

Partial Adherence to Antipsychotic Medication Impacts the Course of Illness in Patients With Schizophrenia: A Review

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Objective: Although many clinicians acknowledge the occurrence of adherence problems with medication regimens among patients with schizophrenia, the problem shows no sign of improving. This may be because, in thinking about the issue, clinicians have tended to focus on patients who openly refuse or repeatedly discontinue treatment. While this description applies to only a minority of patients, in our experience, full adherence is rare; most patients are only partially adherent at best. This article examines the issue of adherence behavior in schizophrenia, focusing on the impact of partial adherence on treatment outcomes, particularly early in the course of illness. We also review potential strategies for managing the problem.

Data Sources: Original research and review articles published in English from 1980 to 2008 were identified using the PubMed database, with the search terms *schizophrenia* or *psychosis* combined with *compliance*, *noncompliance*, *partial compliance*, *adherence*, *nonadherence*, or *partial adherence*.

Study Selection: Articles were selected by the authors on the basis of the hypotheses and/or data described.

Data Synthesis: Failure to adhere to medication as prescribed can have a major impact on the course of illness and treatment outcomes in patients with schizophrenia. Even relatively short gaps in medication coverage increase the risk of relapse. Problems with adherence are common early in the course of illness, when the consequences of relapse can be particularly devastating.

Conclusion: Clinicians in primary care and psychiatric settings need to be vigilant for signs of adherence problems among their patients and to act when necessary to prevent or alleviate the consequences of inadequate medication cover. Relapse prevention strategies, particularly for patients with early psychosis, should include ensuring that medication lapses are minimized or eliminated.

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The failure by patients to take medication as prescribed is a phenomenon that is well known to clinicians in all medical specialties. Among patients with schizophrenia, adherence issues can severely limit the clinical improvement that is achievable with even the best available treatments. There is, however, no evidence that the situation has improved over the last 30 years, and, despite the introduction of new medications with improved tolerability profiles, poor adherence remains a problem. This may be because in both clinical research and day-to-day practice, adherence has often been portrayed as an all-or-nothing issue, with patients being regarded as either adherent or nonadherent. When considering interventions for adherence problems, clinicians have therefore tended to focus on those patients who openly refuse or repeatedly discontinue treatment and are regarded as difficult-to-treat cases. While this description applies to only a limited proportion of patients, in our experience, full adherence is rare. In reality, most patients are partially adherent to some extent, but the focus on treatment discontinuation may have led clinicians to discount partial adherence as an issue worthy of their attention, perhaps regarding it as inevitable and unavoidable. Unless clinicians appreciate

the impact that relatively minor deviations from prescribed treatment regimens can have on treatment outcomes,¹ they are unlikely to take the problem seriously or to devote sufficient time and attention to addressing suspected adherence problems among their patients.

Notably, treatment adherence is considered to have a major influence on achieving clinical remission.² Failure to achieve remission is a predictor for poor prognosis, psychiatric complications, treatment resistance, and even death from medical comorbidities and suicide.³ Moreover, patients who fail to take their medication as prescribed are at a greatly increased risk of relapse.^{1,4,5} Given the devastating impact of psychotic relapse on the course of illness, relapse prevention strategies should encourage greater awareness of the impact of partial adherence and should incorporate appropriate steps to minimize or eliminate the problem, particularly during the early stages of the illness.

This article examines the issue of adherence behavior and its impact on treatment outcomes, with particular reference to early psychosis and first-episode patients, and provides observations on suggested strategies for managing these issues in patients with schizophrenia.

A search of the published literature from 1980 to 2008 was performed using the PubMed search engine. Articles written in English (original research and reviews) were identified using the following keywords: *schizophrenia* or *psychosis* combined with *compliance*, *noncompliance*, *partial compliance*, *adherence*, *nonadherence*, or *partial adherence*. Additional references were identified through citations in relevant articles.

