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# Addressing Nonadherence in the Schizophrenic Population

Angela C. Singh, PharmD, Angela J. Massey, PharmD, BCPP, Michael D. Thompson, PharmD, BCNP, Leonard R. Rappa, PharmD, BCPP, and Marlon S. Honeywell, PharmD

*Nonadherence within the schizophrenic population is a challenge for both the patient and the clinician. This problem not only causes an increase in health care use and cost but also places the patient at risk of relapse and dissatisfaction with medical care. Nonadherence is influenced by several factors including disease, treatment, and*

*psychological and social factors. All of these factors must be addressed if the clinician hopes to reduce nonadherence within this patient population. This article will attempt to identify factors that contribute to nonadherence and review strategies that can be implemented to address each of these factors.*

KEY WORDS: Nonadherence, schizophrenia, addressing, strategies, treatment, psychosocial, disease, factors.

**S**CHIZOPHRENIA AFFECTS approximately 1% of the worldwide population and is considered a chronic illness.<sup>1</sup> Nonadherence is a challenge faced by both the patient and the clinician. Although the terms *compliance* and *adherence* are used interchangeably, adherence infers a collaborative relationship between the patient and the practitioner in achieving therapeutic goals whereas compliance implies that the patient is passive and obedient to the practitioner.<sup>1,2</sup> Nonadherence among the psychiatric population can be defined as a failure to enter a treatment program, premature termination of treatment, or incomplete implementation of instructions, including those that pertain to medication administration. Although treatment adherence is crucial for achieving the desired therapeutic outcomes, it is estimated that nonadherence ranges from 20% to 89% among schizophrenic patients, with an average of 50%.<sup>3</sup>

Studies have shown a direct correlation between nonadherence and rates of relapse in schizophrenia; on average, nonadherent patients have a risk of relapse that is 3.7 times greater than their adherent counterparts.<sup>1,4</sup> Relapse places a tremendous economic burden on our society in terms of both health care costs and the cost of disability, with schizophrenia being among the top 10 causes of long-term disability in the world.<sup>1,5</sup> Patients who are nonadherent are at an increased risk of housing instability and violent behavior.<sup>1,6</sup> Additionally, nonadherence may result in reduced or lack of treatment benefit, decreased patient

satisfaction with medical care, and increased health care use including emergency room visits and hospitalizations.<sup>2</sup> Physicians, who may perceive poor adherence as poor medication response, may make unnecessary changes in treatment regimens, which may result in increased costs to the patient.<sup>6</sup>

There are numerous factors that place patients with schizophrenia at increased risk for nonadherence,

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including the chronic nature of the illness, the stigmatization associated with the disease, cognitive disturbances, poor insight, and intolerable side effects associated with treatment options.<sup>7</sup>

Furthermore, nonadherence may be either inadvertent or intentional. Inadvertent nonadherence is a result of the symptoms of the illness, such as poor insight or cognitive impairment. Intentional nonadherence is a direct result of a conscious decision by the patient to terminate treatment.<sup>6</sup> To address adherence in the schizophrenic population, practitioners must be able to differentiate between different types of nonadherence as well as identify and prevent modifiable risk factors.

### DEFINING AND ASSESSING NONADHERENCE

The definition of medication nonadherence in the schizophrenic population differs among the literature; however, the American Psychiatric Association has defined adherence as missing <20% of medication, partial adherence as missing between 20% to 80% of medication, and nonadherence as missing >80% of medication.<sup>8</sup>

The task of assessing adherence offers many challenges. Often clinicians must rely on subjective and indirect methods for monitoring compliance, such as self-reporting, significant other reporting, and chart reviews. Velligan and associates conducted a review of 161 articles exploring definitions and assessment of adherence. The results demonstrated that the most common method used was self-reporting, and in 77% of the studies, subjective and indirect methods were used.<sup>9</sup> These methods frequently lead to exaggerated or inaccurate responses, particularly with self-reporting. Lastly, reporting by caregivers or significant others is dependent on the degree of involvement of that individual with the administration of the patient's medication.<sup>10</sup>

