Awareness of Illness and Nonadherence to Antipsychotic Medications Among Persons With Schizophrenia

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Objective: The purpose of this study was to assess the effects of patients' awareness of their illness on the clinical presentation, management, and course of nonadherence to antipsychotic medications among patients with schizophrenia. Methods: A national survey was conducted of psychiatrists who were treating patients with schizophrenia. The survey was sent to 771 psychiatrists, of whom 534 responded, for a response rate of 69 percent. The psychiatrists were asked to report on presentation, management, and course for one adult patient with schizophrenia who had been under their care for at least one year and who had been nonadherent to oral antipsychotics at some point in the past year. Patients who were aware that they had a mental illness were compared with those who were not aware. Results: Of the 534 respondent psychiatrists, 310 reported on an eligible patient, and 300 of these patients were classified by illness awareness. Ninety-seven patients, or 32 percent, were not aware that they had a mental illness. These patients who lacked awareness had significantly longer episodes of antipsychotic nonadherence, were more likely to completely cease taking the antipsychotic medication, were more likely to have severe positive symptoms, and were more likely to be psychiatrically hospitalized after nonadherence than those who were aware of their illness. Psychological interventions and several types of family interventions were significantly less effective among patients who lacked awareness. Conclusions: A lack of awareness of mental illness is common among patients with schizophrenia who are nonadherent to antipsychotics. Such nonadherence tends to be especially disruptive and unresponsive to simple commonly used psychological interventions. (Psychiatric Services 57:205-211, 2006)

onadherence to antipsychotic medication regimens is a grave and pervasive problem in the clinical management of schizophrenia. Compared with patients who are adherent, patients who are not adherent have a greater risk of symptom exacerbation (1), psychiatric hospitalization (2), housing instability (3,4), and violence (5).

Lack of insight or awareness of having a mental illness is commonly cited as a primary reason for nonadherence to antipsychotic medications (6,7). Psychotic patients who lack such insight are at significantly increased risk of nonadherence and hospitalization (8–12). In addition, a perception of invulnerability to rehospitalization (13,14) and a belief that antipsychotic medications do not prevent relapse (15,16) have been associated with nonadherence to medications.

Limited progress has been made in developing effective interventions to manage insight deficits and nonadherence among psychotic patients. In one controlled trial, a brief cognitivebehavioral intervention was associated with significantly improved insight into illness and reduced symptom severity compared with usual care for patients with schizophrenia (17). A type of cognitive-behavioral therapy that focused specifically on improving antipsychotic adherence also proved to be effective (18) and durable (19) in a mixed sample of psychotic patients. However, a replication of the study in a sample that was limited to patients with schizophrenia did not show a significant improvement in adherence (20). Psychoeducational interventions for schizophrenia have tended to demonstrate little effect on insight (21) or adherence (22).

Little is known about the routine psychiatric management of nonadherence to antipsychotic medications among patients with schizophrenia who lack awareness of their illness. Information is sparse regarding how psychiatrists manage these patients

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and whether and to what extent commonly provided clinical interventions improve adherence among patients who lack insight into their illness. By examining the effects of patients' insight into their illness on the clinical presentation and management of nonadherence as well as the treatment response among patients with schizophrenia, we hope to inform efforts to improve the clinical management of nonadherence to antipsychotics among patients who are not aware that they have a mental illness.

Methods

A nationally representative sample of psychiatrists was surveyed by mail to assess their management of patients with schizophrenia who had been non-adherent to antipsychotic medication regimens. The study was approved by the institutional review boards of New York State Psychiatric Institute and the American Psychiatric Institute for Research and Education. Primary data collection was conducted from September 2003 to January 2004.

A random sample of psychiatrists was selected from the American Medical Association's Masterfile of Physicians. Psychiatrists who were in psychiatric residency training, living outside the United States, over the age of 75 years, and not involved in direct patient care were excluded. Selected psychiatrists (N=1,150) were sent a prescreening postcard to determine whether they had treated at least four patients with schizophrenia in the past typical work month. Analysis of the National Survey of Psychiatric Practice (23,24) indicated that more than 90 percent of patients with schizophrenia who were receiving psychiatric care were being treated by psychiatrists who treated four or more patients with schizophrenia per month.

