interest

None.

Funding

The research was funded only by the authors.

Data availability

The data of this study can be made available upon request.

References

- 1. WHO. Schizophrenia [Internet]. [cited 2023 Mar 6]. Available from: https://www.who.int/news-room/fact-sheets/detail/schizophrenia
- 2. Peritogiannis V, Ninou A, Samakouri M. Mortality in Schizophrenia-Spectrum Disorders: Recent Advances in Understanding and Management. Healthcare. 2022 Dec;10(12):2366.
- 3. Cho SJ, Kim J, Lee JY, Sohn JH. Adherence to Antipsychotic Drugs by Medication Possession Ratio for Schizophrenia and Similar

Psychotic Disorders in the Republic of Korea: A Retrospective Cohort Study. Clin Psychopharmacol Neurosci. 2022 Aug 31;20(3):491–7.

- 4. Yaegashi H, Kirino S, Remington G, Misawa F, Takeuchi H. Adherence to Oral Antipsychotics Measured by Electronic Adherence Monitoring in Schizophrenia: A Systematic Review and Meta-analysis. CNS Drugs. 2020 Jun;34(6):579–98.
- 5. World Health Organization. Adherence to long-term therapies: evidence for action [Internet]. World Health Organization; 2003 [cited 2023 Mar 11]. Available from: https://apps.who.int/iris/handle/10665/42682
- 6. Semahegn A, Torpey K, Manu A, Assefa N, Tesfaye G, Ankomah A. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Systematic Reviews. 2020 Jan 16;9(1):17.
- 7. Osasona SO, Ehimigbai M. Factors associated with non-adherence to medication among psychiatric out-patients in Benin-City, Nigeria. Nigerian Journal of Family Practice. 2021;12(3):63–72.
- 8. James BO, Omoaregba JO. Prevalence and predictors of poor medication adherence among out-patients at a psychiatric hospital in Benin City, Nigeria. Int J Psychiatry Clin Pract. 2011 Mar;15(1):27–34.
- 9. Ibrahim AW, Yahya S, Pindar SK, Wakil MA, Garkuwa A, Sale S. Prevalence and predictors of sub-optimal medication adherence among patients with severe mental illnesses in a tertiary psychiatric facility in Maiduguri, North-eastern Nigeria. The Pan African Medical Journal [Internet]. 2015 May 21 [cited 2023 Mar 11];21(39). Available from: https://www.panafrican-med-journal.com/content/article/21/39/full
- 10. Taru MY, Bamidele LI, Faith AO, Philip TF, Allagoa EL, Izevbokun OH. Medication Non-Adherence and Disability among Outpatients with Schizophrenia in North-Central Nigeria. Journal of Biosciences and Medicines. 2022 Sep 1;10(9):86–117.
- 11. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. J Clin Hypertens (Greenwich). 2008 May 2;10(5):348–54.
- 12. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59 Suppl 20:22-33;quiz 34-57.
- 13. Overall JE, Gorham DR. The brief psychiatric rating scale. Psychological Reports. 1962 Jun 1;10(3):799–812.
- 14. Morrison P, Gaskill D, Meehan T, Lunney P, Lawrence G, Collings P. The use of the Liverpool University Neuroleptic Side-Effect Rating Scale (LUNSERS) in clinical practice. The Australian and New Zealand journal of mental health nursing. 2001 Jan 1;9:166–76.
- 15. Sowunmi OA. Psychometric properties of Drug Attitude Inventory among patients with schizophrenia. The South African Journal of Psychiatry: SAJP: the Journal of the Society of Psychiatrists of South Africa [Internet]. 2022 [cited 2023 Mar 11];28. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9082242/
- 16. Daneault JG, Maraj A, Lepage M, Malla A, Schmitz N, Iyer SN, et al. Medication adherence in first episode psychosis: The role of pre-onset sub-threshold symptoms. Acta Psychiatr Scand. 2019 Apr;139(4):336–47.
- 17. Tan C, Abdin E, Liang W, Poon LY, Poon NY, Verma S. Medication adherence in first-episode psychosis patients in Singapore. Early Interv Psychiatry. 2019 Aug;13(4):780–8.

