

Adherence to Antipsychotic Medication by Community-Based Patients With Schizophrenia in China: A Cross-Sectional Study

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Objective: Nonadherence to antipsychotic medication is a major health concern. Identification of risk factors associated with nonadherence is a useful initial step toward designing an effective intervention. This study compared the characteristics of medication-adherent and -nonadherent outpatients with schizophrenia in a Chinese community setting.

Methods: In a naturalistic, multicenter, and cross-sectional design, 601 outpatients with schizophrenia served by the National Continuing Management and Intervention Program for Psychoses (the “686 program”) were surveyed from June 2013 to January 2014 in four Chinese cities. On the basis of self-reported behavior, the patients were divided into medication-adherent and -nonadherent groups. Logistic regression analyses were performed to identify potential risk factors associated with nonadherence.

Results: The analyses included 554 patients, 20% of whom were considered to be nonadherent. Compared with the adherent group, the nonadherent group had a longer period of untreated psychosis (odds ratio [OR]=1.09), lower body mass index (OR=.94), higher rate of rural residency (OR=2.01), and lower monthly household income per capita (OR=.94/100 renminbi) ($p<.05$ by hierarchical analysis). Other characteristics (age, gender, occupation, education, marital status, living with family, age at initial presentation of symptoms, duration of illness, and type of antipsychotic medication) did not differ significantly between the groups.

Conclusions: Medication-adherent and -nonadherent groups differed significantly in some social and treatment characteristics. These findings may be useful in informing the development of strategies for reducing medication nonadherence.

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The World Health Organization has promoted the term “adherence” for use in treatment of chronic disorders to mean “the extent to which a person’s behavior—taking medication, following diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider” (1). Poor medication adherence is a major concern in all fields of medicine (2). Systematic reviews estimate that the rates of medication nonadherence among patients with schizophrenia range from 20% to 56% (3), depending on clinical settings, methods of investigation, criteria for and definition of adherence, duration of study, and characteristics of the studied population. In general, poor adherence in schizophrenia treatment is associated with illness relapse, hospitalization, elevated health care costs, and suicide, making an already challenging illness that much more difficult to manage (4–9).

Many factors affect medication adherence, and there is general agreement that it is mediated by major, broad factors, including patient, environment, and treatment-related

risk factors (3,10). Typically, studies in the West have found that the factors most associated with nonadherence include poor insight about the illness, negative attitudes toward medication, previous nonadherence, substance abuse, shorter illness duration, inadequate discharge planning or aftercare environment, and poorer therapeutic alliance with therapists (5). No similar studies have been done in China, where different cultures and health care systems exist. Identifying culturally meaningful risk factors is a logical step toward addressing this common problem.

Since 2004, China has initiated one of the world’s largest efforts in expanding community mental health, covering more than 43 million people in what is known as the “686 program” (named for its initial funding of 6.86 million Chinese Yuan) (11). This national program aims to build a suitable and practical model for China through provision of key mental health treatments to a wide range of urban and rural populations suffering from serious mental illnesses, largely psychosis, with regular follow-up and continuity of

care that is free of charge up to a reasonable set limit. It has been one of the first and largest mental health reforms in China to date (11), shifting psychiatric care from a hospital-based system to an outpatient-centered and community-oriented one.

In this context, to improve clinical outcome, it is particularly salient and timely to study antipsychotic medication adherence in a community setting in China, where there have been no previous studies on associated risk factors for patients with schizophrenia. Although the concept of medication adherence is relatively simple, its measurement is complex. A universally accepted standardized measure is lacking (12,13). The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Medication Compliance and Persistence Work Group has provided a useful measure that is studied over a period of time and reported as a percentage (14). Using this approach, we aimed to quantify the factors associated with medication nonadherence among Chinese patients with a diagnosis of schizophrenia in the context of the 686 program.

METHODS

Procedure

A multicenter cross-sectional study was carried out between June 2013 and January 2014 in four geographically diverse and economically representative cities across China that provided 686 programs: Chaoyang in the capital Beijing, Harbin in Heilongjiang Province (northern China), Mianyang in Sichuan Province (southwestern China), and Xiamen in Fujian Province (southeastern China). Each city included a mixture of urban and rural populations.

