



Improving medication adherence in patients with severe mental illness

American Pharmacists Association

Abstract

Objectives: To provide information that will help pharmacists to understand and identify medication nonadherence among patients with severe mental illnesses and to present interventions that pharmacists can use to help improve patients' medication adherence.

Summary: Poor medication adherence, which is common among patients with severe mental illness, leads to poor health outcomes and increased health care costs. Many barriers to adherence exist, including patient and family attitudes, treatment-related issues, health-system factors, cultural influences, and stigma. This report describes tools to help pharmacists assess adherence and interventions to overcome adherence barriers.

Conclusion: Pharmacists and other health professionals need education and training to help patients with severe mental illness improve medication adherence. Multidisciplinary patient-tailored interventions can help to improve adherence.

Keywords: Psychopharmacology, medication adherence, nonadherence, pharmacist interventions.

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Learning objectives

At the conclusion of this knowledge-based activity, the pharmacist will be able to:

- Describe the causes and impact of medication nonadherence in patients with serious mental illness, including schizophrenia, bipolar disorder, and depression.
- Cite research demonstrating the impact of pharmacists' interventions on outcomes for patients with serious mental illness.
- Identify tools and strategies for assessing medication adherence in patients with serious mental illness.
- Discuss how to apply strategies to overcome barriers to medication adherence for patients.

Preactivity questions

Before participating in this activity, test your knowledge by answering the following questions. These questions also will be part of the CPE exam.

1. **What is the most accurate measure of adherence?**
 - a. Self-report
 - b. Pharmacy refill records
 - c. Direct observed therapy
 - d. Medication Event Monitoring System

2. **Four-times-a-day dosing regimens may result in nonadherence rates of:**
 - a. 30%.
 - b. 40%.
 - c. 50%.
 - d. 60%.

3. **Pharmacist interventions for depression treatment usually:**
 - a. Involve Medication Electronic Monitoring Systems.
 - b. Incorporate patient education or drug monitoring.
 - c. Show improvement in depressive symptoms and adherence.
 - d. Have been shown to be cost effective to a health system.

Nonadherence in community-treated patients

Medication adherence is a serious challenge for providers treating patients with many types of illness. Patients with acute conditions are more likely to be adherent than those with chronic disorders. Nonadherence rates in patients with schizophrenia, bipolar disorder, and depression are often greater than 50%, which is not very different from patients with nonpsychiatric chronic diseases.¹⁻³ Nonadherence in patients with mental illness can have severe consequences, such as relapses and rehospitalizations.

As drug therapy experts, pharmacists can help ensure that patients receive safe and effective medication therapy, receive the most benefit from the medication that is prescribed, and achieve optimal medical therapy outcomes. To do this effectively, community pharmacists must be aware of the barriers to adherence in patients who are mentally ill and knowledgeable about intervention strategies that can improve adherence.

What is adherence? Why do we care about it?

Medication nonadherence occurs when a patient does not initially fill or refill a prescription, discontinues a medication before therapy is complete, or does not follow instructions for dosing and schedule.⁴

Patients who take medications as directed and agree with the provider about the recommendations are considered adherent. An older term, compliance, assumes that the patient is taking the medication as directed but without a discussion of the medication or acknowledged agreement between the patient and provider. Concordance is another older term not frequently used today that assumes an equal relationship between the patient and clinician. Persistence is a method of assessing adherence based on the percentage of doses taken, with no gaps in treatment (Table 1).^{5,6}

Table 1. The lexicon of adherence

Term	Definition
Nonadherence	Medications are not taken at all or are not taken as prescribed.
Adherence	Following instructions for medication use. Patient and provider agree with recommendations.
Compliance	Passively complying with medication regimen; patient does not necessarily agree with the prescriber's recommendations.
Concordance	Clinician and patient have an equal relationship.
Persistence	Measure of the number of days a patient takes medications without any gaps in treatment.

Source: Reference 6

"Drugs don't work in patients who don't take them."⁷
 —C. Everett Koop, MD, former U.S. Surgeon General

Prevalence of nonadherence

Rates of adherence are typically highest in patients with acute conditions such as a bacterial infection. Patients are only required to take their antibiotics for short periods and quickly experience relief. Most patients with nonpsychiatric chronic diseases such as diabetes, hypertension, coronary artery disease, dyslipidemia, and asthma require lifelong treatment with multiple medications. Their adherence rates are lower than those for patients with acute conditions. The mean rate of adherence among people with physical disorders has been reported to be 76%. A considerable drop in medication adherence has been seen in these patients within 6 months of initiation of drug therapy and sometimes within 1 month.^{8,9} Even in clinical trials, which use intensive monitoring and vigorous measures aimed at adherence, the adherence rate ranges from 43% to 80%.¹⁰

Nonadherence among patients with severe mental illness has been estimated to be between 30% and 65%.^{11,12} The following nonadherence rates have been reported: 30% to 66% for major depression, 30% to 65% for bipolar disorder, and 40% to 50% for schizophrenia.

Adherence rates for patients with different psychiatric disorders are not very different from one another and are similar to rates among patients with physical disorders.

