Antipsychotic-Free Status in Community-Dwelling Patients With Schizophrenia in China:
Comparisons Within and Between Rural and Urban Areas

Cai-Lan Hou, MD, PhD[a]; Miao-Yang Chen, MD[b]; Mei-Ying Cai, MD[c]; Zi-Lang Chen, MD[b]; Shou-Bin Cai, MD[b]; Yao-Nan Xiao, MD[b]; and Fu-Jun Jia, MD, PhD[a,*]

ABSTRACT

Objective: To date, no study has specifically compared antipsychotic-free patients with schizophrenia living in the community between rural and urban areas. This study examined the rural-urban differences among antipsychotic-free community-dwelling individuals with schizophrenia in China.

Methods: Data on 1,365 community-dwelling patients with schizophrenia (n = 742 in a rural area and n = 623 in an urban area) with diagnoses according to *DSM-IV* or *ICD-10* were collected by interviews during 2013–2014 and 2015–2016. Data on patients' sociodemographic and clinical characteristics, prescriptions of psychotropic drugs, and antipsychotic treatment status were recorded using a standardized protocol and data collection procedure.

Results: The prevalence of antipsychotic-free status in the total sample (N = 1,365) was 27.3%; the proportion of antipsychotic-free patients was significantly lower (17.5%) in the urban area (17.5%) than in the rural area (35.4%; χ^2 = 55.03, P < .001). Binary logistic regression analysis revealed that antipsychotic-free patients, whether from the urban area or the rural area, were older (P = .001, odds ratio [OR] = 0.95 in urban; P = .006, OR = 0.97 in rural) and had poorer attitude toward medication treatment (P < .001, OR = 1.21 in urban; P < .001, OR = 1.31 in rural). Antipsychotic-free patients from the urban area also had fewer admissions, lower education level, and greater likelihood of living by themselves. Antipsychotic-free patients from the rural area also had worse insight into the disease, fewer anxiety symptoms, more prominent positive symptoms, and lower body mass index and were more likely to be women.

Conclusions: Antipsychotic-free status was more common in community-dwelling patients with schizophrenia in the rural area than in the urban area. Older age and poorer attitude toward medication treatment were common features of antipsychotic-free patients. There were correspondingly different risk factors for antipsychotic-free status between rural and urban areas. Building a positive medication treatment attitude is an important strategy for establishing medication adherence in older, community-dwelling patients with schizophrenia.

J Clin Psychiatry 2018;79(3):17m11599

[a]Guangdong Mental Health Center, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangdong Province, China
[b]The Third People's Hospital of Luoding, Guangdong Province, China
[c]Guangzhou Yuexiu Center for Disease Control and Prevention, Guangzhou Province, China
*Corresponding author: Fu-Jun Jia, MD, PhD, 7/F, Guang Dong Mental Health Centre, Guangzhou, Guangdong Province, China (jiafujun@126.com).

Antipsychotic medications represent the cornerstone of treatment programs for individuals with schizophrenia.[1] The standard of care for patients with schizophrenia includes prompt initiation of antipsychotic treatment. The value of medication maintenance treatment in schizophrenia is now generally accepted.

However, previous studies (eg, Yen et al[2]) reported that a high proportion of patients with schizophrenia do not fully comply with treatment. A major barrier to the effective treatment of individuals with schizophrenia is nonadherence to the medication regimen, with estimated 1-year rates of treatment discontinuation or interruption ranging from 40% to 75%.[3,4] The discontinuation of antipsychotic medication has been shown to be associated with a 5-fold increased risk of relapse during a 5-year follow-up period compared with maintenance therapy[5,6] and greater likelihood of hospital admission.[7] In addition, a proportion of patients in real-world settings (ie, not in controlled research settings) with schizophrenia are antipsychotic-naive for different reasons.

Individual patients discontinue, interrupt, or never accept treatment due to a variety of factors, including a lack of insight into their illness, forgetfulness, a lack of social support, tolerability issues, conscious choice, and refractory or nonresponsive symptomatology.[8] However, studies concerning the proportion of antipsychotic-free status in patients with schizophrenia and related risk factors have not yet been conducted. The majority of studies of urban-rural differences in schizophrenia focused on epidemiology and etiologic factors,[9–11] but urban-rural differences in antipsychotic-free status among people with schizophrenia living in the community are not well studied.

A large proportion of clinically stable patients with schizophrenia are managed by primary care physicians in the community.[12] However, there are no data on the prevalence of and risk factors associated with being antipsychotic-free in community-dwelling individuals with schizophrenia. It is of interest and makes sense to survey antipsychotic-free subjects with schizophrenia in a real-world setting.

Therefore, the aims of this study were (1) to examine the proportion of antipsychotic-free patients with schizophrenia treated by primary care physicians in China and (2) to compare the demographic and clinical correlates of antipsychotic-free status between rural and urban areas.