When the psychiatrists who reported treating fewer than four patients with schizophrenia per month were excluded, the sample was reduced from 1,150 to 880. An additional ten psychiatrists were excluded from the sample because the screening postcards were returned with "addressee unknown" indicated and a follow-up telephone inquiry revealed no forwarding contact information. These

exclusions resulted in a final sample of 771 psychiatrists who met eligibility criteria and had a serviceable mailing address.

In this sample, 534 psychiatrists responded to the survey, for a response rate of 69 percent. Of these 534 psychiatrists, 310 reported on an eligible patient who met the study criteria of being older than 18 years; being under the psychiatrist's care for at least one year; being nonadherent to oral antipsychotics at some point in the past year, defined as taking less than half of the prescribed medication for at least two consecutive weeks; not receiving an injection of depot antipsychotic medication during the two months before nonadherence to oral antipsychotics; and being the last patient the psychiatrist saw who had these characteristics. The other participating psychiatrists (N=224) provided general information about their management of medication nonadherence among patients with schizophrenia, but not individual patientlevel information. This information was not analyzed for this study.

Psychiatrists were asked, in characterizing the selected patients, to determine whether the patient generally believed he or she had a mental illness. This item was used to define the two study groups: patients who were aware that they had a mental illness and those who were not. Data were missing for ten patients for this variable.

Psychiatrists' assessments of patients who were and were not aware of their illness were compared in terms of basic sociodemographic and clinical characteristics, including selected lifetime mental disorders and prescribed psychotropic medications. The study groups were also compared in terms of the perceived primary cause of the patient's last episode of medication nonadherence: denial of illness, paranoia, grandiosity, cognitive disorganization (difficulty following a medication regimen), motivation deficits (indifference, apathy), intolerable side effects, nonresponse of symptoms to medications, patient's belief that his or her symptoms did not respond to medications, stigma associated with taking medications, lack of family support for medications, lack of support in the patient's living environment for medications, substance use problems, problems with the therapeutic alliance, and cost of medications.

The groups were compared on the frequency and perceived effectiveness of several pharmacologic, psychological, behavioral, and family interventions that were used to manage the most recent episode of nonadherence. For these items, the psychiatrists were asked to indicate whether they used each intervention, and, among those they used, to assess the effectiveness of each on a 5-point scale from 1, ineffective in maintaining adherence, to 5, extremely effective.

Bivariate statistical comparisons were based on chi square tests for categorical variables and t tests for continuous variables. Multiple linear regression analyses examined associations between insight into illness and perceived effectiveness of the intervention, with potentially confounding sociodemographic and clinical patient characteristics controlled for. All analyses included weighting to account for nonresponse.

Results

Sociodemographic and clinical characteristics

Approximately one-third of the non-adherent patients (97 patients, or 32 percent) were reported by their psychiatrists as being unaware that they had a mental illness. Compared with the patients who were aware of their mental illness, patients who lacked awareness were significantly less likely to be working at either paid or volunteer employment (Table 1). Both patient groups were predominantly white males who were not married or employed.

Patients who were reported to be aware of having a mental illness were significantly more likely than those without such an awareness to have a lifetime history of major depression, to have a substance use disorder, and to have been homeless for at least 48 hours. By contrast, awareness of illness was not significantly related to deficits in intellectual functioning, having made a previous suicide attempt, or having intentionally physically injured

someone. Immediately before the index nonadherence episode, the vast majority of both groups were managed with second-generation antipsychotic medications. Some patients in each group received adjunctive mood stabilizers, antidepressants, or anxiolytic medications.

Nonadherence episodes

The psychiatrists were asked to select, from a list of 15 possible responses, the primary factor that they believed was most important in the development of the patient's last episode of nonadherence. Denial of illness was cited for nearly threequarters of the patients who lacked an awareness of their illness (70 patients, or 72 percent). By contrast, denial of illness was cited as the primary factor for 35 of the patients who were aware of having a mental illness (18 percent) (Table 2). Interestingly, stigma associated with taking an antipsychotic medication was not cited as the primary contributing factor for any of the patients who lacked awareness of having a mental illness.