Other studies in this area have shown the following¹³⁻¹⁶:

- One-half of patients with major depression will not be taking prescribed antidepressants by 3 months after they were prescribed.¹⁷
 - In a health maintenance organization sample, 32% to 42% of patients did not fill their prescriptions 6 to 8 weeks after starting treatment.
 - Adherence was somewhat better for patients taking selective serotonin reuptake inhibitors (SSRIs) than among those prescribed tricyclic antidepressants (TCAs): 34% of patients taking SSRIs and 20% taking TCAs filled four or more prescriptions within 6 months.
- Researchers use a number of methods for measuring ad-

herence. One is the compliant fill rate, which is the proportion of prescriptions that are filled. Using this method, researchers determined that the fill rate for antipsychotic medications was slightly more than 60%, which is somewhat lower than that for antihypertensives but higher than the rates for cholesterol-lowering drugs and antidiabetes agents.¹⁸

Another measure is the cumulative mean gap ratio, which is determined by dividing the number of days that medication was unavailable as a result of delayed refill by the total number of days during the same time interval.¹⁸ Mean possession ratio also has been used to measure adherence; it is the ratio of days of medication supply divided by the number of days during the same period of time.¹⁹

A study of adherence in bipolar disorder showed that slightly more than one-half of the patients studied were fully adherent, 20% were partially adherent, and nearly 30% were nonadherent. Risk factors for nonadherence in this group included younger age, minority status, substance abuse, and homelessness.²⁰

Nonadherence to antipsychotics, lithium, and antidepressants among patients with schizophrenia was 20%, 38%, and 36%, respectively. Nonadherence to antipsychotics was slightly higher (23%) among those with bipolar disorder but lower for lithium and antidepressants (26% and 22%, respectively). Lithium was associated with the highest rates of nonadherence in both groups, which reflects the adverse effect burden of the medication.²¹

Impact of nonadherence

Poor medication adherence has a substantial impact on disease progression, disease complications, functional outcomes, and quality of life.

Self-care often is affected in patients with depression, and coexisting chronic conditions may not be managed adequately. Pregnant women often refuse to take their antidepressants because of fear of teratogenicity. Unfortunately, pregnant women who are depressed often have inadequate self- and prenatal care, which can lead to adverse pregnancy outcomes.²² Nonadherence also may increase the risk of toxicity among patients who adjust their own medications. Patients with mental illness who are nonadherent also are at risk for homelessness, incarceration, and violence.

Poor adherence can be responsible for avoidable hospital admissions and increased visits to the emergency department. The cost of rehospitalizations has been estimated to be \$100 billion per year. Overall, the estimated cost of nonadherence is \$290 billion.²³

Barriers to adherence

Many factors influence adherence, including factors that are related to the patient and the treatment, as well as social, cultural, and economic issues. Other obstacles arise from the health system or the provider(s) treating the patient.

Patient-related factors

One theory about patient adherence is the common sense model of self-regulation. It posits that individual adherence

is more likely if adherence makes sense within the individual's concept of illness, considering previous experience with illness and medication, potential outcomes of medication adherence, and personal beliefs about illnesses.^{24,25} Working with patients to achieve this core understanding can take months or years.

Lack of insight. Many patients with mental illness suffer from anosognosia, which is a lack of insight into their condition. They do not understand the need for treatment or the rationale for treatment. According to the National Alliance on Mental Illness, this lack of insight is believed to be the leading cause of nonadherence among individuals with schizophrenia and bipolar disorder. Anosognosia is caused by anatomical damage to the brain and affects approximately 50% of individuals with schizophrenia and 40% of individuals with bipolar disorder.^{26,27}

Attitudes toward medications. Patients who have taken multiple psychotropic medications for many years are concerned about adverse effects. Patients' attitudes toward certain medications may be influenced by their past experiences, those of family or friends, and perspectives of the media. Psychotropic medications are known to have a wide range of acute and chronic adverse effects that many patients want to avoid.

Numerous studies have examined patients' attitudes toward medications and adherence. One 5-year prospective study of patients with depression (Vantaa Depression Study) found that 74% of patients reported good adherence to antidepressants. Among those who were not adherent, researchers found that the main reason was a negative attitude toward pharmacotherapy. Other reasons included a lack of motivation, adverse effects, fear of addiction, economic reasons, lapse of memory, and substance abuse. Some patients felt that taking medication was a punishment for their illness.²⁸

In this study, 79% of the patients had a positive attitude toward medications. An analysis of the 21% of patients with a negative attitude revealed that they were most often female, literate, employed, and well educated. They also had had fewer previous major depressive episodes, a lower incidence of social phobias, less alcohol dependence, and fewer comorbid psychiatric disorders than those with a positive attitude. Overall, adherence to psychosocial treatment improved in these patients, but they were not more adherent to pharmacotherapy. Patients were much more interested in cognitive behavioral therapy or counseling than in taking medications.²⁸

"In my practice, the patients with more negative attitudes toward medications are those who are more literate, better educated, and with more access to the Internet and to other resources. That's something we have to struggle with."