Clinical Points

- Previous studies reported that a high proportion of patients with schizophrenia do not fully comply with treatment. However, antipsychotic-free status in community-dwelling patients with schizophrenia is not well studied in real-world settings.

- This study found that being antipsychotic-free was more common in community-dwelling patients with schizophrenia in a rural area than in an urban area. Older age and poorer attitude toward medication treatment were risk factors associated with being antipsychotic-free.

METHODS

Study Design and Participants

This study was a cross-sectional epidemiologic survey of community-dwelling individuals with schizophrenia in China using a standardized protocol and data collection procedure. The survey was conducted between August 1, 2013, and July 31, 2014, in Guangzhou and between January 1, 2015, and March 31, 2016, in Luoding. Guangzhou is the capital of Guangdong Province and belongs to an urban area, while Luoding lies at the western side of Guangdong Province and is located in a rural and underdeveloped area. Consensus meetings to discuss data collection were held prior to each survey.

The subjects had to meet the following criteria: (1) age of at least 18 years, (2) diagnosis of schizophrenia per *DSM-IV* or *ICD-10*, (3) receipt of mental health services and treatment in community-based settings provided by primary health care physicians, (4) capacity to read the survey instructions, and (5) capability to sign an informed consent form. The study was approved by the ethics committee of Guangdong Mental Health Center.

There are a total of 92 primary care services in the Guangzhou major metropolitan area and a total of 63 small town primary care services in Luoding under the jurisdiction of Yunfu City. Twenty-two primary care services in Guangzhou and 21 small town primary care services in Luoding were selected using a random numbers table.

All local community-dwelling patients with schizophrenia who have presented to primary care services are registered in the Chinese National Psychiatric Management System,[13] in which individuals with severe mental disorders, including schizophrenia, bipolar disorder, paranoid psychosis, schizoaffective disorder, mental disorder related to epilepsy, and mental disorder–related mental retardation, are required to enroll. The total number of patients with schizophrenia in the System of Guangzhou on August 1, 2013, was 3,861, and the number on January 1, 2015, in Luoding was 5,842.

We attempted to contact all patients treated in the selected primary care services by telephone and provided a detailed explanation about the study. If patients agreed to participate, 3 trained psychiatrists from each site made a special appointment for the interview to be conducted at the local primary care service.

Assessments

Data on basic sociodemographic and clinical characteristics were collected using a form designed for the study. The patients' basic demographic and clinical characteristics as well as medication prescriptions and duration of untreated psychosis (DUP) were recorded by with electronic chart management system. In this study, the definition of antipsychotic-free status was having discontinued antipsychotics for at least 1 month or being antipsychotic-naive. It is also important to note that the subjects did not receive psychological treatment, rehabilitation treatment, or electroconvulsive therapy in the community.

Eligible patients were examined consecutively at each site. Data on sociodemographic and clinical characteristics, including age, sex, antipsychotic-free status, dangerous behavior, and intervention methods for dangerous behavior and significant psychotic symptoms in the past month, were collected using a form designed for the study.

The Brief Psychiatric Rating Scale (BPRS) was used to assess psychotic symptoms; it has 3 subscales: positive, negative, and anxiety/tension.[14,15] Adverse reactions were assessed using the Simpson-Angus Scale of extrapyramidal symptoms (SAS).[16] The SAS is a 10-item scale used to rate adverse neurologic effects of antipsychotic medications, including gait, arm dropping, shoulder shaking, elbow rigidity, wrist rigidity, leg pendulousness, head dropping, glabella tap, tremor, and salivation. The 10-item Montgomery-Asberg Depression Rating Scale (MADRS),[17] which has a validated Chinese version,[18] was selected to measure depressive symptoms in the previous week. Insight was evaluated using the Insight and Treatment Attitudes Questionnaire (ITAQ).[19] This is a semistructured scale with 11 questions measuring awareness of illness and attitudes toward treatment. Higher scores reflect better insight.

A total of 6 interviewers (3 from Guangzhou and 3 from Luoding) were trained in the use of these assessment tools prior to the main study. The interrater reliability of the rating instruments and the judgment of antipsychotic-free status in 20 patients with schizophrenia between the raters yielded satisfactory agreement (> 0.90).

Statistical Analysis

SPSS 20.0 for Windows (2011; IBM Corp, Armonk, New York) was used to analyze the data. The comparisons between antipsychotic-free and antipsychotic-treated patients in urban and rural areas with respect to sociodemographic and clinical characteristics were performed using independent samples *t* test, Mann-Whitney *U* test, χ^2 test, and Fisher exact test as appropriate. Binary logistic regression analysis with the "Enter" method was used to adjust for the relevant demographic and clinical covariates and to determine the independent contribution of antipsychotic-free versus antipsychotic-treated patients in rural and urban groups. The 1-sample Kolmogorov-Smirnov test was used to check the normality of distribution for continuous variables. The 2-tailed significance level was set at .05.