Episodes of nonadherence tended to be more severe among patients who were assessed as being unaware of having a mental disorder than among patients who were assessed as being aware. Specifically, episodes of nonadherence among patients who were unaware of their illness were significantly longer, more commonly involved complete cessation of medication, and more often resulted in a psychiatric hospitalization. However, complete cessation of medication was common in both groups. Compared with patients who were aware of having a mental illness, patients who lacked such awareness had significantly more severe positive symptoms immediately before, during, and after the nonadherence episode and significantly more severe negative symptoms after the episode (Table 2).

Management of medication nonadherence

There was little evidence that management of nonadherence with antipsychotic medications varied across the two patient groups. The vast majority of both groups were urged by their psychiatrists to take their an-

Table 1

Background sociodemographic and clinical characteristics of patients with schizophrenia who were nonadherent to antipsychotic medications, by whether their psychiatrist reported them as being aware of their mental illness^a

	Unaware (N=97)		Aware (N=203)		т.		
Characteristic	N	%	N	%	Test statistic	df	p
Age (mean±SD years)	39.7± 12.4		38.9± 11.5		t=.54	297	.59
White	61	64	134	66	$\chi^2 = .09$	1	.76
Male	67	70	149	73	$\chi^{2}=.42$	î	.52
Never married	81	84	167	83	$\chi^{2}=.08$	î	.78
Living alone	37	38	81	40	$\chi^{2} = .09$	1	.76
Employed	13	14	59	29	$\chi^2 = 7.99$	î	.005
Public health insurance	61	68	112	58	$\chi^2 = 2.58$	1	.11
Treatment setting	01	00	112	90	$\chi^2 = 5.22$	4	.27
Public clinic	44	47	71	36	χ -3.22	•	
Private clinic	11	12	41	21			
Solo or group practice	26	28	60	30			
Day or partial hospital	5	5	8	4			
Other	8	8	16	8			
Lifetime mental disorders ^b	9		10	9			
Anxiety disorder	46	50	114	58	$\chi^2 = 1.56$	1	.21
Major depression	39	42	115	58	$\chi^2 = 6.58$	1	.01
Substance use	15	16	53	27	$\chi^2 = 4.64$	1	.03
Mania	23	25	44	22	$\chi^2 = .20$	1	.66
Had ever been homeless for					,		
more than 48 hours	18	22	61	38	$\chi^2 = 6.02$	1	.01
Had ever injured someone	31	34	53	27	$\chi^2 = .12$	1	.72
Had ever made a serious					,,		
suicide attempt	18	20	36	18	$\chi^2 = .048$	1	.52
Borderline intellectual					,,		
functioning (IQ<85)	23	24	45	22	$\chi^2 = .12$	1	.72
Psychotropic medications ^c							
Second-generation							
antipsychotic	84	87	182	92	$\chi^2 = 2.36$	1	.12
First-generation							
antipsychotic	20	21	30	15	$\chi^2 = 1.90$	1	.17
Mood stabilizer	13	13	27	13	$\chi^2 = .004$	1	.95
Antiparkinsonian agent	25	26	34	17	$\chi^2 = 3.27$	1	.071
Antidepressant	8	9	23	11	$\chi^2 = .48$	1	.49
Anxiolytic	4	4	2	1	$\chi^2 = 2.93$	1	.086

^a Data are weighted to account for nonresponse. Ns vary because of missing data.

tipsychotic medications. In addition, psychiatrists commonly discussed the risks of medication nonadherence, main effects and side effects of the medications, the patients' reasons for nonadherence, and what taking medications meant to the patients' identity. Efforts were made to connect medication adherence to patients' personal goals. A substantially smaller proportion of patients in each group received family, behavioral, or pharmacologic interventions aimed at managing their nonadherence. In both groups, simplifying the dosage regimen was the most

common pharmacologic intervention (Table 3).

Perceived effectiveness of interventions

All the psychological interventions studied were reported by the treating psychiatrists to be significantly less effective among patients who lacked awareness of having a mental illness than among patients who were aware (Table 4). These group differences remained significant after group differences in background sociodemographic and clinical characteristics were controlled.