NONADHERENCE AND PARTIAL ADHERENCE IN SCHIZOPHRENIA: DEFINITIONS AND PREVALENCE

It has been known for many years that a substantial proportion of patients with schizophrenia do not take their medications as prescribed.^{6,7} Strictly speaking, *nonadherence* means failing to take any prescribed doses (although patients who discontinue their medication after an initial period of adherence can also be correctly described as nonadherent). Full adherence (taking all doses as prescribed) represents the other end of the spectrum of adherence behaviors. The term *partial adherence* can be used to describe all other patterns, from prolonged gaps in medication to infrequent lapses, including occasional missed or incorrect doses.⁷⁻⁹ In the past, the terms *adherence* and *compliance* have been used interchangeably, although some authors have used compliance to describe only the extent to which a patient takes his or her medication and have used adherence to describe a broader concept that encompasses lifestyle, habits, and diets and implies a collaborative attitude on behalf of the patient that leads to active involvement in the therapeutic strategy. Compliance is now perceived to betray a paternalistic attitude toward the patient, however,¹⁰ and so is declining in use.

In an early review, Young et al.¹¹ found that reported rates of adherence varied widely. This partly reflects the inconsistency between the definitions of adherence/partial adherence/nonadherence used in the different studies. In some, occasional missed doses were not regarded as nonadherence,⁶ while in others, patients were deemed to be adherent if they took as little as 70% of the prescribed medication.¹² The studies cited below are limited to those in which the definitions used were clearly stated. Differences between the populations studied and the methods used to quantify adherence behavior may also influence the estimates.

Full adherence is uncommon in schizophrenia, as is the case with most illnesses. Thus, Oehl et al.⁹ estimated that only about one third of patients with schizophrenia are fully adherent, with one third being partially adherent and one third nonadherent. Other authors suggest that at least 50% of patients are not fully adherent with their medication at some time during their illness.^{13,14} With regard to the other extreme of adherence behavior—treatment discontinuation—Young et al.¹¹ concluded that up to 40% of patients treated with conventional antipsychotics stop taking their medication within a year.¹¹ Other studies have reported similar rates of discontinuation in outpatients (50%–75%) during the 2 years following hospital discharge.^{15,16}

Partial adherence appears to be an even more pervasive and insidious problem than treatment refusal or discontinuation; several studies have indicated very high rates of partial adherence among patients with schizophrenia. For example, McCombs et al.¹⁷ examined data for 2655 patients and concluded that one quarter had taken no antipsychotic drugs during the year of the study, but another quarter had delayed using antipsychotic drugs for 30 or more days. Ninety-two percent had at least 1 disruption in treatment. In a study of 565 patients with schizophrenia or schizoaffective disorder, a similar proportion (90%) showed some level of partial adherence during a year of follow-up.¹⁸

DETECTION OF ADHERENCE PROBLEMS

Another factor that may contribute to the variability in published rates of nonadherence and partial adherence is that adherence behavior is not easy to detect and quantify, and all methods of detection have some drawbacks. First, even when asked directly, patients often deny being partially adherent or nonadherent.⁷ For example, in a study of 68 patients with schizophrenia 3 months after discharge from hospital, the majority (55%) rated themselves as fully adherent, but, according to pill counts, only 40% were adherent (> 80% of doses taken) and only 9% of these were fully adherent. Measurements of plasma drug concentrations suggested an even lower adherence rate (23%).¹⁹ Valenstein et al.²⁰ also found that patients

overestimated their level of adherence compared with their physicians, but physicians themselves have been found to overestimate their patients' levels of adherence.¹⁵ For example, in one 3-month study, none of the physicians rated their patients as nonadherent (≤ 4 on the Clinician Rating Scale) but an electronic Medication Event Monitoring System indicated that 48% had $\leq 70\%$ daily adherence.²¹

Medication possession ratio information derived from pharmacy data can be a useful tool for identifying patients requiring assistance with adherence,²² but the use of these data in studies of adherence has major limitations.^{12,22} Although patients may collect their prescriptions on a regular basis, they may not be taking the medication as prescribed. Other changes in clinical circumstances could cause changes in dosing patterns that are interpreted as being indicative of partial adherence.

As partial adherence tends to be covert, accurate measurement is likely to be particularly difficult. A prospective study examining agreement among measures of adherence to oral antipsychotic medications in 52 outpatients with schizophrenia found that, while pill count and electronic monitoring appeared to identify adherent patients (those who were at least 80% adherent), self-report and physicians' ratings failed to accurately differentiate between patients with or without adherence problems.²³

Although direct indicators (such as concentrations of medication in blood) are less subject to bias than indirect measures (self-reports, chart reviews, pill counts, or refill rates), every detection method has its limitations,²⁴ and none of the available methods are ideal.