Table 1. Sociodemographic and Clinical Characteristics of Antipsychotic-Free and Antipsychotic-Treated Patients in Rural and Urban Areas[a]

| | Urban Area | | | | | | | | Rural Area | | | | | | | |
| | Antipsychotic-Free (n = 109) | | Antipsychotic-Treated (n = 514) | | | | | | Antipsychotic-Free (n = 263) | | Antipsychotic-Treated (n = 479) | | | | | |
Characteristic	n	%	n	%	χ^2	df	P		n	%	n	%	χ^2	df	P
Male	68	62.4	273	53.1	3.12	1	.07		149	**56.7**	313	**65.3**	5.45	1	**.01**
Married	39	35.8	182	35.4	0.005	1	.94		117	44.5	211	44.1	0.01	1	.90
Employed	65	59.6	342	66.5	1.89	1	.16		169	64.3	319	66.6	0.41	1	.52
First episode	21	**19.3**	163	**31.7**	6.69	1	**.01**		24	9.1	56	11.7	1.16	1	.28
Living with others	92	**84.4**	477	**92.8**	8.01	1	**.005**		244	92.8	450	93.9	0.38	1	.53
Personal income > 3,000 yuan	5	4.6	19	3.7	0.19	1	.66		0	0	5	1.0	…	…	.16[b]
Private expenses	28	25.7	122	23.7	0.18	1	.66		1	0.4	4	0.8	…	…	.66[b]
Current drinker	13	11.9	39	7.6	2.21	1	.13		12	4.6	16	3.3	0.69	1	.40
Current smoker	29	26.6	120	23.3	0.52	1	.46		56	21.3	110	23.0	0.27	1	.60
Psychiatric family history	25	22.9	137	26.7	0.64	1	.42		38	16.2	58	13.3	1.00	1	.31
Past physical violence	8	7.3	36	7.0	0.01	1	.90		106	40.3	208	43.4	0.67	1	.41
Treatment for violence	9	8.3	69	13.4	2.52	3	.47		135	51.3	245	51.1	0.00	1	.96
Medical conditions	37	33.9	201	39.1	1.01	1	.31		19	7.2	30	6.3	0.25	1	.61
	Mean	SD	Mean	SD	t/U	df	P/Z		Mean	SD	Mean	SD	t/U	df	P/Z
Age, y	**51.4**	9.9	46.8	10.2	4.20	621	**<.001**		40.5	13.4	39.4	11.8	1.10	740	.23
Education, y	**9.2**	3.1	**10.5**	2.8	−4.20	621	**<.001**		8.01	2.1	8.3	2.2	−1.90	740	**.04**
Age at onset, y	**28.1**	11.9	**25.1**	8.9	3.01	621	**.003**		26.7	9.9	26.09	10.3	0.82	740	.41
Illness duration, y	23.2	14.1	21.7	10.3	1.31	621	.18		13.8	11.3	13.3	10.1	0.65	740	.51
DUP, mo	…	…	…	…	…	…	…		34.4	76.5	67.9	504.3	−2.53	…	**.01[c]**
No. of admissions	**1.2**	1.7	**2.4**	2.7	−5.70	…	**<.001[c]**		1.8	1.7	2.1	2.0	−1.20	…	.21[c]
BMI, kg/m²	24.09	5.3	24.7	4.8	−1.10	610	.23		**20.2**	1.6	**22.5**	2.4	−13.26	740	**<.001**
MADRS total score	**12.1**	10.3	**10.01**	9.3	2.07	621	**.03**		5.2	5.9	4.7	5.7	1.12	740	.26
BPRS score															
Positive	6.6	3.5	6.1	3.1	1.59	621	.11		**6.6**	3.0	**5.8**	2.4	4.24	740	**<.001**
Negative	**7.08**	5.1	**6.2**	3.1	2.34	621	**.02**		**5.8**	3.1	**5.3**	2.5	2.50	740	**.01**
Anxiety	3.1	1.6	3.2	1.7	−0.26	621	.79		**4.8**	1.3	**5.2**	1.8	−3.29	740	**.001**
SAS total score	12.3	4.5	12.9	5.2	−1.23	621	.21		**10.02**	1.9	**10.4**	2.2	−2.53	740	**.01**
ITAQ score															
Total	**10.6**	7.9	**16.5**	5.0	−9.94	621	**<.001**		**8.1**	7.9	**10.6**	7.5	−4.22	740	**<.001**
Insight	**4.9**	4.1	**7.6**	3.1	−7.97	621	**<.001**		**4.2**	4.2	**5.2**	3.9	−3.16	740	**.002**
Medication	**5.7**	4.2	**8.8**	2.4	−10.40	621	**<.001**		**3.9**	3.8	**5.4**	3.7	−5.16	740	**<.001**

[a]Boldface indicates a statistically significant difference (P < .05).
[b]Fisher exact test was used.
[c]Mann-Whitney U test was used.
Abbreviations: BMI = body mass index, BPRS = Brief Psychiatric Rating Scale, DUP = duration of untreated psychosis, ITAQ = Insight and Treatment Attitudes Questionnaire, MADRS = Montgomery-Asberg Depression Rating Scale, SAS = Simpson-Angus Scale.