Another dilemma is the fact that clinicians have difficulty accurately detecting or predicting nonadherence in a majority of patients.<sup>11</sup> Byerly and associates recently conducted a study comparing the detection of adherence using the Medication Event Monitoring System (MEMS) and the Clinician Rating Scale.<sup>12</sup> The clinical assessment of the patient was conducted by an experienced mental health counselor and involved questions regarding the patients' symptoms, sense of well-being, functional status, attitude toward taking medication, medication side effects, and a specific

question regarding the number of days the patient was adherent over the past month. The results were significant; nonadherence was detected in 48% of patients evaluated with MEMS and 0% of patients evaluated with the Clinician Rating Scale.<sup>12</sup> Furthermore, physician assessment of efficacy may be incorrectly based on worsening of clinical symptoms, which could also be attributed to lack of adherence with current medications. This misinterpretation can lead to the prescriber discontinuing medications, increasing doses, or adding unnecessary adjuvant therapy.<sup>6</sup>

Direct methods of assessing nonadherence, including pill counts, electronic monitoring, and refill monitoring, can also be problematic.<sup>10</sup> Utilization of pill counts requires the patient to bring in his or her medication, which can lead to an inaccurate assessment, if the patient decides to bring only the correct number of pills, leaving the others at home. Pill counts and refill monitoring can also be influenced by samples of medication that may be given to patients. Lastly, electronic monitoring, a system that records the time and date that a bottle is opened, may be influenced by patients not replacing the caps or the use of medications from another prescription bottle.<sup>12</sup>

### FACTORS CONTRIBUTING TO NONADHERENCE

The issue of adherence is a complex, multifaceted one with no one specific factor that is solely predictive of nonadherence. Rather, it should be viewed as an interconnected relationship between several factors, and each factor must be addressed individually to improve adherence. Factors contributing to nonadherence may be disease related, treatment related, or patient related, or nonadherence may be related to social and psychological factors.<sup>13</sup>

#### Disease-Related Factors

Disease-related factors include characteristics of schizophrenia, which places the patient at an increased risk of nonadherence. For example, poor insight may be the single most important factor leading to nonadherence. Insight may be defined as a general recognition of mental illness, the capacity to correctly attribute symptoms to the pathology of the illness, and the ability to recognize the benefits of and consequently cooperate with treatments.<sup>14</sup> Lack of insight not only plays a major role in nonadherence but can also be a result of nonadherence, creating a vicious circle leading to

increased relapse and inpatient admissions.<sup>1,5,7</sup> Agarwal and associates found that there was a consistent trend toward adherent patients being more aware of their symptoms and being able to relate their symptoms to their disease.<sup>15</sup> In addition, in a study evaluating 300 schizophrenic patients, it was determined that those who lacked insight had significantly longer periods of nonadherence.<sup>1</sup> There is also some evidence that there is a relationship between insight and perceived benefit. Patients who are aware of their symptoms will have a more favorable view of their medications, because they are able to correctly identify the medications' benefit through a reduction of their symptoms.<sup>16</sup> Additionally, several studies have shown that patients who are adherent have positive attitudes toward their medications and report a better subjective response.<sup>15-19</sup>

Disease severity also appears to be a contributing factor to nonadherence. Patients experiencing grandiose delusions may not perceive the need for their medication, and those exhibiting suspiciousness may be less adherent as a result of fear of the medication.<sup>20</sup> Nonadherent patients also show higher levels of agitation, whereas those patients experiencing depression or anxiety may be more adherent.<sup>1,21</sup> Patients recovering from an acute exacerbation of their disease, who may still be experiencing psychotic symptoms, are highly unlikely to remain adherent to their medications after discharge from inpatient facilities. This is not only related to their psychosis but also to the fact that these patients may not have the cognitive skills necessary to understand and implement the instructions that are given to them by the hospital staff regarding their medications. Velligan and associates found that patients who were discharged after a short length of stay in an inpatient facility often mismanaged their medications. They had bottles of the same medication from the outpatient and inpatient pharmacies, and several of the participants had planned on taking both the medications, from the inpatient and outpatient pharmacies, because they did not understand that one medication replaced the other. They also found bottles containing different strengths of the same medication, as well as different medications in the same bottle.<sup>9</sup>