- 18. Ogunnubi OP, Olagunju AT, Aina OF, Okubadejo NU. Medication Adherence Among Nigerians with Schizophrenia: Correlation Between Clinico-Demographic Factors and Quality of Life. Ment Illn. 2017 Mar 22;9(1):6889.
- 19. Adewuya AO, Owoeye OA, Erinfolami AR, Coker AO, Ogun OC, Okewole AO, et al. Prevalence and correlates of poor medication adherence amongst psychiatric outpatients in southwestern Nigeria. Gen Hosp Psychiatry. 2009;31(2):167–74.
- 20. Eticha T, Teklu A, Ali D, Solomon G, Alemayehu A. Factors Associated with Medication Adherence among Patients with Schizophrenia in Mekelle, Northern Ethiopia. PLOS ONE. 2015 Mar 27;10(3):e0120560.
- 21. Brodeur S, Courteau J, Vanasse A, Courteau M, Stip E, Fleury MJ, et al. Association between previous and future antipsychotic adherence in patients initiating clozapine: real-world observational study. The British Journal of Psychiatry. 2022 Jun;220(6):347–54.
- 22. Elowe J, Ramain J, Solida A, Conus P, Golay P. Dynamics between insight and medication adherence in first-episode psychosis: Study of 3-year trajectories. Eur Psychiatry. 2022 Aug 15;65(1):e49.
- 23. Vega D, Acosta FJ, Saavedra P. Nonadherence after hospital discharge in patients with schizophrenia or schizoaffective disorder: A six-month naturalistic follow-up study. Comprehensive Psychiatry. 2021 Jul 1;108:152240.
- 24. Nagai N, Tani H, Yoshida K, Gerretsen P, Suzuki T, Ikai-Tani S, et al. Drug Attitude, Insight, and Patient's Knowledge About Prescribed Antipsychotics in Schizophrenia: A Cross-Sectional Survey. Neuropsychiatr Dis Treat. 2020 Mar 23;16:781–7.
- 25. Aguglia A, Fusar-Poli L, Natale A, Amerio A, Espa I, Villa V, et al. Factors Associated with Medication Adherence to Long-Acting Injectable Antipsychotics: Results from the STAR Network Depot Study. Pharmacopsychiatry. 2022 Nov;55(6):281–9.
- 26. Abdisa E, Fekadu G, Girma S, Shibiru T, Tilahun T, Mohamed H, et al. Self-stigma and medication adherence among patients with mental illness treated at Jimma University Medical Center, Southwest Ethiopia. International Journal of Mental Health Systems. 2020 Jul 29;14(1):56.
- 27. Masa R, Zimba M, Tamta M, Zimba G, Zulu G. The association of perceived, internalized, and enacted HIV stigma with medication adherence, barriers to adherence, and mental health among young people living with HIV in Zambia. Stigma and Health. 2022;7:443–53.
- 28. Buchman-Wildbaum T, Váradi E, Schmelowszky Á, Griffiths MarkD, Demetrovics Z, Urbán R. Targeting the problem of treatment non-adherence among mentally ill patients: The impact of loss, grief and stigma. Psychiatry Research. 2020 Aug 1;290:113140.
- 29. El Abdellati K, De Picker L, Morrens M. Antipsychotic Treatment Failure: A Systematic Review on Risk Factors and Interventions for Treatment Adherence in Psychosis. Front Neurosci. 2020 Oct 9;14:531763.
- 30. Lin SK. Antipsychotic Polypharmacy: A Dirty Little Secret or a Fashion? International Journal of Neuropsychopharmacology. 2020 Mar 25;23(2):125–31.