—Kelly Lee, PharmD

A study reported nonadherence rates of 41% to 43% among patients with bipolar disorders. Risk factors for nonadherence included minority status, single status, and substance abuse. Reasons for nonadherence in this study in-

cluded forgetting to take medications (55%) and adverse effects (20%). Other factors included a disorganized home environment, concern about taking medications long term, fear of adverse effects, and lack of information about the illness. One-third of these patients had individuals in their core social network (e.g., family, spouse, close friends) who advised against medications.²⁹

Attitudes toward condition. Psychological reasons, such as insight, beliefs, and guilt, as well as lack of information about disorders, also play a role in patients' attitudes toward medications. These issues may be more amenable to modification; education can correct incorrect assumptions about treatment and overcome patient lack of information. Some people feel that psychiatric treatment (i.e., receiving treatment in a mental health clinic instead of a primary care physician's office) is punishment for some wrongdoing, and they experience extreme guilt and shame. These stigmas are not easy to overcome.

Relationships. Many patients rely on advice from family members, friends, and acquaintances. Although the intentions may be good, the advice often is not, such as when a friend urges a patient to ask for a specific medication "that works for my friend" or one that they read about on the internet. In such cases, the pharmacist should involve the patient's family because they also need to be educated.

"In a face-to-face conversation with a patient's family members who are advising against taking medication, I say, 'You are preventing this person from getting well.'"
—Kelly Lee, PharmD

Cognitive defects. Many people with schizophrenia start declining cognitively after 20 years to 30 years of disease. They may be developing dementia or experiencing the natural sequelae of schizophrenia. This can be problematic when trying to educate or reason with patients.

Physical conditions. Some patients must deal with comorbidities that affect many aspects of their lives. These include patients with diabetes, obesity, cardiovascular disease, and other disorders, as well as those with physical disabilities such as paralysis.

Treatment-related factors

In some cases, the elements of a patient's treatment actually become barriers. As iterated by Weiden et al.,³⁰ these elements include dosing regimen, adverse drug reactions, fear of addiction potential, and concern about drug-drug interactions. Another study looked at medication schedules and concluded that the adherence rate dropped as the number of doses climbed. The adherence rate was about 50% among patients taking medications on a four-times-a-day schedule.³¹

Health-system and provider factors

Awareness of adherence issues among many clinicians and health-system managers is generally lacking. Education about adherence is needed within the hospital, clinic, and medical group. Health professionals need to understand the

importance of adherence and that psychopharmacology is more than just recommending the right drug for the right patient. Providers need to understand patient barriers; they need to appreciate the state of patients who must take five antidepressants, antipsychotics, and mood stabilizers for the rest of their lives. According to a World Health Organization (WHO) report, this lack of knowledge likely is a reason for the lack of adherence tools to assist health professionals in evaluating and intervening in adherence programs. Adherence would likely improve if allied health professionals such as psychologists, social workers, or behavioral health therapists were available to help patients develop the skills that will improve adherence.³²

The WHO report also noted gaps in access to care for patients with mental illness plus other chronic conditions and suboptimal communication between patients and health professionals as barriers to improving adherence.³²

In addition to lack of education among health professionals, a patient's relationship with providers (e.g., physicians, pharmacists, nurses) can be a barrier. This is especially true when the therapeutic alliance is poor. The provider can distinguish among patients who are just going through the motions and those who are truly invested in their treatment. Providers must strive for a strong therapeutic alliance; this is particularly true when dealing with patients with mental illness.

Also, studies have shown that physician bias exists toward patients with mental illness and their conditions and medications. This situation occurs more often among students and trainees who make faulty assumptions about mental illness (i.e., that the patient is not educated or lacks intelligence). They may expect these patients to exhibit violence or an inability to communicate and express surprise when a patient appears normal.

Condition-related issues

The characteristics of an individual's condition can be barriers in themselves. These may include the patient's stage of treatment (e.g., early or late), severity of the treatment, number of hospitalizations, and symptom chronicity. Other factors related to a patient's condition may affect his or her mood, even when the antidepressant is effective. Impairments from conditions such as cognitive deficits, physical disabilities, or metabolic syndromes from taking antipsychotics for 20 years can increase nonadherence.

Cultural influences

Although many cultures accept the reality of mental illness, some consider it taboo. Identifying the barriers presented by patients' beliefs is important. They may identify the illness as "nerves," possession by spirits, somatic complaints, or inexplicable misfortune. In immigrant families, many times the children accept Western mores and beliefs about many things, including mental illness, while the adults continue their taboo attitudes. In such situations, encouraging family support for the patient is difficult. Other individuals rely

on their cultural attitudes and feel great shame in having a mental disorder, seeking help, being hospitalized, and taking medications. In some cultures, however, having symptoms of a mental illness is quite acceptable.

