Persistence in Treatment for One Year Among Patients in Nigeria With First-Episode Schizophrenia

Oluyomi Esan, M.B.B.S., F.W.A.C.P.

Objective: **The aim of this study was to examine the magnitude of poor persistence in treatment among patients with schizophrenia and to identify associated factors.** ***Methods:*** **All eligible patients (N=216) seen at the University College Hospital in Ibadan, Nigeria, over a five-year period were retrospectively followed up until the time of their last visit. Time to first default was examined by Kaplan-Meier survival analyses. A log-rank test was used to compare survival times for different variables. The contribution of the variables that affected time to default was examined by Cox regression analysis.** ***Results:*** **Only 24% of the sample remained in treatment at the one-year follow-up. Persistence as measured by mean±SE time to all-cause treatment default was 17.80±1.44 weeks. Of several variables examined, including whether patients were taking first- or second-generation antipsychotics, none were found to predict persistence.** ***Conclusions:*** **Persistence in treatment of patients with a first episode of schizophrenia was low. (*Psychiatric Services* 65:1174–1176, 2014; doi: 10.1176/appi.ps.201300294)**

Effective control of schizophrenia symptoms depends largely on persistence in treatment. Treatment persistence, unlike treatment adherence, refers to the act of continuing a treatment for the prescribed duration. Adherence refers to the degree of conformity to the provider's recommendations about day-to-day treatment with respect to timing, dosage, and regularity. However, persistence and adherence are highly correlated (1). Poor persistence, like poor adherence, may increase the personal burden and economic cost of schizophrenia (2) by increasing the risk of relapse, hospitalization, and poor outcomes (3). Poor persistence may also increase morbidity and mortality, and it has been estimated to incur costs in excess of $100 billion per year in the United States (4).

In the management of patients with a first episode of schizophrenia, better outcomes are expected if treatment persistence is good. Experiencing multiple psychotic episodes as a result of nonpersistence not only leads to a poor prognosis but may also lower the odds of a full recovery and incur substantial avoidable costs. Few studies have examined persistence in treatment of patients with a first episode of schizophrenia. A study of treatment persistence among these patients and associated factors will not only provide an estimate of the magnitude of the problem but will also help inform strategies aimed at overcoming barriers to treatment persistence. The aim of this study was to examine the degree of poor treatment persistence among patients with a first episode of schizophrenia in a sub-Saharan African country and to identify factors associated with it.

Methods

The study was conducted among patients in the psychiatry unit of the University College Hospital in Ibadan, Nigeria, an 812-bed teaching hospital located in the southwestern part of the country. The estimated population of southwestern Nigeria is about 28 million. The hospital receives referrals specifically from health facilities in the southwest geopolitical zone of Nigeria and frequently from all geopolitical zones of the country. Psychiatry is one of the major specialties in the hospital. The Department of Psychiatry has seven subspecialties and runs three adult clinics weekly and a 24-hour emergency service. Antipsychotic medication is the mainstay of treatment for patients with schizophrenia in the department. Social skills training, cognitive-behavioral therapy, and other psychosocial interventions are offered as indicated. At follow-up appointments, patients are examined and medication adjustments are made. At each follow-up appointment, patients obtain medications or prescriptions that will last until the next appointment. Most patients are managed on an outpatient basis unless hospital admission is indicated. The section of medical records in the department classifies all psychiatry cases on the basis of *ICD-10* diagnoses.

Data for all the patients who were admitted to the ward or seen in the outpatient clinics of the department were collected. Only case records reviewed by a consultant psychiatrist were included in the study. The study population consisted of all patients with a first episode of schizophrenia between the ages of 18 and 65 who were seen between January 1, 2006, and December 31, 2010, who met *ICD-10* criteria for schizophrenia and who had not previously received any

Dr. Esan is with the Department of Psychiatry, University of Ibadan, Ibadan, Nigeria (e-mail: oluyomie@yahoo.com).

form of treatment. Sociodemographic and clinical data were extracted from the case notes of patients by using a case record form, which collected data on age at first episode, sex, marital status at presentation, employment status, and family history. Sociodemographic data were extracted by two research assistants after I (principal investigator) provided three weeks of training. I extracted the clinical data. Data were collected over a period of ten weeks from February 1 to April 14, 2012. Approval to conduct the study was obtained from the University College Hospital.

The event of interest in this study was default from treatment. The primary outcome was time to default from treatment (that is, persistence in treatment). Persistence was defined as the total number of weeks from the initiation of treatment to the last documented visit to the hospital. All eligible patients were retrospectively followed up until the time of the last visit. For participants who did not default from treatment, observations were right-censored at one year. These participants were considered to have persisted until one year after initiation of treatment. Participants who left treatment before one year were classified as having defaulted, and persistence was then calculated (that is, the day of first visit until the last documented appointment). For example, if a participant had been seen in the tenth month after treatment initiation and was given an appointment for three months later, the participant would be right-censored at the tenth month if he or she did not keep the appointment at 13 months and if records showed that the patient had kept no appointment thereafter.

A descriptive analysis of the major quantitative and categorical variables was performed. Time to default from treatment was calculated in weeks from the day of initial assessment in the hospital. Time to first default was examined by Kaplan-Meier survival analyses (5). The log-rank test was used to compare survival times of the different strata of variables. The contribution of the variables that affected time to default was examined by Cox regression analysis. All analyses were performed with SPSS version 16, and all reported p values are two-tailed.