### Treatment-Related Factors

Treatment-related factors associated with nonadherence include side effects, efficacy of the regimen, complexity of the regimen, and cost. In the past, nonadherence related to side effects was often associated with the use of conventional agents. These agents

predominantly produce anticholinergic and extrapyramidal symptoms, which are considered generally unacceptable to the patient. The introduction of atypical antipsychotics brought the hope that nonadherence related to these side effects would decline; however, clinical trials have not substantially proven this theory.<sup>3,17</sup> Although the atypical agents do not cause anticholinergic and extrapyramidal side effects to the degree of the conventional agents, they do produce side effects that are often unacceptable to some patients including galactorrhea, weight gain, and alterations in lipid and glucose metabolism. Currently, the literature does not provide a clear picture of the degree to which side effects are related to nonadherence. However, although the incidence and type of side effects do seem to play some role in causing nonadherence, they are probably not a major influence.<sup>9,22</sup>

The efficacy of the medication appears to play a major role in determining whether a patient will be adherent to his or her medication. Kikkert and associates found the subjective efficacy of the medication, as evidenced by symptom relief, was the most important factor contributing to adherence among caregivers and patients. Surprisingly, practitioners in the study rated efficacy as significantly less important and rated improved side effect profile as one of the leading factors contributing to adherence.<sup>17</sup> Another treatment-related cause of nonadherence involves the complexity of the patient's regimen. Often, patients may be on several different medications, which may require administration at different times of the day. One practice that increases the complexity of psychiatric regimens is the addition of medications before appropriate time has been given to allow current medications to achieve their maximum therapeutic response. This often occurs in the inpatient setting, where occasionally, the goal of the institution is to control the patient's symptoms rapidly to facilitate the discharge of the patient. The end result is a patient being discharged with a very complex regimen, which may contain multiple antipsychotic medications. As stated previously, these patients are prone to cognitive impairment, which leaves them subject to inadvertent nonadherence. Additionally, as the complexity of the regimen increases, so does the potential for an increase in the incidence and severity of side effects, as well as an increase in cost. Collectively these may contribute to intentional nonadherence. Furthermore, in the outpatient setting, failure of monotherapy to effectively manage symptoms is a common rationale for the addition of adjunctive medications. This is unlikely to be of benefit, as a patient

who fails to respond due to nonadherence or partial adherence will not experience improved response from the addition of another medication. Instead, the additional medication will only lead to continued nonadherence and increased cost to both the patient and society.<sup>23,24</sup>

### Psychological and Social Factors

Psychological and social factors that contribute to nonadherence include stigmatization of both the disease and antipsychotic medications, stressors in the patient's surrounding environment, a poor support system, and a failure to develop a therapeutic alliance with the clinician. Patients and caregivers rate support, information, and involvement as important factors contributing to adherence.<sup>17</sup> A patient's social support system appears to play a vital role in whether or not he or she is adherent to the medications. For example, patients who live alone are less likely to be adherent with their medications than their counterparts, who live with their family or in a group home. Those patients whose families are involved in their care are more likely to be adherent with their medications, unless the caregiver has a negative attitude toward the patient's medications.<sup>20,25</sup> A good therapeutic alliance between the patient and clinician is also strongly associated with adherence; however, even a strong therapeutic alliance may not be effective in preventing nonadherence related to severe psychotic symptoms.<sup>26</sup> Lastly, the study conducted by Olfson and associates found that substance abuse disorders emerged as the strongest predictor of medication nonadherence. The effect of substance abuse on adherence is related to its ability to cause impaired judgment, reduced motivation, and a decreased appreciation for the benefits of antipsychotic therapy.<sup>25</sup>