RESULTS

A total of 1,391 patients with schizophrenia living in a community were enrolled in the study, including 634 from the urban area and 757 from the rural area. Of the participants, 26 (1.9%) did not complete the interview, so a total of 1,365 patients, including 623 from the urban area and 742 from the rural area, were included in the final analysis.

The prevalence of antipsychotic-free status in the total sample was 27.3% (372/1,365). It was 17.5% (109/623) in the urban area and 35.4% (263/742) in the rural area, a significant difference (χ^2 = 55.03, P < .001).

Table 1 shows the sociodemographic and clinical characteristics of antipsychotic-free and antipsychotic-treated patients separately by urban and rural areas. Antipsychotic-free patients from the urban area were significantly older, had a later age at onset, had more prominent depressive and negative symptoms, had fewer admissions, were less likely to be experiencing a first episode, were less likely to be living with others, had a lower education level, and had poorer insight and attitude toward medication treatment compared to antipsychotic-treated patients. Antipsychotic-free patients from the rural area were more often female and had a lower education level; lower body mass index (BMI); more prominent positive and negative symptoms; significantly lower BPRS anxiety scores; fewer EPS; shorter DUP; and poorer insight and medication treatment attitude compared to antipsychotic-treated patients.

Concerning EPS, there was a significant difference between antipsychotic-free patients and antipsychotic-treated patients in the rural area (P = .01). More specifically, mean ± SD scores for gait (0.9 ± 0.2 vs 1.06 ± 0.3, P = .006), elbow rigidity (0.9 ± 0.2 vs 1.02 ± 0.2, P = .03), glabella tap (0.9 ± 0.2 vs 1.03 ± 0.2, P = .009), and salivation (1.07 ± 0.3 vs 1.1 ± 0.4, P = .05) were significantly lower for antipsychotic-free patients than for antipsychotic-treated patients in the rural area. Although there was no significant difference in SAS total score between the 2 groups in the urban area, differences in scores for glabella tap (1.03 ± 0.1 vs 1.08 ± 0.2, P = .054) and salivation (1.06 ± 0.4 vs 1.1 ± 0.6, P = .059) approached significance, with lower scores for antipsychotic-free patients than for antipsychotic-treated patients.

Table 2. Binary Logistic Regression Analysis of Differences Between Antipsychotic-Free and Antipsychotic-Treated Patients in Urban and Rural Areas (N = 1,365)[a]

	Urban Area			Rural Area		
Factor	P	OR	95% CI	P	OR	95% CI
Age	.001	0.95	0.92–0.98	.006	0.97	0.95–0.99
ITAQ medication score	<.001	1.21	1.09–1.35	<.001	1.31	1.16–1.48
Education	.006	1.12	1.036–1.23	.604	1.02	0.93–1.11
No. of admissions	<.001	1.35	1.15–1.58	.26	1.05	0.95–1.17
Living with others	.025	2.405	1.11–5.17	.50	0.76	0.34–1.68
Sex	.07	1.601	0.95–2.67	<.001	2.36	1.52–3.66
BMI	.73	0.99	0.94–1.04	<.001	1.83	1.64–2.05
BPRS positive score	.84	1.009	0.91–1.108	.006	0.87	0.80–0.96
BPRS anxiety score	.85	0.98	0.83–1.16	<.001	1.35	1.16–1.56
ITAQ insight score	.13	1.08	0.97–1.19	.005	0.85	0.76–0.95
First episode	.41	1.302	0.69–2.45	.53	1.21	0.65–2.27
Age at onset	.92	0.99	0.97–1.02	.24	1.01	0.99–1.03
MADRS total score	.16	0.97	0.94–1.01	.53	0.98	0.94–1.03
BPRS negative score	.13	1.06	0.98–1.16	.15	1.06	0.97–1.16
SAS total score	.46	1.02	1.09–1.35	.09	1.09	0.98–1.21
DUP	…	…	…	.09	1.002	1.0–1.004

[a]Boldface indicates a statistically significant difference (P < .05).
Abbreviations: BMI = body mass index, BPRS = Brief Psychiatric Rating Scale, CI = confidence interval, DUP = duration of untreated psychosis, ITAQ = Insight and Treatment Attitudes Questionnaire, MADRS = Montgomery-Asberg Depression Rating Scale, OR = odds ratio, SAS = Simpson-Angus Scale.