One study examined the attitudes of Chinese Americans toward seeking help for a physical condition compared with seeking help for a psychiatric condition. Participants were asked to indicate how likely they were to seek care from a health care provider using Western medicine or to seek traditional Chinese medicine (TCM). For physical conditions, very little difference was observed in willingness to see a physician using Western medicine versus TCM (~10% and ~20%, respectively). For psychiatric conditions, however, nearly 60% of patients reported that it would be shameful to seek help from a Western-trained physician and 30% would be ashamed to seek help from TCM. Even though 90% of patients believed that seeking help from a mental health professional would be helpful, they still were not going to seek one out because their shame superseded their perceptions of the benefits.³³

Research has documented disparities in rates of nonadherence among different ethnic groups. Nonadherence rates are higher among blacks and Mexican Americans compared with whites. A database claims survey identified gaps in adherence of 19 days in minorities. Controlling for demographics, comorbidities, medication history, and previous use of services, the authors concluded that differences in adherence resulted from ethnicity.³⁴

Potential causes of these disparities have been suggested. For example, physicians may be biased toward the clinical presentation of ethnic minorities: do they prescribe stronger medications that would be less tolerated? Another reason is bias by ethnic groups regarding illness, treatment, and providers, as discussed above. Access to health care services is a major issue that affects medication adherence, as does the use of alternative therapies among minorities (Table 2).^{16,35–38}

Case vignette: Ms. Blue

Ms. Blue is a 35-year-old Mexican American immigrant who is admitted to the inpatient psychiatric unit for delusions, depression, and recurrent suicidal thoughts. She doesn't want her family to know about her admission because they question her symptoms and have not acknowledged that she may have mental illness.

She is obese, has type 2 diabetes, and has obsessive-compulsive disorder. She has had bad experiences with medications in the past and cites adverse effects as a reason for her nonadherence. She is unemployed and has no insurance.

What are the barriers to her adherence? See sidebar at end of article for answers.

What tools can help assess adherence?

A 2010 medication adherence e-survey by the Healthcare Intelligence Network (HIN) categorized methods used by health care organizations to measure adherence. Of the 65% of organizations that have programs to improve medication adherence (n = 70), the most common measurement tools were prescription refill patterns (75.5%), health claims data (43.4%), and evidence-based standards (43.4%).⁴²

Table 2. Factors influencing adherence

Patient	Poor insight, fear of adverse effects, physical and psychiatric conditions, attitude toward medications
Treatment	Complex regimen, partial or no efficacy, unresolved symptoms
Social/economic	Financial, transportation, homelessness, stigma
Relationships	Lack of family/social support, therapeutic alliance, family or friends' beliefs about mental illness

Source: References 39–41.

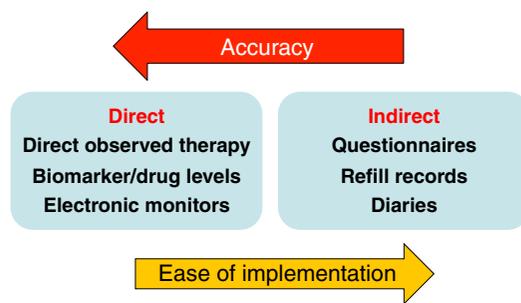


Figure 1. Methods to measure adherence

A common method is self-report. Although easy and quick, questions exist regarding the reliability of this measure. Most organizations use pharmacy refill records, which provide data on the proportion of days on which medication is available during a defined time period; the result is called the medication possession ratio (MPR). Few organizations use drug levels or pharmacologic markers to assess adherence; blood levels for most antipsychotic agents are not measurable.

The Medication Event Monitoring System (MEMS) is most often used in clinical studies. It consists of a bottle with an electronic recorder that is activated when the bottle is opened. MEMS involves reliability concerns, as patients can open bottles but not take medications.

The most accurate method is direct observed therapy. This is the long, intensive process that is used in hospitals to watch the patient take the medicine. It is not practical for routine use among outpatients. Biomarkers for assessing drug levels are not always available and don't account for variations in metabolism; also, the assays are expensive. Electronic monitors such as those used for MEMS are very costly.

Indirect methods such as questionnaires, pharmacy refill records, and patient diaries are much easier to use. Unfortunately, an inverse relation exists between accuracy and ease of implementation: The most accurate methods are the most difficult to administer (Figure 1).

Questionnaires

Numerous questionnaires for assessing medication adherence have been developed and validated. Clinicians prefer them for ease of administration, but patients can easily distort the results.

Beliefs About Medicines Questionnaire. The Beliefs About Medicines Questionnaire (BMQ) is the most common and well-validated tool. It is based on the assumption that patients' attitudes toward medications affect their adherence. Validated for use in schizophrenia and numerous other conditions, it has been translated for worldwide use. BMQ is an 11-item questionnaire with two scales: (1) a 5-item Necessity Scale assessing perceived personal need for medication and (2) a 6-item Concerns Scale appraising concerns about potential adverse effects (e.g., dependence).²⁴

Morisky Medication Adherence Scale. The eight-item Morisky Medication Adherence Scale (MMAS-8) is a self-report scale that also is used commonly. It has been validated for use in depression and physical conditions such as hypertension and asthma.⁴³ The strength of this questionnaire is its informality. It puts the patient at ease by acknowledging that many people face the same issues, thereby normalizing the responses.

MMAS-8: Yes or no questions⁴³

1. Do you sometimes forget to take your medication?
2. During the previous 2 weeks, were there any days when you did not take your medication?
3. Have you ever cut back or stopped taking your medication without telling your physician because you felt worse when you took it?
4. When you travel or leave home, do you sometimes forget to bring along your medications?
5. Did you take your medication yesterday?
6. When you feel like your depression is under control, do you sometimes stop taking your medication?
7. Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your antidepressant treatment plan?
8. How often do you have difficulty remembering to take your medication (never/rarely, once in a while, sometimes, usually, or all the time)?