## ADDRESSING NONADHERENCE

### Disease-Related Factors

Interventions that address disease-related factors that may improve adherence include supportive devices such as cognitive adaptive therapy (CAT), cognitive behavioral therapy (CBT), and psychoeducation. Each intervention addresses specific factors that contribute to nonadherence. For example, supportive devices improve nonadherence related to cognitive impairment or disorganization. Velligan describes a "systematic approach to using environmental support

devices for patients with schizophrenia known as Cognitive Adaptive Therapy (CAT)." CAT utilizes alarms, single-dose containers, and journals for recording side effects to cue behaviors. In a randomized study involving 42 patients, those randomized to CAT treatment groups were significantly more likely to be adherent at the end of 6 months than those who were not in the CAT treatment groups.<sup>6</sup> Psychoeducation involves the delivery of information about schizophrenia, treatment, and medications without placing an emphasis on attitudes or beliefs with regard to treatment. Although this intervention may be effective in patients who are nonadherent as a result of side effects or through a conscious decision to terminate treatment, it is less effective in patients who lack insight or are experiencing denial. Patients who do not believe that they are ill will not be receptive to interventions addressing nonadherence. For these patients, CBT offers a more successful approach because it addresses the attitudes and beliefs of the patient. Often, in clinical practice, the patient's perspective is interrupted with counseling regarding the positive benefits of the medication and the importance of adherence. CBT, however, follows the patient's agenda, and therefore clinicians must respect and gain an understanding of the patient's perspective for the therapy to be successful. This approach is based on the notion that thoughts influence feelings; therefore, the focus is placed on recognizing and challenging irrational, unhealthy, or self-defeating thoughts from a patient's perspective and then developing a plan to replace them with rational and healthy thoughts.<sup>4,6</sup>

### Psychological and Social Factors

Interventions addressing psychological and social factors include providing support groups; assisting the patient with treatment of substance abuse disorders; educating the patient, family members, and caregivers; and lastly developing a strong therapeutic alliance. A therapeutic alliance may be defined as a collaboration between the patient and the provider where there is a mutual agreement on goals and outcomes of selected treatments.<sup>27</sup> Kirsh and Tate conducted a study that combined the results of a literature review with interviews conducted with service providers and mental health patients. Their study revealed that there are 3 basic themes that highlight dimensions of and operations within the therapeutic alliance between the consumer and service provider: (1) building and negotiating

**Table 1**  
**Strategies for Building a Therapeutic Alliance<sup>27</sup>**

Theme	Category	Comments
Building and Negotiating Trust	Laying the Foundations of the Relationship	Engagement of the relationship is related to its perceived benefit. Important to convey to the client the ability to assist with his or her basic needs. Pace the relationship; this should take place within the client's comfort zone. Learn about the client.
	Predictors of a Sound Relationship	Predictors of a strong alliance include service intensity and client characteristics such as level of need.
	Choice as an Essential Ingredient in Relationship Building	Engagement in the relationship should result in increased feelings of power and control for the client. Educate patient about options and consequences and allow him or her to participate in the decision-making process.
"I'm on Your Side"	Being There	Should be accessible, in regular contact and actively listening.
	Knowing the Person Well	Allows the provider to understand the patient's perspective, anticipate his or her needs, and avert crisis.
	Sharing, Accepting, Caring	Invokes the idea of reciprocity in the relationship, respect for individuals and their differences, and concern for their well-being.
Tools and Strategies	Moving Forward	Characterized by staff attitudes that promote personal growth. Improves insight, self-awareness, and self-confidence.
	A Problem-Solving Approach	Break tasks into steps, which allows client to analyze and understand the components as parts of the whole. Role playing; may be helpful in addressing how a client might deal with a particular situation.
	Responsibility for Well-Being; A Key Person Environment as a Tool: The Importance of Location.	Identify one person who is accountable and responsible for the well-being of the client; this solidifies the relationship and provides comprehensive care. Address disabling environments. Provide an environment that is inviting for the client.

trust, (2) I'm on your side, and (3) tools and strategies.<sup>27</sup> Table 1 details the findings of their study.