Several, but not all, of the behav-

b According to psychiatrists' assessments

^c Medications prescribed just before the episode of nonadherence

Table 2

Characteristics of episodes of nonadherence to antipsychotic medications among patients with schizophrenia who were aware of their mental illness and those who were not aware^a

	Unaware (N=97)		Aware (N=203)		т.		
Characteristic	N	%	N	%	Test statistic	df	p
Primary cause of nonadherence							
Denial of illness	70	72	35	18	$\chi^2 = 79.99$	1	<.001
Paranoia	4	4	24	12	$\chi^2 = 4.22$	1	.040
Grandiosity	1	1	3	2	$\chi^2 = .90$	1	.75
Side effects	6	6	21	11	$\chi^2 = 1.47$	1	.22
Substance abuse	2	2	24	12	$\chi^2 = 8.0$	1	.005
Cognitive disorganization	2	2	14	7	$\chi^2 = 3.22$	1	.073
Treatment nonresponse					χ		
Patient's perception	1	1	14	7	$\chi^2 = 4.72$	1	.03
Physician's perception	1	1	3	2	$\chi^2 = .13$	1	.72
Motivational deficit	4	4	17	8	$\chi^2 = 1.64$	1	.20
Stigma associated with	-	-			χ 1.01	-	0
taking an antipsychotic	0		8	4	$\chi^2 = 3.96$	1	.047
No family support for taking	· ·		0		χ =0.00	_	.011
an antipsychotic	3	3	7	4	$\chi^2 = .07$	1	.79
No support in the patient's		9	•		λ01	_	
living environment for							
taking an antipsychotic	1	1	4	2	$\chi^2 = .16$	1	.6
Cost of the antipsychotic	0		11	6	$\chi^{2}=5.41$	1	.020
Problems with the thera-	U	_	11	U	χ -5.41	1	.020
peutic alliance	0		0				
Other	1	1	3	2	$\chi^2 = .90$	1	.75
Duration of nonadherence	1	T	J	4	χ30	1	.10
episode ^b (mean±SD weeks)	16.1±		6.8±		t=2.48	283	.014
episode (mean±3D weeks)	51.1		8.3		t=2.40	200	.014
Completely stopped taking	51.1		0.0				
	74	78	130	64	$\chi^2 = 5.36$	1	.021
the antipsychotic	74	10	130	04	χ = 5.50	1	.021
Severe positive symptoms	1.9	13	12	G	2 1 56	1	.03
Before nonadherence episode	13			6	$\chi^2 = 4.56$		
During nonadherence episode	67	70	98	48	$\chi^2 = 12.27$	1	<.001
After nonadherence episode	18	19	16	8	$\chi^2 = 8.10$	1	.004
Severe negative symptoms	-	_	_	0	.2 2 15	1	10
Before nonadherence episode	7	7	7	3	$\chi^2 = 2.45$	1	.12
During nonadherence episode	27	29	44	22	$\chi^2 = 1.70$	1	.20
After nonadherence episode	13	14	11	6	$\chi^2 = 5.6$	1	.018
Hospital admission after			0.0	0.4	2 0 60		005
nonadherence	50	52	68	34	$\chi^2 = 9.60$	1	.002

^a Data are weighted to account for nonresponse. Ns vary because of missing data

ioral and family interventions were also reported to be significantly less effective among patients who were unaware of their mental illness than they were among patients who were aware. The effectiveness of teaching family members to use positive reinforcement and cueing pill taking to reminders, such as an alarm clock, did not significantly differ in perceived effectiveness between the study groups, although each approach tended to be more effective among patients who were aware that they had a mental illness (Table 4).

The perceived effectiveness of the pharmacologic interventions, with the exception of simplifying the dosage regimen, did not significantly differ between the two study groups in the adjusted models. In both groups, the most effective intervention was reported to be the initiation of a depot antipsychotic medication.

Discussion

Our findings, in line with previous research (6,8,9), indicate that patients with schizophrenia who are not adherent to antipsychotic medication

regimens commonly lack an awareness of having a mental disorder. We estimate that approximately one-third of psychiatric outpatients with schizophrenia in the United States who are nonadherent are not aware that they have a mental illness.

