Optimizing Treatment Choices to Improve Adherence and Outcomes in Schizophrenia

John M. Kane, MD, and Christoph U. Correll, MD

Schizophrenia is a serious, lifelong mental illness. Recovery is possible with consistent, supportive treatment, but relapse is common. A frequent contributor to relapse is treatment nonadherence. Long-acting injectable (LAI) antipsychotics can improve treatment adherence and continuity, potentially improving outcomes for patients, but these agents are underused. Experts John M. Kane, MD, and Christoph U. Correll, MD, described the frequency and consequences of nonadherence and strategies to improve adherence and overall patient outcomes.

MONITORING ADHERENCE IN PATIENTS WITH SCHIZOPHRENIA AND IDENTIFYING CANDIDATES FOR LAI ANTIPSYCHOTICS

Medication adherence is a major problem in all areas of medicine, not just psychiatry, whether patients have heart disease, diabetes, asthma, epilepsy, or any other condition that requires daily medication.[1,2] According to a report by the World Health Organization, poor medication adherence for chronic diseases is a worldwide problem of enormous importance—the rate of adherence averages 50% in developed countries and is lower in developing countries.[3] As many as two-thirds of patients with schizophrenia are estimated to be at least partially nonadherent to oral antipsychotic treatment.[4] Clinicians need to address the problem of nonadherence with patient-tailored interventions and education. In his presentation, Dr Kane offered insight into communication with patients about adherence and about interventions to diminish nonadherence.

Factors in Nonadherence

Prescribers would like for patients to believe that their medicine is beneficial, makes them feel better, and is worth the cost. However, many factors contribute to nonadherence. It may be related to patient issues, specific treatments (eg, side effects, lack of efficacy), or the patient's overall condition.[3] Individuals with schizophrenia face special challenges in taking medication as prescribed. The illness is often complicated by poor insight and cognitive dysfunction; poor symptom control can contribute to nonadherence; patients are less likely to take medicine if they cannot see the value in taking it; adverse effects may be intolerable; patients may have poor social support; and substance abuse is common and can contribute to

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This Academic Highlights activity is derived from the planning teleconference series "Optimizing Treatment Choices to Improve Adherence and Outcomes in Schizophrenia," which was held in March and April 2019. This report was prepared and independently developed by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Indivior Inc.

The teleconference was chaired by **John M. Kane, MD,** Department of Psychiatry, The Zucker Hillside Hospital, Glen Oaks, New York. The faculty was **Christoph U. Correll, MD** from the Department of Psychiatry, The Zucker Hillside Hospital, Glen Oaks, New York.

CME Objectives

After studying this article, you should be able to:

- Monitor adherence to treatment in patients with schizophrenia
- Identify patients who would benefit from LAI treatment
- Address somatic and psychiatric comorbidities in the care of patients with schizophrenia

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The faculty member(s) agreed to provide a balanced and evidence-based presentation and discussed the topic(s) and CME objective(s) during the planning sessions. The faculty's submitted content was validated by CME Institute staff, and the activity was evaluated for accuracy, use of evidence, and fair balance by the Chair and a peer reviewer who is without conflict of interest.

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nonadherence.[5–7] Social, economic, and health system factors may interfere as well.

Keeping up with daily medications can be difficult, as one person shared about her brother with schizophrenia:

Family Perspective

"It seems that deciding to take medication is one thing for diagnosed people, but deciding to ensure that it is taken exactly as prescribed at the exact right time is another issue entirely. My brother is proof that it is extremely difficult to keep track of many different medications simultaneously. . . . A single mismanaged dose can potentially lead to weeks of hardship. . . . Going without has caused a lot of unnecessary hardship for my brother and it's possible that some of his visits to the emergency room for psychological distress could have been avoided entirely."[8]

Assessing Nonadherence

Unfortunately, many physicians overestimate treatment adherence.[9,10] Dr Kane said that clinicians' perceptions of their own patients can be biased and may reflect the view that nonadherence is a problem that *other* clinicians have. Physicians may think that their patients are better with compliance or are more likely to listen to them than the patients reported in the literature,[11] even though this may not necessarily be the case.