In stepwise binary logistic regression analyses, the variables with significant differences by analysis of variance, including age, sex, education, first episode status, age at onset, number of admissions, living with others, BMI, MADRS total score, BPRS positive score, BPRS negative score, BPRS anxiety score, SAS total score, DUP, ITAQ insight score, and ITAQ medication score, were entered into the logistic regression models. Table 2 displays the independent demographic and clinical correlates of antipsychotic-free status. Antipsychotic-free patients from both the urban area and the rural area were older and had poorer medication treatment attitude than their antipsychotic-treated counterparts. Antipsychotic-free patients from the urban area had fewer admissions, a lower education level, and greater likelihood of living by themselves compared to antipsychotic-treated patients. Antipsychotic-free patients from the rural area also had worse insight into the disease, fewer anxiety symptoms, more prominent positive symptoms, and lower BMI and were more often female. Together, these variables accounted for 39.8% of the variance of antipsychotic-free status in the rural area (P < .001) and 40.4% of the variance of antipsychotic-free status in the urban area (P < .001).

DISCUSSION

To the best of our knowledge, this study was the first to compare antipsychotic-free status between rural and urban areas in community-dwelling patients with schizophrenia. This study yielded some major findings. First, the prevalence of antipsychotic-free status is higher in the rural area. Second, the risk factors of antipsychotic-free patients, whether from an urban area or a rural area, were older age and poorer medication treatment attitude. Third, there were other risk factors that differed between rural and urban antipsychotic-free patients.

The overall prevalence of antipsychotic-free status in community-dwelling patients in China was 27.3%, and the percentage (35.4%) in the rural area was higher. Unfortunately, we did not find similar studies concerning the prevalence of antipsychotic-free status in patients with schizophrenia, whether in community-dwelling patients or in outpatients or with a rural-urban comparison. Therefore, this study was the first focusing on the prevalence of antipsychotic-free status and exploring the correlates of antipsychotic-free status in rural and urban areas. The different proportions of antipsychotic-free patients in rural and urban areas could be attributed to several factors, including differences in regions and culture.[20]

Antipsychotic-free community-dwelling patients with schizophrenia were older than those on antipsychotic therapy in this study. This result was consistent with results of some previous studies. Compared with a control group of patients admitted to acute inpatient units who accepted prescribed antipsychotic treatment, 103 patients who refused such treatment were older.[21] Due to a natural tendency for improvement in the symptoms, as well as increased risk of adverse effects, a reduction in dose or gradual tapering and discontinuation of antipsychotics may be possible in later years in a proportion of aging patients with schizophrenia.[22] However, there were also other studies with contrasting findings. One study[23] indicated that older age is associated with better adherence to antipsychotic treatment for patients with acute schizophrenia in the routine clinical practice setting. Another study[24] also reported that noncompliant patients were younger. A systematic review[25] reported that younger age is one of the main risk factors for medication nonadherence in schizophrenia. This topic deserves more study concerning patients living in real-world community settings in the future.

In this study, poor attitude toward medication treatment was found in both rural and urban antipsychotic-free patients. This finding is perhaps not so surprising given the evidence that antipsychotic-free status is a complex issue, influenced by a number of variables. Nonetheless, important questions remain about the correlates of antipsychotic-free status in community-dwelling patients with schizophrenia, and data on the characteristics of antipsychotic-free patients are limited and inconclusive. Treatment noncompliance should be considered an important factor related to antipsychotic-free status. Although treatment compliance is the foundation of favorable therapeutic outcomes,[26,27] it is unfortunate that noncompliance to antipsychotics is common among people with schizophrenia.[28,29] Lambert et al[30] reported that the prevalence of long-term refusal of antipsychotic treatment in first-episode psychosis was 18.8%.

One of the most heavily researched risk factors of nonadherence is insight into illness. Insight should be viewed as a multidimensional construct that assesses patients' awareness that they have a psychiatric illness, their ability to relabel their psychotic symptoms as being a consequence of mental illness, and their recognition of the need for treatment.[31,32]

Some studies[33,34] found that only insight into treatment adherence or only insight into psychotic experiences was associated with medication adherence, whereas another study[35] reported that insight into both illness and treatment was associated with medication adherence. On the other hand, other research[2] found that in subjects with schizophrenia, those who had greater insight into treatment had higher medication adherence, whereas insight into mental health status or psychotic experiences among subjects with schizophrenia was not correlated with their medication adherence. Noncompliant patients had a more negative and subjective response to medication.[24] Meanwhile, individuals who hold negative attitudes toward antipsychotic medication are more reluctant to adhere to prescribed medications.[36] When subjects with schizophrenia do not have good insight, they are less inclined to begin or remain in treatment, underappreciate the benefits of medication, and put themselves at higher risk of discontinuing treatments, with concomitant increase in the risk of relapse.[37]