In this study, awareness of illness was related to a history of comorbid depression. A recent meta-analysis also indicated a positive relationship between insight and depressive symptoms (25). More severe depression has been strongly associated with greater insight early in the course of illness (26) and among patients with multiple episodes (27-29). In one study, insight into illness was related to suicidal ideation (30). As clinical efforts are made to extend and broaden insight into illness among persons with schizophrenia, it may be important to monitor patients closely for changes in mood state and suicidal behavior (17).

Patients who were aware of having a mental illness were approximately twice as likely to be engaged in paid or volunteer employment as patients who lacked such awareness. This finding is consistent with previous research linking impairments in insight occupational performance (31,32). In one study of adults with schizophrenia, those with poor insight into their illness had greater difficulties cooperating with coworkers, poorer work habits, and poorer quality of work than their counterparts whose insight was intact (32). Improvements in vocational rehabilitation have also been related to improved insight (33).

In this study, a history of substance abuse and homelessness was related to an awareness of illness. Longitudinal research is needed to help define the extent to which awareness of schizophrenia increases vulnerability to substance abuse or housing loss, or whether these adversities tend to lead to a greater awareness of having a mental disorder among individuals with schizophrenia.

Several investigators have reported that cognitive impairment in schizophrenia is related to deficits in insight (32,34–36). In our study, which involved comparisons among patients who had recently been nonadherent

^b Defined as the number of weeks separating the start of the episode and the end of the episode

to medications, awareness of mental illness was not significantly related to general intellectual functioning. Because nonadherence is also significantly related to poor intellectual functioning (36), it is possible that, because the samples were limited to patients who were nonadherent, group differences in intellectual functioning were attenuated.

Denial of illness was cited as the primary cause of nonadherence for a majority of patients who lacked awareness of their illness. By contrast, paranoia was less commonly related to nonadherence among patients who lacked awareness than among those who were aware of having a mental illness. This finding, together with the lower rates of depressive disorder in the group that lacked insight, is consistent with research linking the evolution of insight to development of depression and paranoia in early-stage schizophrenia (37).

The consequences of nonadherence to antipsychotic medications may be especially serious for patients who lack awareness of having a mental disorder. Compared with patients with intact insight, patients with impaired insight have a significantly longer duration of nonadherence, are more likely to completely cease taking antipsychotic medications, have more severe positive psychotic symptoms, and are more likely to be psychiatrically hospitalized.

In routine psychiatric practice, management of nonadherence to antipsychotic medications does not appear to vary markedly with awareness of illness. No significant differences were found by illness awareness in the frequency with which patients received a wide range of pharmacologic, psychological, behavioral, and family interventions. Simple psychological interventions, such as urging the patient to maintain medication adherence or discussing the risks of nonadherence, were almost universally provided to both patient groups.

In clinical treatment research, cognitive-behavioral and motivational approaches have shown some promise in building insight (17) and improving adherence (18,19) among persons with psychotic disorders. By contrast, the common—and presum-

Table 3

Frequency of interventions used to manage episodes of nonadherence among patients with schizophrenia, by whether their psychiatrist reported them as being aware of their mental illness^a

	Unaw	vare (N=97)	Aware (N=203)			
Type of intervention	N	%	N	%	$\chi^{2\dagger}$	p
Pharmacologic						
Change antipsychotic dosage	31	34	74	32	.09	.76
Switch antipsychotic	25	29	61	32	.20	.56
Add another antipsychotic	11	13	31	16	.48	.49
Simplify dosing	48	51	98	48	.23	.63
Start depot medication	21	22	30	15	2.60	.11
Change medications for side						
effects	20	21	51	25	.64	.43
Psychological						
Urge adherence	89	95	196	96	.48	.49
Discuss risks of nonadherence	90	95	197	97	.78	.37
Explore reasons for						
nonadherence	89	94	194	95	.36	.55
Link adherence to personal						
goals	66	70	155	76	1.50	.22
Discuss main effects and side						
effects	84	89	178	87	.10	.75
Explore the meaning of taking						
antipsychotic medications	70	74	133	67	2.23	.14
Behavioral						
Daily observation	39	42	71	35	1.19	.28
Cue with reminders	17	18	50	25	1.60	.21
Compartmentalized pill box	34	36	91	45	1.96	.16
Medication diary	20	21	41	20	.02	.90
Family						
Explore attitudes	46	49	101	50	.02	.90
Encourage family support	60	63	119	58	.51	.47
Psychoeducation						
General	57	60	114	56	.37	.54
Adherence assessment	52	54	100	49	.70	.40
Positive reinforcement	42	44	83	41	.27	.61