Expert consensus recommendations are to assess adherence via not only self-report but also objective tools.[12] For example, the Medication Adherence Rating Scale can be used with patients who have schizophrenia.[13,14] Pill counts and informant ratings can also be useful.[15]

To improve the accuracy of patients' self-report, asking about their experiences taking medication may be more useful than asking a direct question about nonadherence (Figure 1).[6,16] Dr Kane recommended that clinicians avoid conveying an attitude that patients who miss or stop taking medications are "bad patients"; instead, they should communicate that nonadherence is human nature and happens frequently and that doctors want to help patients benefit from their medications as much as possible.

Relationship Between Nonadherence and Relapse

Poor adherence to oral antipsychotics is the most common cause of relapse.[4] A summary of 5 studies compared continuous antipsychotic treatment with intermittent treatment (ie, patients were treated only when clinicians thought they were experiencing early signs of relapse).[17] All 5 studies showed a significantly lower rate of relapse in patients with continuous treatment than in those with intermittent treatment.

Patients with schizophrenia are at risk for relapse and hospitalization after intervals of missed medication as short as 10 days or less (Figure 2).[18,19]

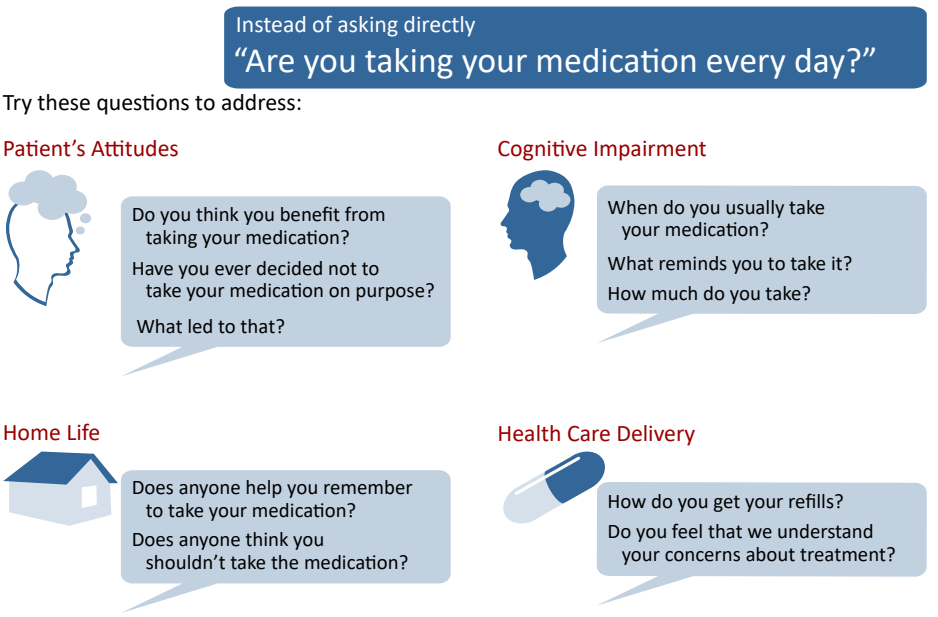
A systematic review[20] of 6 studies assessing the risk of relapse after treatment discontinuation found that 77% of patients relapsed within 1 year. The rate of relapse among these patients jumped to 90% after 2 years. In comparison, the rate of relapse among patients with good adherence has been reported as 18%.[21]

A study[22] by Robinson and colleagues followed 104 first-episode patients and found that after 5 years, 82% of the cohort had experienced at least one relapse. Stopping medication was found to be the most powerful predictor of relapse; patients who stopped were 5 times more likely to relapse than patients who continued with their medication.

Consequences of Relapse

Dr Kane noted that, with each relapse, the onset of therapeutic effect of medication may be slower, treatment may be less effective, and patients can experience greater hardships and illness burden. Relapses have been associated with progressive decline in brain

Figure 1. Communication Strategies to Ascertain Medication Adherence in Schizophrenia Patients More Accurately[a]



[a]Based on Velligan et al[6]; reprinted with permission from Kane.[16]

Figure 2. Odds Ratio for Hospitalization in Patients With Schizophrenia, by Gap in Antipsychotic Treatment[a]

[a]Data from Weiden et al[18]; adapted with permission from Correll.[19]

volume.[23] Ramifications of relapse among patients with schizophrenia include the following[24]:

- Increased risk of self-harm
- Increased risk of harm to others
- Increased distress for patients and families
- Increased strain on friendships and relationships
- Disruptions in education
- Disruptions in vocational functioning
- Decreased patient autonomy
- Increased social stigma
- Increased economic burden associated with treatment
- Increased risk of not returning to baseline functioning
- Increased resistance to treatment

A study[25] that followed 130 patients showed that reaching the same degree of improvement after a relapse took longer with the second episode than the first. The illness, in other words, became less responsive to treatment.