Based on the ISPOR proposal, the 686 Implementation and Evaluation research team at Peking University Institute of Mental Health (PKUIMH) designed a questionnaire and guideline for the survey. A pilot study with six patients and their families was conducted before the full survey was implemented. Two key investigators each from Chaoyang and Xiamen and one key investigator each from Mianyang and Harbin were trained together for one day in Beijing. The training covered in detail the research protocol, the questionnaires to be used, and the physical measurements involved, with a period for fielding questions from the investigators. The study was approved by the Ethics Review Board at PKUIMH.

Participants

The inclusion criteria for the study included being 16–60 years old, having a primary diagnosis of schizophrenia according to the *ICD-10*, being of Han ethnicity, living in the study community for at least six months, and taking any oral antipsychotic medication. The exclusion criteria were actively abusing substances and being pregnant. Patients and caregivers were enrolled only if both agreed to provide written informed consent.

Data Collection

The researchers recruited patients who were participating in the 686 program from the four participating cities. The

recruitment target was >550 participants, based on the formula $N = Z_{\alpha}^2 P(1-P)/d^2$ (15), where $\alpha = .05$ and $Z_{\alpha} = 1.96$, and there was an estimated acceptable margin of error for proportion d of .05, an estimated refusal rate of 30%, and—according to review of the literature—an estimated rate of nonadherence (P) of 50% (3). A total of 601 patients participated in the study from 31 of the 686 program community centers across the four cities. For each participant, researchers arranged face-to-face interviews for the patient and a key caregiver. Interviewees were assured that their participation was voluntary and would not affect their treatment or therapeutic relationship. Interviewers were known to the patients and were not involved with patients' clinical care. A typical interview took place at the patient's home or in the community center and lasted 15–25 minutes. Participants received no incentive or compensation for their interviews.

Measures

Data regarding age, gender, social characteristics (occupation, marital status, education, monthly household income, number of family members, place of residence, and living with family), clinical and treatment characteristics (age at initial symptoms, duration of illness, duration of untreated psychosis, types of antipsychotic medication, height, weight, name of antipsychotic medication, dosage per pill, number of pills taken in the past month, and psychiatrists' prescription) were collected from patients and caregivers.

The final adherence rate was calculated with the formula of dosage taken divided by the dosage prescribed. Also, in accordance with recent recommendations from experts in the field (16), the adherence threshold was established at 80% of the prescribed medication. An adherence rate below 80% was defined as nonadherent. We also defaulted to the category of nonadherent if either the patient or the caretaker reported a level that qualified as nonadherence.

Body mass index (BMI) was calculated with the formula of weight divided by the square of height in meters (kg/m^2).

Monthly household income per capita was calculated with the formula of monthly household income divided by number of family members, with the result rounded to the nearest 100 renminbi (RMB).

Statistical Analysis

Descriptive summaries of sociodemographic and treatment data for all patients were analyzed and compared between the adherent and nonadherent groups. Student's t tests were used for normal numerical variables, Kruskal-Wallis tests were used for abnormal numerical variables, and chi square tests were used for categorical variables.

Logistic regression was used because it was ideally suited to identify risk factors among a large pool of available variables in this study, and the dependent variable was dichotomous (adherent or nonadherent in this study). The independent variables included were specified a priori, based on the literature reviewed (17). Two kinds of logistic

regression were used. To analyze the impact of the variables on the risk of nonadherence, a univariate logistic regression analysis was applied for each variable. Furthermore, hierarchical logistic regression was applied to analyze the relationship between the dependent variable and combination of independent variables, presented as odds ratios (ORs) and 95% confidence intervals (CIs) (18). Independent variables were entered as two blocks. Block 1 included sociodemographic variables, and block 2 included treatment variables. For continuous independent variables, the ORs indicated an increased or decreased likelihood of nonadherence as a function of any quantitative increase in that variable; for categorical independent variables, the ORs indicated an increased or decreased likelihood of nonadherence compared with a reference category.