### Treatment-Related Factors

Pharmacological interventions to improve adherence include optimization of doses to minimize symptoms, use of an appropriate trial period before increasing the dose or adding medications, use of orally disintegrating tablets or long-acting injections, dose reductions or switching medications to minimize side effects, regimen simplification, and observation of pill taking.<sup>1,8,13</sup> The intervention selected to improve adherence may vary depending on the causes of the patient's nonadherence. For example, a patient who is nonadherent as a result of psychotic symptoms may need to be considered for depot therapy. But, a patient who is experiencing intolerable side effects may need a dose reduction or to be switched to another agent.

Regimen complexity significantly contributes to nonadherence, and studies have demonstrated that the prescribed number of doses per day is inversely related to adherence. By optimizing the dose of a medication and allowing the appropriate time for that medication to achieve its maximum therapeutic

response, before adding extra medications, clinicians will minimize nonadherence related to polypharmacy. Additionally, prescribing medications that require once to twice daily dosing may also minimize the complexity of the regimen and therefore improve adherence. Patients who exhibit cognitive dysfunction or disorganization may find it difficult to manage complex medication regimens and may benefit from simplification of their regimen or a long-acting injectable. A review of studies in which compliance was monitored using electronic monitoring devices was conducted to determine the association between dose frequency and medication compliance. A total of 76 studies were evaluated, and the reviewers found that compliance was significantly higher for once-daily versus 3 times daily ( $P = .008$ ), once daily versus 4 times daily ( $P < .001$ ), and twice daily versus 4 times daily regimens ( $P = .001$ ).<sup>28</sup>

Changing from an oral formulation to long-acting injections is also helpful in addressing adherence issues, not only related to cognitive dysfunction and disorganization but also in those patients experiencing unresponsive psychotic symptoms. The use of a long-acting injection reduces the occurrence of covert nonadherence. It provides the clinician with the ability

**Table 2**  
**Dosing Comparison of Long-Acting Injectables<sup>31</sup>**

<b>Fluphenazine Decanoate Dosing</b>		
<b>Patient</b>	<b>Dose</b>	
Stabilized on oral formulation	12.5 mg of depot formulation is equivalent to 10 mg of oral formulation	
Treatment Naive	12.5 mg every 3 weeks	
Titration	Individualized according to therapeutic response or adverse events	
<b>Haloperidol Decanoate Dosing</b>		
<b>Patient</b>	<b>Initial Dose</b>	<b>Maintenance</b>
Stabilized on low daily oral doses up to 10 mg/day	10-15 times the daily oral dose	10-15 times the previous oral dose
Elderly or debilitated	10-15 times the daily oral dose	10-15 times the previous oral dose
High dose	20 times the oral daily dose	10-15 times the previous daily dose
Risk of relapse		
Tolerant to oral haloperidol		
Titration	Dose should be titrated up or down depending on the clinical response of the patient	
<b>Risperidone (Risperdal Consta® Dosing)</b>		
<b>Patient</b>	<b>Dose</b>	
No previous treatment with risperidone	Pretreat oral risperidone for at least several days to assess tolerability before the first injection	
Documented exposure and toleration of oral risperidone within the last year but not stabilized	25 mg Risperdal Consta every 2 weeks	
Stabilized patient on a fixed dose of oral risperidone for 2 weeks or more	Oral dose of <4 mg = 25 mg every 2 weeks Oral dose 4-5 mg = 37.5 mg every 2 weeks Oral dose of >5 mg = 50 mg every 2 weeks	
Elderly (Age > 65)	Risperdal Consta® 25 mg every 2 weeks	
Titration schedule	Increase Risperdal Consta® by 12.5 mg every 4 weeks	