A Dutch study[26] of 603 patients with schizophrenia investigated the relationship between an interruption in medication of at least 30 days and suicide. After adjusting for age and gender, the relative risk of suicide attempt was found to increase approximately 4-fold among patients with a 30-day or more interruption compared with patients who did not have an interruption.

Cooperation between patients and clinicians is necessary to minimize relapses and their consequences such as lost jobs, as illustrated by a patient who experienced multiple relapses:

Patient Perspective

"I was diagnosed as schizophrenic when I was 13 years old. I spent the better part of my adolescence and young adulthood in hospitals. . . . I fought my disease and the stigma of mental illness in my struggle for employment. I learned from my mistakes which cost me several jobs, and along with my psychiatrist, we experimented with different medications. Fortunately, we found a combination of medications which kept me out of hospitals and I kept employment."[27]

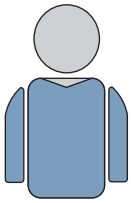
Using Long-Acting Injectable Antipsychotics

Long-acting injectable (LAI) antipsychotics can play a role in helping patients with schizophrenia remain adherent.[4,28,29] Research indicates that patients treated with LAI antipsychotics have decreased hospitalization and use of emergency services compared with those treated with oral antipsychotics.[30–32] A real-world comparative effectiveness trial[33] that included almost 30,000 patients found that LAIs and clozapine were the most effective treatments for preventing schizophrenia relapse; rehospitalization rates among patients receiving LAIs were 20%–30% lower than for patients receiving equivalent oral formulations. However, this treatment modality is not prescribed as often as oral antipsychotics.[4,34]

Figure 3. Perceptions of Clinicians vs Patients Toward Long-Acting Injectable (LAI) Antipsychotics[a]

Clinician Perceptions

- Patients have refused or will refuse LAIs
- Patients will always prefer oral medications
- Patients are sufficiently adherent to oral medication
- An LAI would be too expensive
- Use of LAIs should be avoided if patients are in their first episode
- My patients have been adequately informed about LAI options



Patient Perceptions

- My doctor has never informed me about LAI options
- I may prefer LAIs to oral treatments after trying LAIs
- LAIs may prevent relapse better than oral treatments
- I feel better supported with injections than with oral drugs because of regular contact with health professionals

[a]Based on Heres et al,[35] Patel et al,[36] Jaeger and Rossler,[37] Walburn et al,[38] Iyer et al,[39] and Caroli et al.[40]

Many factors play a role in the underuse of LAIs. Clinicians may have inaccurate perceptions about the medications and their patients' attitudes toward them (Figure 3).[35–40] Additionally, clinicians may think that they have clearly explained the treatment options to patients, but the conversation may be interpreted differently by patients. A survey[37] of patients being treated for schizophrenia and having no prior experience with LAIs, as well as psychiatrists, highlighted the disconnect between patients and clinicians. Only 21% of the patients reported that they had been informed of LAI options by their psychiatrist. Yet, 75% of the psychiatrists surveyed said that they had informed their patients about different formulations of antipsychotics, including LAI options.

Patient attitudes toward LAIs are frequently positive.[38] In a survey of patients with > 3 months of experience with an LAI formulation, LAIs were preferred, and 70% of patients felt better supported in their illness (compared with oral medication) because of regular contact with the clinician who administered their injection.[40]

What Can Clinicians Do to Improve Adherence?