 $^{^{\}rm a}$ Data are weighted to account for nonresponse. Ns vary because of missing data. $^{\dagger}{\rm df}{=}1$

ably much less intensive—psychological interventions we assessed in routine practice were perceived as relatively ineffective in managing antipsychotic nonadherence, especially among patients who lacked awareness of having a mental disorder. Differences between patient groups in perceived effectiveness tended to be less evident for several of the pharmacologic interventions.

For both patient groups, starting a depot medication (38) and observing pill taking on a daily basis were rated as the two most effective interventions. Expanding the use of these interventions might improve the management of nonadherence. At the same time, more work is needed to develop and test intensive psychological approaches to the prevention and

management of nonadherence to antipsychotic medications among patients with schizophrenia.

This study had several limitations. First, the data are based exclusively on the psychiatrists' assessments. Although we limited the study to patients who had been under the psychiatrists' care for at least a year and who therefore were presumably well known to the psychiatrists, the absence of patient-reported or family-reported data imposes significant and obvious limitations. For example, patients may have a different view than their psychiatrist of the effectiveness of treatment. In addition, the exclusion of patients who were seen for less than a year is likely to have eliminated many highly nonadherent patients.

Second, the accuracy of clinicians'

Table 4Perceived effectiveness of interventions to manage episodes of nonadherence to antipsychotic medications among patients with schizophrenia, by whether their psychiatrist reported them as being aware of their mental illness^a

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Switch antipsychotic 20 3.0 ± 1.4 51 3.5 ± 1.2 1.2 69 .22 .04 Add another antipsychotic 9 2.8 ± 1.6 25 3.6 ± 1.1 1.6 32 .12 .20 Simplify dosing 45 2.7 ± 1.3 90 3.3 ± 1.2 2.8 133 .006 .67 Start depot medication 20 3.9 ± 1.0 26 3.9 ± 1.1 .05 44 .96 12 Change medications for side effects 18 3.1 ± 1.4 46 3.3 ± 1.0 .54 62 .59 28 Psychological Urge adherence 86 2.0 ± 1.0 182 3.0 ± 1.2 7.1 266 <.001	.89
Add another antipsychotic 9 2.8 ± 1.6 25 3.6 ± 1.1 1.6 32 .12 .20 Simplify dosing 45 2.7 ± 1.3 90 3.3 ± 1.2 2.8 133 .006 .67 Start depot medication 20 3.9 ± 1.0 26 3.9 ± 1.1 .05 44 .9612 Change medications for side effects 18 3.1 ± 1.4 46 3.3 ± 1.0 .54 62 .5928 Psychological Urge adherence 86 2.0 ± 1.0 182 3.0 ± 1.2 7.1 266 <.001 .96 Discuss risks of nonadherence 86 2.1 ± 1.0 182 3.1 ± 1.1 7.1 266 <.001 .92	.90
Simplify dosing 45 2.7 ± 1.3 90 3.3 ± 1.2 2.8 133 .006 .67 Start depot medication 20 3.9 ± 1.0 26 3.9 ± 1.1 .05 44 .96 12 Change medications for side effects 18 3.1 ± 1.4 46 3.3 ± 1.0 .54 62 .59 28 Psychological Urge adherence 86 2.0 ± 1.0 182 3.0 ± 1.2 7.1 266 <.001 .96 Discuss risks of nonadherence 86 2.1 ± 1.0 182 3.1 ± 1.1 7.1 266 <.001 .92	.61
Start depot medication 20 3.9±1.0 26 3.9±1.1 .05 44 .96 12 Change medications for side effects 18 3.1±1.4 46 3.3±1.0 .54 62 .59 28 Psychological Urge adherence 86 2.0±1.0 182 3.0±1.2 7.1 266 <.001	.007
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Psychological Urge adherence 86 2.0±1.0 182 3.0±1.2 7.1 266 <.001	.45
Urge adherence 86 2.0±1.0 182 3.0±1.2 7.1 266 <.001	
Discuss risks of nonadherence 86 2.1±1.0 182 3.1±1.1 7.1 266 <.001 .92	<.001
Explore reasons for nonadherence 84 2.1 ± 1.1 180 3.2 ± 1.2 7.3 262 <.001 1.08	<.001
	<.001
Link to personal goals 62 2.1±1.1 145 3.1±1.1 6.9 205 <.001 1.00	<.001
Discuss main effects and side effects 80 2.2 ± 1.1 159 3.1 ± 1.2 5.8 237 < .001 .91	<.001
Explore the meaning of taking	
antipsychotic medications 68 1.9±1.0 124 2.8±1.2 5.2 190 <.001 .78	<.001
Behavioral	
Daily observation $37 3.2\pm 1.4 64 3.9\pm 1.3 2.3 100 .025 .69$.002
Cue with reminders 17 2.6 ± 1.0 50 3.0 ± 1.1 1.4 65 .18 .58	.14
Compartmentalized pill box 34 2.5 ± 1.1 82 3.2 ± 1.1 2.9 114 .004 .59	.011
Medication diary 19 $1.8\pm .8$ 38 2.6 ± 1.1 2.6 55 .011 .68	.07
Family	
Explore attitudes 42 2.5 ± 1.4 94 3.2 ± 1.3 2.7 134 .008 .68	.01
Encourage family support 53 2.7 ± 1.5 108 3.2 ± 1.2 3.4 159 < .001 .70	.003
Psychoeducation	
General $53 2.8\pm1.3 106 3.5\pm1.2 3.3 157 .001 .59$.004
Adherence assessment 49 2.8±1.4 92 3.5±1.2 3.1 139 .002 .68	.021
Positive reinforcement 39 2.7 ± 1.4 77 3.2 ± 1.2 1.9 114 .055 .38	.16