There were many differences among the four cities in economic level, population, and natural conditions, but the detailed information was not collected at the city level, and the difference in city level was embedded within patient level, so all the patients were pooled in the analysis.

The level of statistical significance was set at $p=.05$ for a two-sided test. The analyses were conducted with SPSS version 16.0.

RESULTS

The final sample included 601 eligible patients, with complete data for 554, of whom 440 patients were assigned to the adherent group and 114 to the nonadherent group on the basis of their self-reported medication adherence behavior.

The results of the univariate analysis, summarized in Table 1, showed that four of the sociodemographic characteristics were statistically associated with nonadherence: compared with adherent patients, nonadherent patients had a lower level of education and were from families with less household income. The proportions of patients living in urban areas and who were single were higher for adherent patients than for nonadherent patients. Other sociodemographic characteristics (age, gender, occupation, and living with family) and all treatment characteristics (BMI, age at initial symptoms, duration of illness, duration of untreated psychosis, and types of antipsychotic medication) did not differ significantly between the two groups.

Furthermore, binary univariate logistic regression analysis was used to model each variable's role in adherence (Table 2). This analysis showed that medication nonadherence was positively associated with duration of untreated psychosis ($OR=1.11$), residence in a rural area ($OR=2.82$), and being either married ($OR=2.10$) or in the divorced or widowed category ($OR=2.07$) and was negatively associated with monthly household income per capita ($OR=.90/100$ RMB).

All variables were classified into two categories—sociodemographic and treatment variables—and entered into hierarchical logistic regression analyses in two separate blocks (Table 2). This analysis indicated that nonadherence

was significantly associated with lower BMI, lower monthly household income per capita, residence in rural area, and longer duration of untreated psychosis.

DISCUSSION

Of the 601 patients surveyed in this naturalistic, multisite study, approximately one-fifth met the criterion for nonadherence. The rate of nonadherence in this study appeared to be consistent with a large ($N=1,579$) three-year naturalistic, prospective, and observational study of community patients in the United States, in which 18.8% were deemed nonadherent (19). Beyond this, several remarkable findings emerged from this pioneering study of Chinese patients with schizophrenia in a community setting.

It is of interest that poor financial condition of a family was a significant risk factor for nonadherence in univariate and multivariate regression analyses, and yet neither the patient's employment status nor marital status was a significant factor. One possible explanation is related to the family construct in China. In this study, 96% of all patients lived with their families, which is consistent with other reports that found over 90% of Chinese patients with schizophrenia lived with their families, compared with only about 40% doing so in the United States (20). These statistics reflect the tightly knit interdependence between individual and family and the importance of family as a basic social unit in China. It may explain why family, and no factor related to the individual, was the unit of significance in this study. In other words, a family's situation may be more representative and informative than that of an individual in a collectivist society such as China.

It is noteworthy that lower income was a risk factor for nonadherence. Low income may be related to larger historical and social factors that impoverished people may be facing in China, such as not being able to afford medication or to attend treatment and having different life priorities with limited resources. The fact that 686 program services and medications were provided for free seemed not to attenuate this phenomenon.

Lack of employment of patients with schizophrenia and key relatives' employment status were associated with medication nonadherence in two European studies (21,22). The authors suggested that medication-adherent patients were receiving more supervision and support from key relatives who were available when needed. According to our study, in the Chinese context, the support provided by living together seems to be more universally available and therefore not a contributing factor to nonadherence. Overall, level of support and socioeconomic factors appeared to influence medication adherence, and they varied in accordance with different cultural settings.