The LAIs used to be considered appropriate for only a subgroup of patients with schizophrenia who had major nonadherence problems and frequent relapses.[41] Recent guidelines,[41,42] however, have noted the potential benefit of using second-generation LAIs following the first episode; LAIs have been found to be effective to prevent relapse in patients experiencing their first episode[43] as well as in those who have already experienced multiple relapses.[44,45] These agents should be "systematically proposed to any patients for whom maintenance antipsychotic treatment is indicated."[41]

Communication issues between clinicians and patients need to be overcome, noted Dr Kane. If clinicians are inadequately aware of data or are ambivalent about the message that LAIs are useful, then the dialogue will be ineffective. Clinicians should reflect on their own beliefs and recognize any negative assumptions about patient preferences. Clinicians with negative assumptions about LAIs will most likely present the option with a pessimistic tone that patients notice.[39]

Dr Kane stated that clinicians should consider the use of LAI formulations for any patient and start the conversation at the beginning of treatment. If the option of LAIs is introduced at a later date, it might be confusing or viewed as a negative response to a patient's hospitalization. Clinicians also need to make sure that their staff members and patients' family members understand why LAI formulations are being offered. A single team member who does not support the use of LAIs can undermine the treatment strategy with the patient.

Recent research showed that, even among first-episode and early-phase patients, the overwhelming majority of patients would consider the use of LAI formulations—only 14.4% of outpatients who were approached declined LAI treatment.[46] Staff education, which was successfully provided for this research, has the potential to substantially enhance the use of LAI antipsychotics. Staff members were trained on the role of nonadherence in relapse and hospitalization and the rationale for using an LAI formulation in patients with early-phase psychosis.[46] They also received education about shared decision-making, communication strategies, and patients' frequently asked questions; role-playing was used to develop their communication skills. Solutions were also devised to overcome logistical barriers to LAI use, and study prescribers received training on prescribing guidelines.

Dr Kane concluded that, if clinicians can employ these strategies for assessment, communication, and education, then far more patients could be engaged in treatment with LAI antipsychotics, which may provide enormous benefit to the patients, their families, and public health.

Case Practice Question

Discussion of the best response can be found at the end of the activity.

Case 1. John is a 33-year-old man who is diagnosed with schizophrenia and in his third hospitalization for psychosis. What should the clinical team consider in terms of preventing future relapses?

a) John has refused LAI antipsychotics in the past, but the options may not have been communicated in the best way.

b) John would be more likely to relapse if his oral medication is switched to an LAI than if he keeps the same regimen.

c) Nonadherence is probably not why John has had relapses, as he says he takes his tablets daily.

d) If John has a problem with adherence to oral medication, he would also have a problem coming in for injections.

TREATING THE WHOLE PATIENT: INCORPORATING THE PHARMACOLOGY OF TREATMENTS FOR SCHIZOPHRENIA AND SPECIAL CONSIDERATIONS FOR COMORBID CONDITIONS

While acute treatment efficacy and early remission of symptoms are important, effective maintenance treatment is crucial in keeping patients with schizophrenia stable.[47,48] Effective maintenance management of schizophrenia starts with efficacious and tolerable treatment. In general, efficacy differences among antipsychotics are relatively small, while tolerability differences are larger, which is true both for acute[49,50] and maintenance[51] treatment. Several LAI antipsychotics are available and differ based on starting dose, maintenance dose, and whether or not oral cotreatment is necessary at initiation (Table 1).[52–61] They also differ in that first-generation LAIs are oil-based, while second-generation LAIs are water-based, which leads to less injection pain and reaction.

In his presentation, Dr Correll reviewed evidence on LAIs and described situations in which LAIs might be especially useful.

Evidence on Discontinuation and Relapse With LAI Antipsychotics

A large meta-analysis[62] of randomized controlled trials (RCTs) was not able to demonstrate LAI superiority over oral agents, but this finding appears to be due to biased populations enrolled in RCTs.[63] Patients in double-blind RCTs tend to be more adherent, tend to have better illness insight, and might not be as severely ill as patients in the "real world."[64] Consistent with this interpretation, in meta-analyses of mirror image[64] and cohort[65] studies, which reflect more real-world patient populations, LAIs have been shown to prevent treatment discontinuation and reduce hospitalizations better than oral treatments.

One reason for the consistent results of LAI superiority over oral antipsychotics in 23 of the 25 meta-analyzed mirror image studies[64] may be improved medication possession. A study[66] of medication possession ratios based on pharmacy records reported that patients were in possession of oral medications only 40% and 42% of the time during a 12-month period, for commercially insured and Medicare-insured groups, respectively. However, when these patients were switched to LAIs for 12 months, the medication possession ratios rose to 67% and 68%.