to differentiate between relapses or lack of symptom improvement due to nonadherence, from those that are due to lack of medication efficacy. Additionally, long-acting injections remain in the patient's system longer than oral products, which will allow the clinician to begin efforts to reinstate therapy before relapse occurs. Potential disadvantages consist of the inability to stop the medication immediately with the development of side effects or lack of patient acceptance.<sup>8</sup> It is a common

misconception that patients prefer oral formulations over long-acting injections. A review of 6 studies comparing patients' attitudes toward oral and long-acting injectables found that a majority of patients prefer long-acting injections over oral formulations in 5 of the 6 studies.<sup>29</sup> Currently, fluphenazine, haloperidol, and risperidone are the only antipsychotics available as long-acting injectable agents. Ziprasidone, aripiprazole, and olanzapine are available as immediate-acting injections; however, they are short-acting formulations, which are typically used in the management of acute psychosis. Table 2 provides a summary of the dosing recommendations for the long-acting injections.

Liquid formulations or orally disintegrating tablets are particularly useful in patients who are nonadherent in the inpatient setting or in an environment where a caregiver either administers the medication or observes the patient taking the medication. Currently, clozapine, olanzapine, and risperidone are the only antipsychotics available in an orally disintegrating formulation, which limits the usefulness of this practice. Additionally, cost must be considered when utilizing orally disintegrating tablets. For example, Zyprexa Zydis® 15 mg is approximately \$125 more than Zyprexa® 15 mg tablets for a 30-day supply. In patients who may not be able to afford an orally disintegrating product, the use of liquid formulation should be considered. Table 3 provides additional information regarding the formulations available for each antipsychotic.

Interventions addressing the tolerability of medications include lowering the dose or switching from one agent to another. Clinicians who choose to lower the dose of a medication must be aware that reducing the dose may result in increased risk of relapse for the patient.<sup>7</sup> If the clinician determines that switching antipsychotics is the most appropriate intervention, he or she must then determine which switching strategy to employ. Both of these interventions can be difficult. Switching strategies for oral antipsychotics generally include 4 approaches: (1) introduction of the new agent with titration to its therapeutic dose and a gradual taper of the prior agent, (2) simultaneous cessation of the prior agent with initiation of the new agent, (3) introduction of the new agent with gradual titration to therapeutic dose and cessation of prior therapy, and (4) gradual cessation of prior therapy with introduction of the new agent at full dose.<sup>30</sup> There are also several strategies addressing switches occurring between oral therapy and long-acting injections. Table 4 outlines switching strategies for both

**Table 3**  
**Antipsychotic Formulations<sup>31,32</sup>**

Drug	Oral Tablet	Oral Capsule	Orally Disintegrating Tablet	Oral Liquid	Suppository	Long-Acting Injection	Immediate-Acting Injection
Chlorpromazine (Thorazine®)	X	X		X	X		X
Thioridazine (Mellaril®)	X			X			
Perphenazine (Tilafon®)	X			X			X
Trifluoperazine (Stelazine®)	X			X			X
Thiothixene (Navane®)		X		X			
Fluphenazine (Prolixin®)	X			X		X	X
Haloperidol (Haldol®)	X			X		X	X
Loxapine (Loxitane®)		X		X			
Clozapine (Clozaril®)	X		X				
Risperidone (Risperdal®)	X		X	X		X	
Olanzapine (Zyprexa®)	X		X				X
Quetiapine (Seroquel®)	X						
Ziprasidone (Geodon®)		X					X
Aripiprazole (Abilify®)	X			X			X