However, antipsychotic-free patients from the rural area had worse insight into disease than antipsychotic-treated patients in this study. High intensity of delusional symptoms and suspiciousness and low socioeconomic status are the main risk factors for medication nonadherence in subjects with schizophrenia. A prospective study[38] of patients' refusal of antipsychotic medication in a setting in which physicians have discretionary power to administer treatment over patients' objections reported that patients who refused treatment were found to have significantly higher BPRS scores than were patients who complied with antipsychotic treatment. The antipsychotic-free patients from the rural area in this study had fewer BPRS anxiety symptoms and more prominent positive symptoms, a finding that perhaps is partly explained by the antipsychotic-free status but still deserves further research. In addition, sociodemographic factors such as sex, education level, socioeconomic status, and living condition have been posited to be correlates of medication compliance,[39,40] but the results are inconclusive.

In this study, antipsychotic-free patients in the rural area were more often female. However, in previous studies, male sex was associated with a lower rate of treatment discontinuation.[20] Male sex is associated with a poorer outcome and disease course than are found in female patients.[41–43] Thus, male patients may show more severe symptoms and self-harming behaviors and greater hostility, resulting in clinicians' or the patients' families' paying more attention to the patients' treatment maintenance.[20] In addition, rural communities have socioeconomic and cultural characteristics distinct from those of non-rural communities.[44] Salient son preference in rural areas in China perhaps made families pay more attention to the treatment of male patients. The fear of weight gain may also undermine medication compliance of female patients,[45] which perhaps partly explains the lower BMI in the rural area.

It is well known that family support is essential for individuals' engagement in medication regimens,[46] and lack of social support and social supervision are common barriers to treatment compliance.[47] A study from Hong Kong[48] showed that medication noncompliance was obvious among individuals who lived alone. Consistent with the findings of previous studies, antipsychotic-free patients from the urban area in this study were inclined to live by themselves. They also had a lower education level. Low level of education has been found to be one of the main risk factors for medication nonadherence in schizophrenia.[25]

Antipsychotic-free patients from the urban area had fewer admissions. Mullins et al[42] reported that having no prior psychiatric hospitalizations was associated with a lower risk of discontinuing treatment. Another study[20] reported that experiences of hospitalization did not affect the likelihood of discontinuing treatment. Factors most consistently contributing to nonadherence in first-episode schizophrenia include lack of insight into having an illness, distress associated with side effects, lack of or partial efficacy with continued symptoms, beliefs that medications are no longer needed, persistent comorbid substance use, poor medication acceptance, and lack of social support.[45,49–53]

Our study has some methodological limitations. Results of the regression analyses should be interpreted with caution as regards causation because of the cross-sectional nature of the study design. First, the causal relationship between antipsychotic-free status and other variables could not be examined because of the cross-sectional design. Second, the reasons for and details regarding duration of antipsychotic-free status were not explored. Third, only 1 urban city and 1 rural city in China were included; thus, the findings cannot be generalized to the rest of China. Fourth, the subjects in this study included only community-dwelling patients with schizophrenia; thus, the findings cannot be generalized to inpatients and outpatients. However, the study yielded some major findings regarding antipsychotic-free patients in China, and our findings have important implications for clinical practice in the treatment of community-dwelling patients with schizophrenia.

In conclusion, antipsychotic-free status was more common in community-dwelling patients with schizophrenia in the rural area than in the urban area. Older age and poorer attitude toward medication treatment were common features of antipsychotic-free patients. The risk factors associated with being antipsychotic-free differed between the rural and urban areas. Building a positive medication treatment attitude is an important strategy for establishing medication adherence in older community-dwelling patients with schizophrenia.

REFERENCES

1. Remington G, Kwon J, Collins A, et al. The use of electronic monitoring (MEMS) to evaluate antipsychotic compliance in outpatients with schizophrenia. *Schizophr Res*. 2007;90(1–3):229–237.

2. Yen CF, Chen CS, Ko CH, et al. Relationships between insight and medication adherence in outpatients with schizophrenia and bipolar disorder: prospective study. *Psychiatry Clin Neurosci*. 2005;59(1):403–409.

3. Masand PS, Roca M, Turner MS, et al. Partial adherence to antipsychotic medication impacts the course of illness in patients with schizophrenia: a review. *Prim Care Companion J Clin Psychiatry*. 2009;11(4):147–154.