A meta-analysis[67] showed that maintenance treatment with either oral or LAI antipsychotics has a strong relapse-prevention effect, translating into in a number-needed-to-treat of 3 versus placebo; however, the injectable formulations were associated with a greater reduction in relapse than oral drugs ($P = .03$).

Unlike with oral medication, clinicians have clear information when a patient misses a dose of an LAI. Furthermore, the window of opportunity to get the patient back into care before a relapse is extended due to the

Table 1. Long-Acting Injectable (LAI) Antipsychotic Differences[a,b]

Antipsychotic	Loading Strategy Upon LAI Initiation: Oral Supplementation	Loading Strategy Upon LAI Initiation: Additional LAI Injection or Higher Initial Dose	Injection Intervals
First-Generation			
Fluphenazine decanoate	No	No	Varies; possibly 3 or 4 wk
Haloperidol decanoate	No	No	4 wk
Second-Generation			
Risperidone microspheres	3 wk	No	2 wk
Risperidone extended-release subcutaneous	No	No	1 mo
Olanzapine pamoate	No	Dose[c]	2 or 4 wk
Paliperidone palmitate	No	Injection	1 or 3 mo
Aripiprazole monohydrate	2 wk	No	1 mo
Aripiprazole lauroxil	3 wk	No	4, 6, or 8 wk
Aripiprazole lauroxil + aripiprazole lauroxil Initio	1 day (30 mg)	Injection	4, 6, or 8 wk

[a]Data from Lauriello and Perkins[52] and antipsychotic package inserts.[53–61]
[b]Always consult current drug labeling for prescribing guidelines.
[c]Except for 300 mg every 2 weeks as the LAI equivalent dose for 20 mg oral olanzapine.

long-acting nature of LAIs. A study[68] indirectly compared relapse rates from separate RCTs, in which patients were switched to placebo following stabilization on 1 of 3 formulations of paliperidone: oral, once-monthly, and every 3 months. The duration until half of the patients relapsed was 59 days after the last dose of oral paliperidone treatment, 200 days after the last dose in patients who had received once-monthly paliperidone, and 479 days among the group that had received every-3-months paliperidone.

Special Populations

In the past, LAI antipsychotics were reserved for patients who had had multiple relapses, showed poor insight into the illness, and demonstrated nonadherence, but, as Dr Kane noted, guidelines now suggest considering LAIs as an initial treatment for any patient. Dr Correll stated that certain subgroups who would especially benefit from this change are those in the early stage of illness, who have substance abuse, and/or who are in contact with the legal system.[43,69–75] Although comorbid depression[76,77] and sleep disruption[78–80] are common in patients with schizophrenia and negatively affect outcome,[81] studies of LAIs in patients with these comorbidities are still lacking.

Early-illness patients. A study[43] of patients hospitalized between 2000 and 2007 with first-episode schizophrenia who were discharged on either oral or LAI treatments showed that the LAI treatment group had a 59% decreased risk for discontinuation and a 64% decreased risk for rehospitalization. A 12-month trial[71] of patients with first-episode schizophrenia (N = 86) found that oral treatment was associated with an observed relapse rate of 33% compared with 5% in the group receiving the LAI. In fact, in survival analyses, the relapse rates were estimated to be 50% vs 8.5% if all patients had been followed for an entire year, and at the end of the study, only 33% of orally treated patients, compared with 95% of LAI treated patients, had "excellent" adherence. Finally, in a study of patients with a recent diagnosis of schizophrenia (within 1–5 years),[69] LAI treatment reduced relapse risk by 29.4% versus oral treatment.

Patients with substance use or legal involvement. Substance abuse occurs more frequently in individuals with schizophrenia than in the general population and is associated with antipsychotic nonadherence.[74] A mother described her son's current situation:

Family Perspective

"My son is 21 and has been living with this horrible disease since he was 18. We have had 4 hospitalizations, each over a month in duration. We seem to be in a rut right now. He is non-med-compliant, refuses to go to treatment. . . . Before his hospitalization he was drinking heavily."[82]

A naturalistic 3-year study[75] of patients treated for first-episode schizophrenia who had substance use disorder found that, despite worse prognostic factors in the group receiving LAIs (eg, history of homelessness), these patients fared better than those taking oral antipsychotics. The LAI group experienced a lower relapse rate (68% vs 77%) and a longer time to relapse (694 days vs 447 days).