^a Data are weighted to account for nonresponse.

assessments of adherence to antipsychotic regimens has been questioned (39,40). Although a more intrusive method of adherence measurement, such as pill counts, serum levels, and electronic MEMS (Medication Event Monitoring System) caps, would likely have yielded more accurate information, the promise of improved accuracy of measurement must be weighed against substantial selection biases that are likely to have been introduced by limiting the sample to patients who were willing to submit to intrusive adherence monitoring.

Third, illness awareness was measured with a single survey item. A more extensive assessment of insight into illness (41–43) would have provided a more informative description. For some patients, illness awareness

may fluctuate and cannot be captured by a dichotomous measure.

Fourth, salience of individual cases may have biased patient selection and produced a sample of memorable patients rather than representative patients (44). Fifth, no information was collected for patients who consistently adhered to their antipsychotic therapy. For this reason, the results do not address patients who, despite reporting that they were not ill, came to appointments and took their antipsychotic medications as prescribed. Finally, survey nonresponse may have biased the reported rates and group associations. Although we adjusted the results for nonresponse related to known characteristics of the study psychiatrists, we cannot exclude the possibility that response patterns related to unmeasured respondent characteristics biased study findings.

Conclusions

Lack of insight into mental illness is common among patients with schizophrenia who are nonadherent to antipsychotic medication regimens. For patients with schizophrenia who lack such awareness, nonadherence tends to be prolonged and especially clinically disruptive. Simple psychological approaches were often used to manage medication nonadherence in this patient sample but were reported by the treating psychiatrists as being relatively ineffective. By contrast, initiation of depot medications, daily observation of medications, and family psychoeducation were less commonly used but were reported to be more

b Measured on a 5-point scale from 1, ineffective in maintaining adherence, to 5, extremely effective

^c Adjusted for patient's age, gender, race, employment status, living arrangement, payment source, intellectual functioning, lifetime episode of mania, major depression, substance use disorder, having injured someone, having been homeless for 48 hours, and treatment with an antidepressant, anxiolytic, mood stabilizer, or antiparkinsonian medication

effective than the psychological interventions. Developing and testing new strategies to enhance adherence to antipsychotics among patients with schizophrenia who lack insight into their illness remains a high priority.

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