RECOGNITION OF ADHERENCE PROBLEMS IN CLINICAL PRACTICE

Beyond the research setting, the failure of physicians to recognize adherence problems among their patients can have an important impact on prescribing behavior, patient outcomes, and healthcare costs,²³ but relatively few studies have examined clinicians' awareness of adherence problems in patients with schizophrenia. Giner et al.²⁵ described the results of a survey of 330 Spanish psychiatrists on their perceptions of adherence behavior among their patients. Nearly one half thought that patients should be classed as nonadherent if they missed 10% to 25% of their prescribed medication. Another third felt that 5% to 10% of missed doses should be regarded as nonadherence. Most (49%) thought that between one quarter and one half of their patients had adherence problems, but some (10%) saw adherence as a problem in up to three quarters of patients. Poor insight was identified as an important factor by 90% of physicians; the doctor-patient relationship was also thought to have an important influence. Eighty-five percent of physicians identified nonadherence as the main cause of relapse among their patients.

A larger survey conducted in 11 European countries revealed that psychiatrists think that the majority of their patients have problems with adherence; two thirds (60%) were suspected of forgetting to take their medication at some time in the previous month.²⁶ Many patients (57%) were thought to be incapable of noticing a worsening in their health after interrupting treatment, and a similar proportion (66%) were thought to lack awareness of their illness. About two thirds of patients were suspected of discontinuing their medication at some time because they felt better. Cognitive deterioration sufficient to affect adherence was identified in about 50%. Most were thought to need their family or others to remind them to take their medication but had life circumstances that were not conducive to adherence. Embarrassment or being upset at having to take tablets every day was seen as a contributing factor in two thirds. Similar results have been found in other national surveys.^{27,28}

Thus, when asked specifically, clinicians suspect many of their patients have problems taking their medication as prescribed. The surveys did not ask whether they act on their suspicions, however, and the fact that poor adherence remains a common problem suggests that the issue is not being adequately addressed. It may be that clinicians do not fully appreciate the impact of gaps in treatment coverage on disease course and outcome. They may assume that a chronic course of illness with multiple relapses is to be expected. In fact, as described below, for many patients with unsatisfactory outcomes, poor adherence is likely to be an important contributory factor.

THE IMPACT OF NONADHERENCE AND PARTIAL ADHERENCE

Failure to adhere to antipsychotic regimens is associated with exacerbation of psychotic symptoms,²⁹ increased aggression against self and others,³⁰ worse prognosis,^{31,32} increased use of inpatient and acute outpatient services,³³ and increased costs.³⁴ Importantly, nonadherence to medication has been suggested to be the most important modifiable factor contributing to psychotic relapse that leads to rehospitalization.¹⁴

It is perhaps not surprising that major lapses or discontinuation of therapy can have a profound impact, but partial adherence has also been shown to have important consequences. Using pharmacy refill and medical claims data for 4325 outpatients with schizophrenia, Weiden et al.¹ found that the hospitalization rate was substantially higher in patients who were less than 70% adherent than in those with better adherence (23% vs. 13.8%, $p < .001$). A gap in medication coverage of as little as 1 to 10 days almost doubled the risk of hospitalization, showing that relatively minor deviations from treatment as prescribed can have a major impact on outcomes. Another analysis of data from approximately 49,000 patients found that

hospital admission was 2.4 times more likely in poorly adherent patients (medication possession ratio, < 0.8) than in those with good adherence (medication possession ratio, 0.8–1.1).¹² The admission rates were 23% and 10%, respectively. Importantly, partial adherence often remains undetected until psychotic symptoms emerge or are exacerbated,³⁵ but the longer patients fail to take their medication as prescribed, the greater is the impact on outcomes.³⁶ The negative consequences of partial adherence may range from increased stress to loss of functioning, breakthrough of symptoms, and, ultimately, relapse.

In addition to the impact on patient outcomes, adherence behavior has also been shown to have an important effect on resource utilization and costs. Thus, Valenstein et al.¹² found that poorly adherent patients spent more days in hospital (33 days per year) than those with good adherence (24 days per year), while Gilmer et al.³⁷ reported that rates of psychiatric hospitalization were substantially lower among adherent (14%) than partially adherent (24%) or nonadherent (35%) patients. Hospital costs were also significantly lower in adherent patients,³⁷ and, in fact, nonadherence to antipsychotic drugs has been suggested to be one of the most significant factors in increasing service costs.³⁸ Marcus and Olfson³⁹ calculated that improving adherence has the potential to reduce Medicaid inpatient care costs by more than \$100 million through reductions in acute-care admissions (12%) and inpatient treatment days (13%).