A 15-month, open-label randomized study[70] of patients with schizophrenia and a history of incarceration demonstrated a lower rate of treatment failure (arrest/incarceration, psychiatric hospitalization, suicide, treatment discontinuation or supplementation, or increased service use to prevent hospitalization) in the LAI treatment group (39.8%) than in the oral treatment group (53.7%).

Patients experiencing breakthrough psychosis. Patients with breakthrough psychotic symptoms while on LAI treatment need special care.[72,83] Dr Correll recommended that clinicians should rule out or address medical illness or substance use, identify and address stressors, optimize nonpharmacologic treatments, and treat comorbidities that could contribute to the exacerbation. Clinicians must also review whether the LAI administration was properly handled. The medication could have been mixed improperly or not injected deeply enough, reducing the rate of distribution.

If doses have been missed or delayed, the patient's next injection could be scheduled earlier than usual while staying within the recommended interval.[72] Clinicians could also increase LAI doses if not at the maximum. If doses are at the maximum, a possible solution is to add an extra oral dose of the same medication and monitor for 2–4 weeks. If the patient tolerates the extra dose and responds well, then his or her injection interval could be shortened (an off-label strategy).

The site of injection may also need to be moved because deltoid injections reach higher peak levels but result in a shorter half-life, while gluteal injections reach lower peak levels but result in a longer half-life.[84–86] If the symptoms still persist, clinicians may consider switching from one LAI to another or implementing different oral treatment, possibly clozapine for treatment resistance.[72]

Case Practice Questions

Discussion of the best responses can be found at the end of the activity.

Case 2. Jamal is a 24-year-old man with first-episode schizophrenia who has responded well to an oral second-generation antipsychotic. Which statement about next steps is *most* applicable?

a) Oral treatment that works will have the best chance to limit Jamal's risk of relapse.

b) Because Jamal has had only a first episode of schizophrenia, it is too early to start LAI treatment.

c) An LAI antipsychotic would have the best chance of reducing Jamal's relapse risk.

Case 3. Mateo is a 37-year-old man who has schizophrenia and is abusing marijuana and alcohol. During several inpatient stays, Mateo's schizophrenia stabilized, and he was unable to use drugs. After each discharge, he resumed his drug use and intermittent nonadherence with oral antipsychotics, leading to relapse. Mateo was recently involved in minor criminal activity, arrested, and briefly incarcerated. You need to devise a treatment plan; which statement reflects the *most* evidence-based strategy for Mateo?

a) Because Mateo uses alcohol and marijuana and has had problems with the law, an LAI antipsychotic will not be better than oral treatment for relapse prevention.

b) Relapse prevention with an LAI antipsychotic will most likely be more effective for Mateo than it would if the same LAI antipsychotic were prescribed for a patient without drug or alcohol use.

c) Relapse prevention with an LAI antipsychotic will most likely be similarly effective for Mateo as when the same LAI antipsychotic is prescribed for a patient without drug or alcohol use.

d) Relapse prevention with an LAI antipsychotic will most likely be less effective for Mateo than it would when prescribed for a patient without drug or alcohol use, but it may be more effective than the oral agents for Mateo.

Adverse Effects

When devising a treatment plan, it is very important to consider tolerability,[87] which can affect the likelihood that patients will continue treatment. Dr Correll stated that clinicians should bear in mind that antipsychotic side effect differences are larger and easier to predict than efficacy differences.[50]

A survey of patients with schizophrenia ranked the 5 most commonly occurring adverse effects as weight gain, somnolence or insomnia, problems with concentration, memory loss, and disorganized thoughts.[88] Relatives have reported that particularly unpleasant side effects for patients include sedation, weight gain, and extrapyramidal symptoms.[89] A meta-analysis[90] of RCTs that compared 119 adverse effects found no significant differences among LAI and oral versions of the same antipsychotics for 115 of them. Only 3 adverse effects occurred significantly *more* frequently with LAIs than with oral treatments: akinesia, higher low-density lipoprotein cholesterol, and anxiety. Prolactin change/hyperprolactinemia occurred significantly *less* frequently with LAIs than oral medications. Iatrogenic effects—including weight gain, hyperprolactinemia, diabetes, and extrapyramidal side effects—have been reported to reduce patients' medication adherence[91] and quality of life.[88,92]