Antidepressant Adherence Scale. The Antidepressant Adherence Scale is a condensed version of MMAS-8, with the goal of saving time and increasing ease of use. It asks broad questions covering the previous 4 weeks: (1) How many times did you forget to take your medication? (2) How many times were you careless about taking your medication? (3) How many times when you felt better did you stop taking your medication? (4) How many times when you felt worse did you stop taking your medication?

Responses are converted to a numerical scale. Any patient who missed taking their medication for any reason five or more times during the 4 weeks following their psychiatric consultation is considered nonadherent.

Attitudes Toward Mood Stabilizers Questionnaire. The Attitudes Toward Mood Stabilizers Questionnaire is a modification of the Lithium Attitudes Questionnaire, which

is specific to patients taking lithium. It consists of seven subscales representing the following domains: opposition to prophylaxis, denial of therapeutic effectiveness, fear of adverse effects, difficulty with medication routines, denial of illness severity, negative attitude toward drugs in general, and lack of information about mood stabilizers.⁴⁴

"Some patients who have been hospitalized 10 times still believe they can survive without medications."

—Kelly Lee, PharmD

Medication Adherence Report Scale. The Medication Adherence Report Scale is a five-item self-report scale for schizophrenia. It has been validated in a number of psychiatric disorders; its validation is closely related to results from electronic measures of adherence. It uses statements such as "I forget to take medicine" and "I alter the dose" with response choices ranging from "always" to "never."^{45,46}

Drug Attitude Inventory. The Drug Attitude Inventory is a true/false assessment of patients' attitudes toward antipsychotic drugs. Clinicians can reassure patients that there are no right or wrong answers and that they are simply trying to understand how the patient feels about medications.^{47,48}

Drug Attitude Inventory: True or false statements⁴⁷

- For me, the good things about medication outweigh the bad.
- I feel strange, "doped up," on medication.
- I take medications of my own free choice.
- Medications make me feel more relaxed.
- Medication makes me feel tired and sluggish.
- I take medication only when I feel ill.
- I feel more normal on medication.
- It is unnatural for my mind and body to be controlled by medications.
- My thoughts are clearer on medication.
- Taking medication will prevent me from having a breakdown.

How can we improve adherence?

Although achieving complete remission of symptoms is rare, especially in schizophrenia and bipolar disorder, health professionals must seriously attempt to meet the challenges of adherence. After pharmacists and other professionals are well educated on the factors that contribute to nonadherence, what can be done to improve adherence? Pharmacists must use the tools for measuring adherence and learn how to implement the interventions that are used successfully today.

Case vignette: Mr. Suspicious

Mr. Suspicious is a 45-year-old white man with a 25-year history of schizophrenia (diagnosed at age 20 years). He has not refilled his prescriptions for several months. He says that he takes his medications most of the time but "misses a pill here and there." In the past, he has experienced several adverse effects, including dystonia and akathisia, with older antipsychotic agents. He uses three different pharmacies to "prevent the FBI from tracking my movements." He may be taking double the dose because he doesn't realize that the refills from three pharmacies are likely for the same medications.

How would you manage this patient to improve his adherence?
See sidebar at end of article for answers.

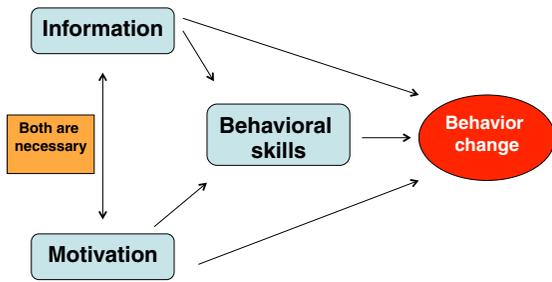


Figure 2. Information–motivation–behavioral skills model
Source: Reference 49.

Many of the psychiatric-focused studies have focused on depression by itself and in combination with other conditions such as HIV and aging. Most interventions have focused on unidimensional factors (i.e., patient-related factors). However, as discussed above, many other factors affect patient adherence. For that reason, multidimensional interventions that also target the cultural, socioeconomic, health-system, and provider barriers that influence adherence are required. Although these multidimensional approaches have shown the best results, their use is limited because they are labor intensive and costly.

The complexity of such a process can be seen in the information–motivation–behavioral skills model (Figure 2). To achieve change in behavior, individuals must be equipped with behavioral skills. Both information and motivation are required to have an effect on behavioral skills, which can lead to changes in behavior (i.e., improved adherence).⁴⁹

The HIN e-survey of 107 health care organizations determined that the top five health professionals responsible for improving medication adherence are primary care physicians (40%), pharmacists (34.7%), case managers (33.3%), health coaches (30.7%), and nurse practitioners (21.3%). All of the professionals involved should be educated in adherence issues so that they can reinforce one another when dealing with patients.⁴²

“Every person who touches a patient should reinforce the same skills, the same knowledge, and the same levels of education to help the patient improve adherence.”