NONADHERENCE AND PARTIAL ADHERENCE IN EARLY PSYCHOSIS: PREVALENCE AND IMPACT

Adherence problems (both treatment discontinuation and partial adherence) appear to be common during the early stages of schizophrenia^{7,40–42} and to have important effects on course and outcome.⁴³ First-episode patients usually respond well to treatment⁴⁴ but relapses are common,⁴ so improving adherence can be of long-term benefit.⁴⁵ Robinson et al.⁴⁶ found that 26% of first-episode patients had stopped taking their medication (against medical advice) in the first year of treatment (43% had discontinued medication after recovery from their first relapse). In another early psychosis program, 39% of patients were nonadherent during the first year, but another 20% were described as poorly adherent (taking medication irregularly).⁴⁷ Focusing on partial adherence, Mojtabai et al.⁴⁸ found 63% of first-admission patients to have 1 or more gaps in their use of typical antipsychotics during the year after hospital discharge. About one half of the gaps were for 30 days or more, most occurred soon after discharge, and 73% were initiated by the patient.

The importance of optimizing adherence early in the course of illness is indicated by a study of 104 first-episode patients who had responded to treatment and

were at risk for relapse.⁴ The risk of a first or second relapse when patients did not take medication was found to be about 5 times greater than when they did take medication (initial relapse, hazard ratio = 4.89; second relapse, hazard ratio = 4.57). Moreover, in a naturalistic study of 65 patients during the 2 years after hospital discharge after a first admission for psychosis, those with poor adherence (at least 1 interruption in medication in 2 years, against medical advice) were 5 times more likely to have an episodic course and were more likely to have been readmitted (the risk of compulsory readmission was increased 3-fold).⁴⁹

RISK FACTORS AND STRATEGIES FOR ADDRESSING ADHERENCE PROBLEMS

Given the impact of adherence behavior throughout the course of illness, we consider it essential for clinicians to be vigilant in recognizing adherence problems among their patients and to act when necessary to prevent or alleviate the consequences of inadequate medication cover. Clinicians first need to be aware of the factors that can lead to adherence problems. On the basis of our experience, we would emphasize the impact of distressing side effects on adherence behavior; other important obstacles include cost and access, the use of complicated treatment regimens, and the impact of cognitive impairment. In this section, we review the published research on risk factors and examine some strategies that have been proposed to address the problem.

Several authors have identified what Tacchi and Scott⁵⁰ described as a “predictable checklist” of features associated with nonadherence, including being young, male, and unemployed or socially isolated; a past history of nonadherence; and, possibly, current use of illicit substances. Based on a review of 39 studies, however, Lacro et al.²⁴ found no association between adherence and either age or gender. The factors that were consistently associated with adherence problems were poor insight, negative attitude or subjective response to medication, previous nonadherence, substance abuse, short illness duration, inadequate discharge planning or aftercare environment, and a poor therapeutic alliance. Surprisingly, the severity of psychotic symptoms or medication side effects did not have notable effects. To date, few studies have adequately quantified the relative importance of the different risk factors, but, in a recent review, Narasimhan et al.⁵¹ concluded that symptomatology, cognitive function, disease insight, and presence of substance abuse were the most important features.

A similar range of factors have been proposed to influence adherence behavior during the early stages of illness. For example, in first-episode patients, Robinson et al.⁴⁶ found that poor premorbid cognitive functioning was an important predictor of treatment discontinuation during

the first year of therapy. After the first relapse, discontinuation was more likely when Parkinsonian side effects were present but less likely in patients with better executive function. In another first-episode study, McEvoy et al.⁵² found that lack of insight was an important risk factor, while Kampman et al.⁵³ concluded that younger age, male sex, lack of social activities, presence of side effects, and high Positive and Negative Syndrome Scale (PANSS) total and low PANSS positive scores were all predictors of nonadherence in first-episode patients. Similarly, Coldham et al.⁴⁷ found that nonadherent early-psychosis patients were younger, had an earlier onset, and lacked a family member with involvement in the treatment plan. In first-episode patients, Verdoux et al.⁴⁹ found that low occupational status, alcohol misuse, and the severity of delusions and suspiciousness were all predictors of poor adherence. There are many contradictory findings, however⁵⁰; this is probably because studies have tended to examine the impact of each risk factor in isolation. One recent study evaluating the relative impact of several putative risk factors⁵⁴ concluded that early psychosis patients who show poor adherence tend to have issues with trusting authority (childhood trauma, severity of symptoms, and a poor therapeutic alliance were also found to be important).