**Table 4**  
**Switching Strategies for Antipsychotic Therapy<sup>33</sup>**

Type	Method
Switching between oral antipsychotic agents.	Titration of new agent to therapeutic dose while gradually reducing the prior agent. Discontinue the prior agent and initiate the new agent.
Switching from a conventional long-acting antipsychotic drug to an atypical oral agent.	Titration of new agent to therapeutic dose and cessation of prior therapy. Initiation of new agent at full dose with gradual tapering of old agent. 1-month cross-titration taper.
Switching to a long-acting atypical antipsychotic.	Continue oral therapy during the first 3 weeks of treatment.
Switching from a conventional long-acting agent to an atypical long-acting agent.	Administer long-acting risperidone 1 week prior to next dose of conventional long-acting agent. Administer long-acting risperidone at the next scheduled dose of conventional long-acting agent.

oral therapy and long-acting injections. Lastly, observing the administration of the medication is a useful intervention for numerous factors; however, it is limited by the fact that the patient must either be institutionalized, participate in a day program, or have a caregiver who is willing to cooperate in the process.

## CONCLUSION

The impact of nonadherence is felt across the full spectrum of our society. Patients who are nonadherent are placed at an increased risk for developing violent behaviors, homelessness, relapse, rehospitalization, and lack of symptom control.<sup>4,20,25</sup> There are multiple contributory factors, and with many patients, nonadherence is a multifactorial problem. To appropriately address nonadherence in this patient population, clinicians must assess each individual situation and address each contributing factor. This approach will typically require more than one type of intervention; however, if successful, these interventions will result



in an improvement of the patient's quality of life and will benefit society.