–Kelly Lee, PharmD

The HIN 2010 e-survey also examined interventions used by pharmacists. Individual coaching was the most frequently reported intervention (64.6%), followed closely by medication reconciliation (58.3%) and medication therapy management (52.1%). Telephone reminders and postdischarge calls ranked lower (27.1% and 12.5%, respectively).⁴²

Therapeutic alliance

Both clinicians and patients commonly struggle with their relationship. A major obstacle to success occurs if the patient doesn’t trust the pharmacist or doesn’t believe that the pharmacist has the knowledge and capability to provide needed

care. A solid therapeutic alliance can set the stage for meaningful two-way communication as the pharmacist seeks to overcome barriers to adherence.

Patient barriers. Patient-related strategies for overcoming barriers are as follows:

- Ask open-ended questions about medication beliefs. (For example: How do you feel about your medications?)
- Discuss health benefits and the risk–benefit ratio of the patient’s medications. Prepare the patient for potential adverse effects while also emphasizing the benefits of the treatment. If a patient is concerned about becoming addicted to a medication, pull the studies that belie that fear and show them to the patient.
- Discuss the patient’s immediate and long-term needs. This can be difficult because patients can’t easily envision what they want to achieve. Help the patient put problems into the context of their lives; when addressing comorbidities, point out to a grandmother, for example, that she must take better care of her diabetes if she wants to be part of her grandchildren’s lives.
- Repetition: talk about the same things on every visit, perhaps from different angles. Be reassuring and consistent in the message.
- Use all available tools (written, verbal, and nonverbal communication) to reinforce the importance of adherence.

Treatment barriers. The pharmacist can help the patient develop realistic expectations about the potential benefits of their medications. Some suggestions for making it as easy as possible for a patient to take medications as directed include the following⁴³:

- Simplify the treatment regimen: use once-a-day long-acting medications as much as possible.
- Provide aids to improve adherence such as pill boxes or blister packs.
- Use depot injections.
- Switch to generic or lower-cost alternatives.
- Make use of pharmaceutical companies’ patient assistance programs.
- Arrange for home delivery of medications.

Health-system barriers. Implementing collaborative care models can achieve the multipronged interventions that have been shown to work best. Having physicians, pharmacists, nurses, care managers, and social workers on the treatment team results in a better outcome than if the pharmacist is acting independently. Constant communication among the team members is essential.

Condition-related barriers. Adherence can be affected by many aspects of the patient’s condition. The pharmacist should identify comorbidities and make sure that the patient is receiving adequate treatment for them. Systematic screening for depression among patients with other mental illnesses can shed light on a patient’s true condition.

Culture-related barriers. With increasing populations of patients from different cultures, pharmacists face new challenges in communication and understanding a patient’s

Table 3. Interventions to improve adherence in depression

Barrier	Intervention
Patient related	Counseling and education, relapse-preventing counseling, family psychotherapy, frequent follow-up interviews, specific advice targeted at patient's individual needs
Treatment related	Education on proper use of medication(s), patient-tailored prescriptions, continuous monitoring and reassessment of treatment
Condition related	Education on the patient's condition, realistic expectations, identify comorbid conditions
Health care team and health system related	Multidisciplinary care, adherence training of health professionals, use of primary care nurse for counseling, telephone consultation and counseling, improved assessment and monitoring of patients

Source: Reference 32.

attitudes toward mental illness and medications. These can be addressed by establishing a therapeutic alliance, identifying barriers and misconceptions, using language/interpreter services, including family members and caregivers in the treatment plan, and/or obtaining information on the patient from collateral sources.⁴⁴

Provider-related barriers. All providers need to increase their cultural competence to help patients effectively. In addition to establishing a therapeutic alliance with the patient and perhaps also with the family, other steps providers can take include expanding knowledge of barriers to adherence, increasing education about the illnesses and medications, and boosting knowledge about resources for patients to help them deal with housing, finance, food, and insurance issues. Local resources such as Section 8 housing units, food banks, homeless shelters, and substance recovery programs should be included.

Interventions to improve adherence in depression are shown in Table 3.

Case vignette: Ms. Distracted

Ms. Distracted is a 28-year-old Asian-American woman diagnosed with bipolar disorder. She is currently taking lithium 300 mg three times a day. She is an attorney and often forgets to take her lithium doses, leading to erratic lithium levels during the previous 6 months. With her irregular work hours, she often forgets to eat and keep hydrated. Her sleep patterns are irregular, and she doesn't have time to exercise.

She complains that she can no longer handle her mood swings and is concerned that her coworkers have noticed her erratic behavior, which varies from hypomania to full-blown mania at times and sometimes depression.

What interventions can you use to help her? See sidebar at end of article for answers.

"Patients are extremely grateful for the little things pharmacists can do that make a huge difference, such as helping them find affordable housing or navigating federal or local resources for them."
—Kelly Lee, PharmD

Do pharmacists' interventions work?

Numerous studies have been conducted to assess the effectiveness of pharmacists' interventions to improve adherence.

Antidepressant adherence

A review article of interventions for adherence to antidepressants showed that the interventions used were primarily focused on patient education, drug monitoring, and frequency of visits or phone follow-up. Adherence measures were primarily self-report and pharmacy refill records. The overall pharmacist impact on adherence ranged from 1% to 33%.⁴⁵ The studies included in this meta-analysis did not use more accurate measures of adherence such as biomarkers and direct observed therapy.