A post hoc analysis of data from German patients in the Schizophrenia Outpatient Health Outcomes study found that adherence to antipsychotic medication was strongly associated with subjective well-being; patients with less severe symptoms (including extrapyramidal symptoms) were more adherent.⁵⁵ The causal relationships are unproven; patients who are more adherent might be expected to be less symptomatic. Conversely, incomplete control of symptoms or persistence of side effects could reduce well-being and so act as a disincentive for patients to continue taking their medication as prescribed. In this regard, it had been assumed that the introduction of the atypical antipsychotic drugs would lead to improvements in adherence,⁵⁶ given their generally favorable tolerability profiles compared with the typical antipsychotics. The results of studies comparing adherence with older and newer antipsychotic drugs are, however, inconclusive and conflicting, and adherence rates with atypical drugs remain lower than had been hoped. For example, using pharmacy refill records to quantify adherence in outpatient veterans, Dolder et al.⁵⁷ found that patients receiving atypical antipsychotics were without medication for 4 days per month on average compared with 7 days per month for those receiving typical antipsychotics (and as previously mentioned, this level of partial adherence can have important effects on outcomes). More recently, in the CUtLASS study, no differences in adherence were found between patients treated with first- and second-generation antipsychotic drugs.⁵⁸ Problems with adherence therefore persist, despite the availability of drugs with improved side-effect profiles.

The need to take medication several times a day can be disruptive to patients' daily routines, thus increasing the risk of missed doses or discontinuation of treatment.⁵¹ Long-acting neuroleptics can address all-cause discontinuation and poor adherence,⁵⁹ and treatment guidelines (e.g., American Psychiatric Association, Schizophrenia Patient Outcomes Research Team, Texas Medication Algorithm Project) strongly recommend using depot formulations for patients who are noncompliant with oral agents, but clinicians seem reluctant to modify their practice, even for patients who are overtly nonadherent. For example, Valenstein et al.⁶⁰ found that almost one half (49%) of 1307 veterans with schizophrenia or schizoaffective disorder were known to have been nonadherent in the previous year, yet only 18% were receiving depot neuroleptics. They concluded that there are barriers to implementing the recommendations but noted that, until recently, only typical neuroleptics were available in long-acting formulations. Others have suggested that long-acting formulations of atypical neuroleptics represent a more promising solution.^{59,61} In one 12-month trial of long-acting risperidone, less than 2% of patients discontinued due to adherence issues, and only 18% had to be readmitted to hospital.⁶² No direct comparisons between long-acting risperidone and depot typical neuroleptics are available, but patients whose symptoms were stable during treatment with typical depots did show improvements after switching to long-acting risperidone.⁶³ Patients switched from oral risperidone also showed improvements,⁶⁴ presumably due to continuity of medication delivery and elimination of covert partial adherence. In daily clinical practice, the use of a long-acting agent means that adherence problems cannot be hidden; as soon as the patient misses an injection, the clinician can take actions to address the issue and to involve the family and other caregivers.⁵¹ Historically, long-acting agents (particularly depot formulations of typical antipsychotic agents) have tended to be reserved for more chronically ill patients with a clear history/high risk of nonadherence, but some authors have suggested a role for such agents earlier in the course of illness, including for first-episode patients.⁶⁵ The feasibility of this approach (i.e., its acceptability to patients) is indicated by the finding that 73% of first-episode patients who were stable after treatment with an oral atypical antipsychotic accepted a recommendation of changing to a long-acting atypical agent when this was discussed as part of an integrated treatment plan.⁶⁶