4. Leucht S, Heres S. Epidemiology, clinical consequences, and psychosocial treatment of nonadherence in schizophrenia. *J Clin Psychiatry*. 2006;67(suppl 5):3–8.

5. Robinson D, Woerner MG, Alvir JM, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry*. 1999;56(3):241–247.

6. Kulhara P, Basu D, Mattoo SK, et al. Lithium prophylaxis of recurrent bipolar affective disorder: long-term outcome and its psychosocial correlates. *J Affect Disord*. 1999;54(1–2):87–96.

7. Haywood TW, Kravitz HM, Grossman LS, et al. Predicting the "revolving door" phenomenon among patients with schizophrenic, schizoaffective, and affective disorders. *Am J Psychiatry*. 1995;152(6):856–861.

8. Tiihonen J, Haukka J, Taylor M, et al. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. *Am J Psychiatry*. 2011;168(6):603–609.

9. Pedersen CB, Mortensen PB. Are the cause(s) responsible for urban-rural differences in schizophrenia risk rooted in families or in individuals? *Am J Epidemiol*. 2006;163(11):971–978.

10. Pedersen CB, Mortensen PB. Why factors rooted in the family may solely explain the urban-rural differences in schizophrenia risk estimates. *Epidemiol Psichiatr Soc*. 2006;15(4):247–251.

11. van Os J, Hanssen M, Bijl RV, et al. Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. *Arch Gen Psychiatry*. 2001;58(7):663–668.

12. Hou CL, Cai MY, Ma XR, et al. Clozapine prescription and quality of life in Chinese patients with schizophrenia treated in primary care. *Pharmacopsychiatry*. 2015;48(6):200–204.

13. National Health and Planning Commission of the People's Republic of China. Measures for the administration of the reporting of serious mental disorders (for trial implementation). *Chinese Practical Journal of Rural Doctor*. 2014;21(2) .

14. Overall JE, Beller SA. The Brief Psychiatric Rating Scale (BPRS) in geropsychiatric research, I: factor structure on an inpatient unit. *J Gerontol*. 1984;39(2):187–193.

15. Zhang MYZT, Tang SH, Chi YF, et al. The application of the Chinese version of the Brief Psychiatric Rating Scale (BPRS) [in Chinese]. *Chin J Nerv Ment Dis*. 1983;9:76–80.

16. Simpson GM, Angus JW. A rating scale for extrapyramidal side effects. *Acta Psychiatr Scand suppl*. 1970;212:11–19.

17. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. 1979;134:382–389.

18. Zhong BL, Wang Y, Chen HH, et al. Reliability, validity, and sensitivity of the Montgomery-Asberg Depression Rating Scale for patients with current major depressive disorder [in Chinese]. *Chin J Behav Med Brain Sci*. 2011;1:85–87.

19. McEvoy JP, Aland J Jr, Wilson WH, et al. Measuring chronic schizophrenic patients attitudes toward their illness and treatment. *Hosp Community Psychiatry*. 1981;32(12):856–858.

20. Jung SH, Kim WH, Choi HJ, et al. Factors affecting treatment discontinuation and treatment outcome in patients with schizophrenia in Korea: 10-year follow-up study. *Psychiatry Investig*. 2011;8(1):22–29.

21. Hoge SK, Appelbaum PS, Lawlor T, et al. A prospective, multicenter study of patients' refusal of antipsychotic medication. *Arch Gen Psychiatry*. 1990;47(10):949–956.

22. Jeste DV, Maglione JE. Treating older adults with schizophrenia: challenges and opportunities. *Schizophr Bull*. 2013;39(5):966–968.

23. Takahashi MFS, Funai J, Alev L, et al. Predictors of discontinuation of antipsychotic therapy in patients with acute schizophrenia: a 1-year observational study with more than 1,000 patients. *Open J Psychiatr*. 2014;4:364–371.

24. Agarwal MR, Sharma VK, Kishore Kumar KV, et al. Non-compliance with treatment in patients suffering from schizophrenia: a study to evaluate possible contributing factors. *Int J Soc Psychiatry*. 1998;44(2):92–106.

25. García S, Martínez-Cengotitabengoa M, López-Zurbano S, et al. Adherence to antipsychotic medication in bipolar disorder and schizophrenic patients: a systematic review. *J Clin Psychopharmacol*. 2016;36(4):355–371.

26. Ludwig W, Huber D, Schmidt S, et al. Assessment of compliance-related attitudes in psychiatry: a comparison of two questionnaires based on the Health Belief Model. *Soc Psychiatry Psychiatr Epidemiol*. 1990;25(6):298–303.

27. Thornley B, Adams C. Content and quality of 2,000 controlled trials in schizophrenia over 50 years. *BMJ*. 1998;317(7167):1181–1184.

28. Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. *Psychiatr Serv*. 1998;49(2):196–201.