## REFERENCES

- Compton M. Treatment nonadherence among individuals with schizophrenia: risk factors and strategies for improvement. 2006. CME. Available at: medscape.com. Accessed September 23, 2006.
- Tabor P, Lopez D. Comply with us: improving medication adherence. *J Pharm Pract.* 2004;17:167-181.
- Dolder C, Lacro J, Dunn L, Jeste D. Antipsychotic medication adherence: is there a difference between typical and atypical agents? *Am J Psychiatry.* 2002;159:103-108.
- Zygmunt A, Olfson M, Boyer C, Mechanic D. Interventions to improve medication adherence in schizophrenia. *Am J Psychiatry.* 2002;159:1653-1664.
- Menzin J, Boulanger L, Friedman M, Mackell J, Lloyd J. Treatment adherence associated with conventional and atypical antipsychotics in a large state Medicaid program. *Psychiatr Serv.* 2003;54:719-723.
- Velligan D, Weiden P. Interventions to improve adherence to antipsychotic medications. *Psychiatr Times.* 2006;23. Available at: www.psychiatristimes.com/article/showarticle.jhtml?articleId=192202943. Accessed September 23, 2006.
- Rittmannsberger H, Pachinger T, Keppelmuller P, Wancata J. Medication adherence among psychotic patients before admission to inpatient treatment. *Psychiatr Serv.* 2004;55:174-179.
- Kane J, Leucht S, Carpenter D, Docherty J. The expert consensus guidelines series; optimizing pharmacologic treatment of psychotic disorders. *J Clin Psychiatry.* 2003;64(suppl 12):42-47.
- Velligan D, Lam F, Ereshefsky L, Miller A. Perspectives on medication adherence and atypical antipsychotic medications. *Psychiatr Serv.* 2003;54:665-667.
- Velligan D, Lam Y, Glahn D, et al. Defining and assessing adherence to oral antipsychotics: a review of the literature. *Schizophr Bull.* 2006;32:724-742.
- Kane J. Reducing nonadherence: new formulations of antipsychotic medications. *Psychiatr Times.* 2006;25(2). Available at: www.psychiatristimes.com/article/showarticle.jhtml?articleId=18020783. Accessed September 23, 2006.
- Byerly M, Risher R, Whatley K, et al. A comparison of electronic monitoring vs. clinician rating of antipsychotic adherence in outpatients with schizophrenia. *Psychiatr Res.* 2005; 133:129-133.
- Marder S. Overview of partial compliance. *J Clin Psychiatry.* 2003;64:3-9.
- Rickelman B. Anosognosia in individuals with schizophrenia: toward recovery of insight. *Issues Mental Health Nurs.* 2004;25:227-242.
- Agarwal M, Sharma V, Kumar K, Low D. Non-compliance with treatment in patients suffering from schizophrenia: a study to evaluate possible contributing factors. *Int J Soc Psychiatry.* 1998;44:92-106.
- Freudenreich O, Cather C, Evins A, Henderson C, Goff D. Attitudes of schizophrenia outpatients toward psychiatric medications: relationship to clinical variables and insight. *J Clin Psychiatry.* 2004;65:1372-1376.
- Kikkert M, Schene A, Maarten W, Koeter J, Robson D, Born A. Medication adherence in schizophrenia: exploring patients', carers' and professionals' views. *Schizophr Bull.* 2006;42: 786-794.
- Garavan J, Browne S, Gervin M, Lane A, Larkin C, O'Callaghan E. Compliance with neuroleptic medication in outpatients with schizophrenia; relationship to subjective response to neuroleptics; attitudes to medication and insight. *Comprehensive Psychiatry.* 1998;39:215-219.
- Suzuki T, Uchida H, Takeuchi H, et al. Simplifying psychotropic medication regimen into a single night dosage and reducing the dose for patients with chronic schizophrenia. *Psychopharmacology.* 2005;181:566-575.
- Fleischhacker W, Oehl M, Hummer M. Factors influencing compliance in schizophrenia patients. *J Clin Psychiatry.* 2003; 64:10-13.
- Yamada K, Watanabe K, Nemoto N, Hidechika F, Chikaraishi C, Yamauchi K. Prediction of medication noncompliance in outpatients with schizophrenia: 2-year follow up study. *Psychiatr Res.* 2006;141:61-69.
- Lieberman J, Stroup S, McEvoy J, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med.* 2005;353:1209-1223.
- Thieda P, Beard S, Richter A, Kane J. An economic review of compliance with medication therapy in the treatment of schizophrenia. *Psychiatr Serv.* 2003;54:508-516.
- Gilmer T, Dolder C, Lacro J, et al. Adherence to treatment with antipsychotic medication and healthcare costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry.* 2004;161:692-699.
- Olfson M, Mechanic D, Hansell S, Boyer C, Walkup J, Weiden P. Predicting medication noncompliance after hospital discharge among patients with schizophrenia. *Psychiatr Serv.* 2000;51:216-222.
- Corriss D, Smith T, Hull J, Lim R, Pratt S, Romanelli S. Interactive risk factors for treatment adherence in a chronic psychotic disorders population. *Psychiatr Res.* 1999;89: 269-274.
- Kirsh B, Tate E. Developing a comprehensive understanding of the working alliance in community mental health. *Qual Health Res.* 2006;16:1054-1075.
- Claxton A, Crame J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther.* 2001;23:1296-1309.
- Walburn J, Gray R, Gournay K, Quraishi S, David A. Systematic review of patient and nurse attitudes to depot antipsychotic medication. *Br J Psychiatry.* 2001;179:300-307.
- Masand P. A review of pharmacologic strategies for switching to atypical antipsychotics. *Prim Care Comp J Clin Psychiatry.* 2005;7:121-129.
- Lacy CF, Armstrong L, Goldman M, Lance L, eds. *Drug Information Handbook.* 14th ed. Hudson, Ohio: Lexi-Comp; 2006.
- Katzung B, Bernstein J, Ransom J, Foltin J, Holton B, eds. *Basic & Clinical Pharmacology.* 9th ed. New York, NY: McGraw Hill; 2001.
- Weiden P. Switching antipsychotics: an updated review with a focus on quetiapine. *J Psychopharmacol.* 2006;20:104-118.