Another notable and robust finding of the study is that living in a rural area was related to nonadherence. There are a number of possible reasons for this finding. First, residents in rural areas typically have lower income than their urban

TABLE 1. Characteristics of 554 antipsychotic-adherent and -nonadherent outpatients with schizophrenia in China

Characteristic	Adherent (N=440)		Nonadherent (N=114)		Test statistic	df	p
	N	%	N	%			
Age (M±SD)	42.6±9.4		42.7±9.8		t=.13	552	.894
Male	230	52	54	47	$\chi^2=.87$	1	.350
Employment					$\chi^2=1.97$	1	.161
Employed	132	30	42	37			
Not employed	308	70	72	63			
Body mass index (M±SD kg/m ²)	25.5±4.2		25.0±4.6		t=1.20	552	.230
Monthly household income per capita (M±SD RMB) ^a	1,077.7±794.0		689.1±508.3		H=28.23	1	<.001
Marital status					$\chi^2=10.93$	2	.004
Single	207	47	34	30			
Married	177	40	61	54			
Divorced or widowed	56	13	19	17			
Living with					$\chi^2=.14$	1	.709
Self	16	4	5	4			
Family	424	96	109	96			
Residence					$\chi^2=24.32$	1	<.001
Urban	306	70	51	45			
Rural	134	30	63	55			
Education					$\chi^2=19.55$	4	.001
None	18	4	7	6			
Primary school (up to 5th grade)	90	20	36	32			
Secondary school (6th to 9th grade)	156	35	50	44			
High school (10th to 12th grade)	123	28	16	14			
College or above	53	12	5	4			
Age at initial symptoms (M±SD)	26.6±8.7		25.9±9.5		H=1.57	1	.211
Duration of illness (M±SD years)	16.2±9.1		17.2±9.3		H=1.00	1	.317
Duration of untreated psychosis (M±SD years)	.4±1.9		1.3±4.4		H=3.69	1	.055
Antipsychotic ^b					$\chi^2=1.84$	2	.398
First generation	41	11	10	11			
Second generation	301	78	68	72			
Both	46	12	16	17			

^a RMB, renminbi^b Denominators vary because some patients could not recall the name of their medication.

counterparts, which may reflect a secondary effect of the previous finding that household income was negatively associated with adherence. Second, nonadherence by rural residents may simply be related to a long-standing lack of services for mental health care. Shortages of mental health specialists are at historic levels in China and are most pronounced in rural areas (23) and worst in remote rural areas (24). The fact that the participants were part of the 686 program did not nearly compensate for this historic level of mental health need, and the 686 program in a rural setting is most likely less resourced than urban 686 program counterparts. Rural areas also typically have health insurance systems of poorer quality compared with systems in more urban areas (25), and rural residents possibly have a lower

level of general knowledge about mental illnesses and their treatment (26). It is worth noting that China has developed separate health insurance systems for urban and rural areas, primarily for inpatient care, and researchers have found that these separate systems have further increased the inequity between rural and urban locales (25).

For other medical services, such as continuity of mental illness treatment, illness prevention, and health maintenance—all of which are crucial for caring for patients with schizophrenia—rural Chinese areas use the New Medical Cooperative Scheme that began in 2003. Although the policy states that it covers up to 50% of the medical expenses, many beneficiaries have reported that the actual reimbursement level is much lower (27), likely contributing to the overall inequity, and perhaps indirectly to the lower medication adherence finding. In general, more equitable medical care systems and better resource distribution are likely other important factors affecting medication adherence. In industrialized countries, similar population-based, cross-sectional surveys in Canada

and Australia did not show a difference in medication adherence between rural or urban patients (28,29).

This study also showed that duration of untreated psychosis was one of the factors strongly associated with nonadherence. This is consistent with international reports (30,31). Longer lack of treatment has been associated with poorer outcomes of psychotic disorders in general (32) and poor general symptomatic outcome, poor social functioning, and global psychosocial outcomes more specifically (33). A recent meta-analysis showed that the average duration of untreated psychosis in schizophrenia is 64 weeks (34), longer than the 32 weeks in this study. Several studies also showed that early intervention services reduced duration of untreated psychosis (35,36). It is encouraging to

see that the new and innovative 686 program has provided responsive and timely services to shorten the time between the onset of psychotic symptoms and initiation of treatment, therefore enhancing the chance of better overall outcome and, by extension, improving medication adherence. On the other hand, more services and attention should be devoted to patients with long durations of untreated psychosis to ensure both their adherence and overall clinical outcome.