Improving antipsychotic adherence

A controlled trial compared a pharmacy-based intervention with usual care (no pharmacist involved) in patients with schizophrenia, schizoaffective disorder, or bipolar disorder. Researchers in four Veterans Affairs facilities used pharmacy refill records to measure MPRs. The Meds-Help intervention consisted of (1) unit-of-use packaging that included all patients' medications for psychiatric and general medical conditions, (2) a medication and packaging education session, (3) refill reminders mailed 2 weeks before scheduled refill dates, and (4) notification of clinicians when patients failed to fill antipsychotic prescriptions within 7 to 10 days of a fill date. Meds-Help staff served as contacts for patient questions regarding pharmacy services or physician prescriptions.

After 12 months, the adherence rate in the intervention group had improved from an MPR of 0.54 at baseline to 0.86—a statistically significant increase. However, measures of symptoms and quality of life did not show improvement.⁴⁶

Treatment adherence therapy

In a controlled trial in patients with schizophrenia and schizoaffective disorders, interventions by psychiatric nurses included motivational interviewing, medication optimization, and behavioral training. At baseline, 18% of the patients were completely nonadherent. One-third of patients were taking second-generation oral antipsychotics and 17% were taking two antipsychotic agents simultaneously. Adherence, which was measured by asking patients about the number of missed doses in the past days and weeks, significantly improved at the end of the study and after 6 months of follow-up.⁴⁷

Ongoing challenges

Substantial room for improvement exists in the adherence arena. Education of pharmacists and other providers is essential, and use of interventions must become more widespread. Three specific areas needing attention are described below.

Further improve adherence

More health care organizations and community pharmacists need to use the available interventions. Nonadherence results in wasted money and resources on emergency department visits and rehospitalizations—situations that can be reduced considerably if greater emphasis is placed on getting patients to take their medications.

Improve outcomes

Most studies in the antidepressant review did not show improvement in depressive symptoms despite improvements in adherence.⁴⁵ Similarly, a study of patients with schizophrenia, schizoaffective disorder, and bipolar disorder showed increased antipsychotic adherence, but no significant improvements in symptoms or well-being were observed.⁴⁶ The apparent lack of effectiveness of improved adherence may be because most of the trials cited lasted 3 to 6 months, which is not enough time to evaluate the overall effects. The cost of conducting long-term studies is prohibitive.

Converting adherence improvement to outcome improvement is a complicated issue. Clearly, many factors other than adherence are involved in determining a patient's ability to recover.

Reimbursement

The HIN Medication Adherence e-survey found that 70.6% of responding organizations said they were not currently reimbursing pharmacists' adherence-related interventions. Pharmacists are reimbursed for the following medication tasks: medication reconciliation/review (26.5%), patient education (17.6%), resolving drug therapy problems (14.7%), and converting regimens to generic drugs or preferred formulary medications (8.8%).⁴² Therefore, securing payment for their time and efforts required to conduct interventions remains an ongoing issue for pharmacists.

Summary

Poor medication adherence in the treatment of chronic disease, including severe mental illness, is a worldwide problem. Poor adherence leads to poor health outcomes and increased health care costs. Nonadherence is multifactorial, and multidisciplinary patient-tailored interventions are required. Improving patient adherence improves patient safety. Health professionals need to be trained in adherence.

"Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific treatments."
—R.B. Haynes

Case vignette answers

Answers to Ms. Blue's adherence barriers: cultural barriers, poor family support, financial, comorbidities, poor experience and nonadherence with previous medications, adverse effects (including weight gain), poor attitude toward medications.

Suggestions for managing Mr. Suspicious: call the three pharmacies to limit the number of prescriptions and the number of refills, educate him about the risks of using three different pharmacies, use injectable medications.

Try to relieve his delusions about the FBI. You could tell him, "If we are careful with your prescriptions, it is less likely that anyone would be able to track your movements." Or tell him you are prescribing a brand-new medication and by increasing the dose quickly, he won't need to use three pharmacies.

Warn him that his continued nonadherence may well worsen his symptoms: "If you continue behaving this way and not taking your medications reliably, ultimately you'll become hospitalized. What is it worth to you to stay out of the hospital?"

Interventions to help Ms. Distracted: Tell her to use a reminder alarm to alert her when she is scheduled to take her medication. Simplify her dosage, reducing her regimen to twice a day. If she is at steady state, combine her doses to be taken at night. Switch to a longer-acting medication that can be taken less often. Emphasize the importance of sleep, diet, and exercise. Point out the danger of becoming dehydrated while taking lithium. Counsel her to provide some structure in her life. Educate her about her disorders and why she has mood swings. Suggest that she get a dog, which she will have to walk every day, thereby providing exercise. Ask her about her immediate and long-term goals in the legal profession, suggesting that adherence can assist her in attaining her goals both immediately and in the future. Reassure her that following your recommendations and taking her medication regularly can overcome her concern about her coworkers' awareness of her behavior.

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CPE assessment

Instructions: This exam must be taken online; please see “CPE information” for further instructions. The online system will present these questions in random order to help reinforce the learning opportunity. There is only one correct answer to each question.