Table 1

Cox regression analysis of variables as predictors of default from treatment among 216 patients with a first episode of schizophrenia

Variable	Hazard ratio	95% CI	p
Age at onset	1.00	.98–1.02	.91
Occupational status (reference: skilled)			
Semiskilled	.92	.59–1.46	.73
Unskilled	1.12	.68–1.82	.66
Unemployed	1.04	.58–1.89	.89
Student	.70	.39–1.25	.23
Marital status (reference: single)			
Married or cohabiting	.84	.43–1.64	.60
Divorced, widowed, or separated	1.27	.69–2.35	.45
Level of education (reference: no formal education)			
Primary	1.03	.41–2.57	.95
Secondary	1.35	.82–2.22	.23
Tertiary	1.03	.73–1.45	.86
Female (reference: male)	1.17	.85–1.60	.34
Employed (reference: unemployed)	1.15	.83–1.61	.40
Second-generation antipsychotic (reference: first-generation antipsychotic)	.72	.50–1.01	.06
Islam (reference: Christianity)	1.32	.93–1.89	.12

Results

A total of 243 participants with an untreated first episode of schizophrenia over the five-year period were included in the study. This total represented 9% of new patients seen at the Department of Psychiatry and reflects the proportional morbidity rate of schizophrenia.

Eighty percent of the sample (N=194) were taking first-generation antipsychotics, the most common of which was haloperidol. Only a small proportion of the 243 patients (16%, N=39) were taking second-generation antipsychotics. Twenty-seven were excluded from the study because their records were not complete. Of the 216 participants who were retrospectively followed up, 165 (76%) defaulted before the end of one year, and 51 (24%) completed the follow-up. An examination of treatment persistence for the first six months showed that only 68 participants (32%) remained in treatment after six months.

The mean±SE duration of persistence, as measured by mean time to all-cause treatment default (in weeks) and by Kaplan-Meier analysis, was 17.80±1.44 weeks (95% confidence interval=14.97–20.62). [A figure showing the overall Kaplan-Meier survival curve is available in an online data supplement to this report.]

Comparison of the survival curves for persistence in treatment of participants by gender did not indicate a significant difference. A similar comparison of the survival curves of patients taking first-generation antipsychotics with those taking second-generation antipsychotics also did not indicate a significant difference. In a Cox regression analysis, employment status, occupational status, religion, marital status, level of education, and the type of antipsychotic medication did not predict persistence in treatment (Table 1).

Discussion

In this retrospective study of untreated patients with a first episode of schizophrenia, only 24% of the sample persisted in treatment for at least one year, and only 32% persisted beyond six months. These findings are suboptimal because persistence is a key factor in the effectiveness of therapies for chronic conditions such as schizophrenia, diabetes, and hypertension.

The low rate is consistent with the results of a U.S. study by Ascher-Svanum and colleagues (1), which showed that the proportion of patients completing at least one year of treatment while taking haloperidol was 23%. However, the same study found that the completion rate was higher for those who were taking clozapine (72%), olanzapine (57%),

risperidone (49%), and quetiapine (46%). Most participants in the study reported here (about 60%) were taking haloperidol, and over 80% of participants were taking first-generation antipsychotics.

Overall, mean persistence in treatment was 17.8 weeks. This rate is very low compared with previously reported rates. For example, Ascher-Svanum and colleagues (6) reported that persistence, as measured by time to all-cause medication discontinuation for haloperidol was 24.7 weeks (172.9 days), and for participants on clozapine it was as high as 43.6 weeks (305 days). These findings suggest that in the management of patients with schizophrenia, time to medication discontinuation for any cause is significantly longer for second-generation than for first-generation antipsychotics. However in our study there was no significant difference in persistence between participants taking first- and second-generation antipsychotics (18.90 weeks versus 14.92 weeks; $p=.29$). Nevertheless, the rates were very low. The nonsignificant findings between participants taking the two types of antipsychotic may result from a lack of statistical power to detect a true difference because so few participants were taking second-generation agents. Another possible explanation is that none of the Nigerian patients were taking clozapine, which has been particularly associated with higher adherence rates. It has been suggested that the regular visits required for monitoring the potentially lethal side effects of clozapine contribute to improved adherence.

Employment status, occupational status, marital status, level of education, and the type of antipsychotic did not predict default from treatment. This is consistent with results from a study by Lacro and colleagues (7) in which gender, race-ethnicity, marital status, education level, severity of psychotic symptoms, severity of medication side effects, presence of mood symptoms, route of medication administration, and family involvement did not predict default from treatment.

This study had some limitations. The first is inherent in the retrospective study design: records were retrieved from case notes, and data were missing in some cases. A prospective approach would have enabled the examination of more factors that could have influenced persistence, such as social and economic factors (for example, income), factors related to the health care system (for example, the provider-patient relationship), and factors related to the patient's condition (for example, the severity of the disorder). Another limitation is the movement of patients between treatment facilities and helping agencies. In Nigeria, it is not uncommon for patients to move from orthodox medical facilities to complementary and alternative mental health care providers and vice versa. Therefore, default from treatment in a particular facility does not necessarily imply that patients are not receiving treatment.

A major strength of the study is the large sample. Also, the study is naturalistic in that the patients were not given any special attention or incentive that could have influenced persistence in treatment, such as in clinical trials.

Conclusions

Poor persistence in treatment of patients with a first episode of schizophrenia is common. It is important for mental health practitioners to increase persistence by collaborating with the patient to solve this problem. Patients who have problems persisting in treatment need a more concentrated approach than do other patients. Also, with more patient and caregiver education, it might be possible to retain younger people in treatment. The relationship between persistence in treatment and outcomes among patients with first-episode schizophrenia should be explored in future studies.

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