Relatively few studies of adherence behavior have examined the impact of personal beliefs and attitudes or of contextual factors such as family environment, but in one study of first-episode patients that did evaluate attitudinal and clinical factors, both negative attitudes to medication and a lack of insight or awareness of illness were significant predictors of poor adherence.⁶⁷ Other authors have suggested that a negative attitude to medication may be

an important factor among many patients with schizophrenia.⁵⁰ Patients may refuse to accept the need for medication, particularly during the early stages of illness when they have experienced only 1 or 2 psychotic episodes.⁷ For young people, the idea of taking medication for the rest of their life can be a worrying prospect. They may also regard the need for daily medication as a sign of weakness or inferiority (a perception that can be reinforced by societal stigma), and it may be difficult for them to understand the benefits of medication, particularly if they regard their condition as temporary and not the result of an illness. They may also need reassurance that the medication is their insurance against symptoms recurring. All these considerations highlight the importance of establishing a strong therapeutic alliance, and, in one study, nonadherence after a recent acute hospitalization was found to be predicted by poor therapeutic alliances with staff as well as refusal of families to be involved in treatment.³³ In contrast, the presence of a positive therapeutic alliance meant that patients took less time to switch from being nonadherent to adherent.⁶⁸

No single factor is likely to explain the adherence behavior of an individual, and, among schizophrenia patients as a group, a number of different factors appears to be important.^{5,14,69} It has been suggested that interventions for adherence problems are particularly relevant to patients with a history of relapse related to poor adherence, to those with limited awareness of their disease, and to those with comorbid substance abuse.²⁸ However, for most patients, adherence issues are multifactorial; there is unlikely to be a single answer to the problem. An individualized approach is needed, based on an evaluation of the factors or combinations of factors likely to have most influence on the individual's adherence behavior. For example, in patients with first-episode psychosis,⁷⁰ it was reported that a structured early intervention program based on specifically adapted interventions (including cognitive-behavioral therapy, medication management, vocational support, and family interventions) significantly reduced treatment discontinuation compared with that achieved by standard community services.

Regular assessment of adherence behavior is essential, but when issues with adherence do become apparent, clinicians may feel that they do not have the time or resources to address the problem adequately. In addition, there is only a limited evidence base on the effectiveness of specific interventions. Studies tend to involve complex approaches, comprising combinations of more convenient care, information, counseling, reminders, self-monitoring, reinforcement, family therapy, and other forms of enhanced supervision or attention.⁷¹ Most interventions have brought only limited improvements, and other approaches are needed.⁷² Interventions that employ educational and behavioral strategies are more likely to be successful than purely didactic approaches.^{5,50,73} Consequently, Tacchi and

Scott⁵⁰ suggested a number of steps toward addressing problems of nonadherence and partial adherence that could be used by any mental health professional without additional training. These include investing time in the development of a strong therapeutic alliance; developing a shared understanding of patients' problems; establishing the acceptability and manageability of possible interventions (before prescribing an evidence-based treatment); establishing positive reasons for accepting treatment, for example, by linking adherence to personal goals (such as returning to work); maintaining vigilance for signs of ambivalence about treatment; checking repeatedly that patients understand the nature of the disorder and the rationale for medication; and incorporating simple interventions for nonadherence into routine clinical practice (involving education, behavioral techniques and interventions, and cognitive techniques).⁵⁰ Other practical steps that could be considered by clinicians include the use of once-daily dosing regimens for oral medications together with various types of medication calendars, diaries or organizers, and electronic reminders and alarms as well as pill dispensers or blister packs.

CONCLUSIONS

Provided that they receive optimal early intervention, patients experiencing their first psychotic episode have good prospects for improved outcome, including long-term remission.⁷⁴⁻⁷⁷ On the other hand, the risk of relapse is high, particularly early in the course of illness,⁴ and the consequences of relapse can be devastating in terms of lost educational, occupational, and social development opportunities. Adherence problems leading to relapse can therefore have profound detrimental consequences for long-term outcomes. A psychotic relapse is a serious medical emergency and should be recognized as such by clinicians. Relapse-prevention strategies should include providing the most appropriate medication and ensuring that medication lapses are minimized or eliminated.

Further research involving longer-term studies of interventions aimed at improving adherence among individuals with schizophrenia is clearly warranted, as few studies have assessed whether positive effects of interventions are maintained in the long term. More methodologically rigorous research on the economic impact of nonadherence and the cost-effectiveness of strategies for enhancing adherence is also needed.

Drug name: risperidone (Risperdal and others).

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