- What is the most accurate measure of adherence**
 - Self-report
 - Pharmacy refill records
 - Direct observed therapy
 - Medication Event Monitoring System
- Four-times-a-day dosing regimens may result in non-adherence rates of:**
 - 30%.
 - 40%.
 - 50%.
 - 60%.
- Pharmacist interventions for depression treatment usually:**
 - Involve Medication Electronic Monitoring Systems.
 - Incorporate patient education or drug monitoring.
 - Show improvement in depressive symptoms and adherence.
 - Have been shown to be cost effective to a health system.
- The rate of adherence among patients with severe mental illness is:**
 - Higher than in those with an acute illness.
 - About the same as those with chronic illnesses.
 - Higher than those with chronic diseases, such as hypertension.
 - Lower than those with physical ailments.
- A patient who is taking medication without any gaps is considered:**
 - Concordant.
 - Obedient.
 - Persistent.
 - Compliant.
- The estimated cost of nonadherence in the United States is:**
 - \$875 million.
 - \$75 billion.
 - \$190 billion.
 - \$290 billion.
- The most commonly used questionnaire for assessing adherence is:**
 - The Medication Adherence Report Scale.
 - The Drug Attitude Inventory.
 - The Attitudes Toward Mood Stabilizers Questionnaire.
 - The Beliefs About Medicines Questionnaire.
- The pharmacist intervention that is used the most by health care organizations with adherence programs is:**
 - Medication reconciliation.
 - Phone reminders.
 - Individual coaching.
 - Medication therapy management.
- The Vantaa Depression Study concluded that the main reason patients do not take their antidepressants is:**
 - A generally negative attitude toward medications.
 - Fear of addiction.
 - Concern about adverse effects.
 - Cost of the drugs.
- According to the National Alliance on Mental Illness, the primary reason why patients with schizophrenia and bipolar disorder do not take their medications is:**
 - Fear of addiction.
 - Anosognosia.
 - Substance abuse.
 - Concern about adverse effects.

CPE information

To obtain 2.0 contact hours (0.2 CEUs) of CPE credit for this activity, you must complete the online Assessment and Evaluation. A Statement of Credit will be awarded for a passing grade of 70% or better on the Assessment. You will have two opportunities to successfully complete the CPE Assessment. Pharmacists who successfully complete this activity before June 1, 2016, can receive CPE credit. Your Statement of Credit will be available upon successful completion of the Assessment, Learning Evaluation, and Activity Evaluations and will be stored in your ‘My Training Page’ and on CPE Monitor for future viewing/printing.

CPE instructions:

- Log in or create an account at pharmacist.com and select LEARN from the top of the page; select Continuing Education, then Home Study CPE to access the Library.
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Live step-by-step assistance is available Monday through Friday from 8:30 am to 5:00 pm ET at APhA Member Services at 800-237-APhA (2742) or by e-mailing education@aphanet.com.

- 11. The Morisky scale for measuring adherence:**
- Is an 11-item questionnaire about a patient's attitudes toward medication.
 - Consists of a Necessity Scale and a Concerns Scale.
 - Has been validated for use in patients with depression and physical conditions.
 - Is a modified version of the Lithium Attitudes Questionnaire.
- 12. Which of the following percentages of the health care organizations surveyed by the Healthcare Intelligence Network (HIN) reported having intervention programs to improve adherence?**
- Less than 25%
 - 50%
 - 65%
 - 78%
- 13. In the HIN report, which of the following was the most common target for adherence interventions reported by health care organizations?**
- Patients with a history of nonadherence
 - Patients who take multiple medications
 - Patients who are concerned about the cost of drugs
 - Patients with severe mental illness
- 14. When meeting a new psychiatric patient with adherence issues, the first thing the pharmacist should do is:**
- Establish a therapeutic alliance.
 - Measure the patient's rate of nonadherence.
 - Provide educational pamphlets.
 - Identify any comorbid conditions.
- 15. The best way to initiate an honest exchange with patients is to:**
- Ask a question such as, "Are you taking your medication as directed?"
 - Give them a list of true/false statements to fill out.
 - Ask an open-ended question.
 - Criticize their lack of adherence.
- 16. The greatest positive impact of adherence interventions occurs when:**
- The patient's family is involved.
 - Cultural barriers are addressed.
 - Multidimensional interventions are used.
 - The intervention focuses on overcoming condition-related barriers.
- 17. The most commonly used measure of adherence in health care organizations' intervention programs is:**
- Claims databases.
 - Refill patterns.
 - Evidence-based standards.
 - Blood tests.
- 18. The statement, "It is unnatural for my mind and body to be controlled by medications," is part of which of the following adherence questionnaires?**
- The Drug Attitude Inventory.
 - The Medication Adherence Report Scale.
 - The Attitudes Toward Mood Stabilizers Questionnaire.
 - The Morisky Medication Adherence Scale.
- 19. Research studies on the effectiveness of adherence interventions have reported:**
- Considerable improvement in patients' depressive symptoms.
 - Lack of improvement in adherence rates for those taking antidepressants.
 - Mild improvement in self-perceived well-being for patients with schizophrenia.
 - Moderate to substantial improvement in adherence.
- 20. In the HIN e-survey, what percentage of health care organizations reported that they do not reimburse for adherence-related interventions?**
- 50.5%
 - 69.3%
 - 70.6%
 - 85.0%