29. Lacro JP, Dunn LB, Dolder CR, et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry*. 2002;63(10):892–909.

30. Lambert M, Conus P, Cotton S, et al. Prevalence, predictors, and consequences of long-term refusal of antipsychotic treatment in first-episode psychosis. *J Clin Psychopharmacol*. 2010;30(5):565–572.

31. David AS. Insight and psychosis. *Br J Psychiatry*. 1990;156:798–808.

32. Amador XF, Strauss DH, Yale SA, et al. Awareness of illness in schizophrenia. *Schizophr Bull*. 1991;17(1):113–132.

33. David A, Buchanan A, Reed A, et al. The assessment of insight in psychosis. *Br J Psychiatry*. 1992;161:599–602.

34. Wong SS, Lee S, Wat KH. A preliminary communication of an insight scale in the assessment of lithium non-adherence among Chinese patients in Hong Kong. *J Affect Disord*. 1999;55(2–3):241–244.

35. Smith CM, Barzman D, Pristach CA. Effect of patient and family insight on compliance of schizophrenic patients. *J Clin Pharmacol*. 1997;37(2):147–154.

36. Cuffel BJ, Alford J, Fischer EP, et al. Awareness of illness in schizophrenia and outpatient treatment adherence. *J Nerv Ment Dis*. 1996;184(11):653–659.

37. Heinrichs DW, Cohen BP, Carpenter WT Jr. Early insight and the management of schizophrenic decompensation. *J Nerv Ment Dis*. 1985;173(3):133–138.

38. Kasper JA, Hoge SK, Feucht-Haviar T, et al. Prospective study of patients' refusal of antipsychotic medication under a physician discretion review procedure. *Am J Psychiatry*. 1997;154(4):483–489.

39. Fleischhacker WW, Oehl MA, Hummer M. Factors influencing compliance in schizophrenia patients. *J Clin Psychiatry*. 2003;64(suppl 16):10–13.

40. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophr Bull*. 1997;23(4):637–651.

41. Limosin F, Loze JY, Philippe A, et al. Ten-year prospective follow-up study of the mortality by suicide in schizophrenic patients. *Schizophr Res*. 2007;94(1–3):23–28.

42. Mullins CD, Obeidat NA, Cuffel BJ, et al. Risk of discontinuation of atypical antipsychotic agents in the treatment of schizophrenia. *Schizophr Res*. 2008;98(1–3):8–15.

43. Siegel SJ, Irani F, Brensinger CM, et al. Prognostic variables at intake and long-term level of function in schizophrenia. *Am J Psychiatry*. 2006;163(3):433–441.

44. Beard JR, Tomaska N, Earnest A, et al. Influence of socioeconomic and cultural factors on rural health. *Aust J Rural Health*. 2009;17(1):10–15.

45. Coldham EL, Addington J, Addington D. Medication adherence of individuals with a first episode of psychosis. *Acta Psychiatr Scand*. 2002;106(4):286–290.

46. Corrigan PW, Liberman RP, Engel JD. From noncompliance to collaboration in the treatment of schizophrenia. *Hosp Community Psychiatry*. 1990;41(11):1203–1211.

47. Hudson TJ, Owen RR, Thrush CR, et al. A pilot study of barriers to medication adherence in schizophrenia. *J Clin Psychiatry*. 2004;65(2):211–216.

48. Tsang HW, Fung KM, Corrigan PW. Psychosocial and socio-demographic correlates of medication compliance among people with schizophrenia. *J Behav Ther Exp Psychiatry*. 2009;40(1):3–14.

49. Kamali M, Kelly BD, Clarke M, et al. A prospective evaluation of adherence to

medication in first-episode schizophrenia. *Eur Psychiatry*. 2006;21(1):29–33.

50. Mutsatsa SH, Joyce EM, Hutton SB, et al. Clinical correlates of early medication adherence: West London first episode schizophrenia study. *Acta Psychiatr Scand*. 2003;108(6):439–446.

51. Novak-Grubic V, Tavcar R. Predictors of noncompliance in males with first-episode schizophrenia, schizophreniform and schizoaffective disorder. *Eur Psychiatry*. 2002;17(3):148–154.

52. Perkins DO, Gu H, Weiden PJ, et al; Comparison of Atypicals in First Episode study group. Predictors of treatment discontinuation and medication nonadherence in patients recovering from a first episode of schizophrenia, schizophreniform disorder, or schizoaffective disorder: a randomized, double-blind, flexible-dose, multicenter study. *J Clin Psychiatry*. 2008;69(1):106–113.

53. Rabinovitch M, Béchard-Evans L, Schmitz N, et al. Early predictors of nonadherence to antipsychotic therapy in first-episode psychosis. *Can J Psychiatry*. 2009;54(1):28–35.