Another interesting finding of the study is that although differences in BMI were not statistically significant between the adherent and nonadherent groups, BMI was significantly associated with the adherent group in the hierarchical regression analysis. This result signifies that outpatients who were adherent with their antipsychotic medications suffered the untoward effects of increased BMI. Of course, weight gain can lead to long-term negative health effects and nonadherent behaviors (37). This finding further illustrates the importance of psychoeducation and wellness programs in promoting healthy diet and lifestyles to prevent and reduce weight gain and risks of metabolic problems associated with antipsychotic medications (38).

Our study did not show any association between adherence and type of antipsychotic medications. Internationally a three-year prospective, nonrandomized, and noninterventive study found that adherence rates were higher for second-generation antipsychotics (39), whereas a recent systematic review that included 13 observational studies found that antipsychotic medication type did not affect medication adherence (40).

There are several limitations to consider when interpreting these findings. First, no single method of assessing medication adherence is flawless. Although self-report is the most commonly used method for gathering information about adherence, it is likely to contain the usual inaccuracies and tends to overestimate the level of adherence (41). Also, this study did not cross-check self-reports with clinical records. Second, the findings may not be applicable to a general patient population, because the study was based on the 686 program, and the registered patients likely received better services and were more likely to be adherent to

TABLE 2. Logistic regression analyses of predictors of nonadherence among 554 outpatients with schizophrenia in China

Variable	Univariate logistic regression			Hierarchical logistic regression		
	OR	95% CI	p	OR	95% CI	p
Age (years)	1.00	.98–1.02	.894	.91	.80–1.04	.172
Male (reference: female)	.82	.54–1.24	.351	.89	.52–1.53	.684
Employment (reference: not employed)	1.36	.88–2.10	.162	1.33	.77–2.31	.309
Monthly household income per capita (per 100 RMB) ^a	.90	.87–.94	<.001	.94	.88–.99	.016
Marital status (reference: single)						
Married	2.10	1.32–3.34	.002	1.66	.82–3.34	.156
Divorced or widowed	2.07	1.10–3.90	.025	1.60	.69–3.73	.271
Living with family (reference: self)	.82	.30–2.30	.709	.91	.24–3.47	.888
Rural residence (reference: urban)	2.82	1.85–4.30	<.001	2.01	1.06–3.82	.032
Education (reference: none)						
Primary school (up to 5th grade)	1.03	.40–2.67	.954	.87	.25–3.05	.828
Secondary school (6th to 9th grade)	.82	.33–2.09	.683	1.18	.33–4.22	.804
High school (10th to 12th grade)	.33	.12–.92	.035	.71	.18–2.80	.627
College or above	.24	.07–.86	.028	.39	.07–2.27	.296
Body mass index (kg/m ²)	.97	.92–1.02	.230	.94	.88–.99	.039
Age at symptom onset (years)	.99	.97–1.01	.435	1.07	.94–1.23	.296
Duration of illness (years)	1.01	.99–1.03	.378	1.12	.98–1.28	.094
Duration of untreated psychosis (years)	1.11	1.03–1.19	.005	1.09	1.00–1.18	.043
Antipsychotic type (reference: first generation)						
Second generation	.93	.44–1.94	.839	.95	.41–2.19	.901
Both	1.43	.58–3.49	.437	1.19	.42–3.34	.747

^a RMB, renminbi

medication than the overall community patient population. Third, there are many differences among the four cities we sampled, but little information was collected on city level and the analysis pooled all of the patients, without any site-specific identity. Finally, the measure of duration of psychosis is always challenging and may lack precision in this retrospective, self-reported study.

CONCLUSIONS

Although medication adherence is driven by multiple, complex, and often overlapping risk factors, this study identified a small and well-defined set of strong psychosocial and clinical variables that were unique and informative about community mental health care in China, enabling future researchers and clinicians to focus on targeted interventions to reduce nonadherence and improve clinical outcomes.

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