Risk of mortality. In a recent, 30-year Finnish study[93] of mortality, the mean age at death was found to have increased among patients with schizophrenia, and the rate of suicide had decreased. However, a gap still exists, with the average age at death in the general population being 77.5 years and in those with schizophrenia being 70.1 years. Increases were found in deaths from cardiovascular diseases and cancer. In a Swedish study,[94] the risk of death was found to be 56% lower among individuals with schizophrenia who were taking antipsychotics than among those taking no antipsychotics. The use of LAI antipsychotics was associated with a 33% lower risk of death compared with equivalent oral formulations.[94]

Offering LAIs

Dr Correll agreed with Dr Kane that prescribers appear to have misconceptions about attitudes their patients may have toward LAI treatment. In a survey of opinions about LAIs among patients and health professionals,[95] the health professionals overestimated many concerns they believed their patients taking oral antipsychotics had about LAIs, including fear of pain at the injection site, embarrassment, reduced autonomy, and stigma. The only concern that patients had to a greater extent than imagined by clinicians was related to the amount of time they would be required to stay in the clinic for the mandatory observation after an injection of olanzapine pamoate.

Clinicians who offer LAIs may require training in communication. In a 2015 study,[96] psychiatrists were recorded while offering LAIs to their patients. In 33 conversations, only 9% of the speech time was dedicated to explaining positive aspects of LAI treatment (eg, no need for daily medication); 91% of the time was spent on the modality ("a shot") or neutral aspects. Two-thirds of patients expressed either a neutral or positive response to

Table 2. GAIN Model for Discussing LAI Antipsychotics With Patients[a]

G	Goal Setting	Discuss realistic goals with patients and ask which ones are most important to them
A	Action Planning	Identify with the patient and family the actions needed to achieve goals and discuss ways that LAIs might further those actions
I	Initiating Treatment	Confirm that the patient and family accept that using an LAI can help reduce relapse risk, review practical aspects of treatment and any potential problems, and begin the treatment
N	Nurturing Motivation	Talk with the patient, family, and treatment team about how the experience is going (both positive and negative aspects) and assess progress toward goals

[a]Based on Lasser et al.[98]

the offer of LAI therapy (with 33% indicating a potential willingness to try it). When another physician trained in delivering a positive message about LAIs and their potential advantages went back a few days later to speak to the patients, as many as 96% stated that they were open to try.

Patients may hear "injection" and not understand what is meant, as the following qualitative study's comments indicate:

Patient Perspectives

"A patient . . . feared that he might get 'addicted' to a[n] LAI as it was administered by an injection. This view related to him associating 'addiction' with injectable 'street drugs.' Another patient queried whether a[n] LAI needed to be injected daily 'like insulin.'"[97]

Dr Correll suggested that clinicians practice motivational interviewing by listening to and understanding the patient's values and fears. Clinicians should be nonjudgmental, respectful, collaborative, flexible, and empathic. The GAIN model[98] to facilitate change is based on the LEAP communication model,[99] in which the steps are Listen, Empathize, Agree, and Partner. The GAIN model can be used to discuss LAI antipsychotics with patients (Table 2).[98] Dr Correll concluded that clinicians should identify patient goals and should help patients recognize the disparity between where they are now and where they would like to be ideally, with medication being one tool to help them reach their goals.

CONCLUSIONS

Acute and long-term objectives must be linked early in the treatment of schizophrenia. Maintenance therapy is pivotal in relapse prevention. Relapses are serious events that alter disease trajectory and are most often related to nonadherence, which can be prevented in many cases with LAI treatments. Long-acting injectable treatments are still underused. Presentation matters for LAI treatments to be accepted by patients and family members. Communication strategies can be improved with clinician/staff training. As always, the risk-benefit ratio of treatment must be considered when choosing among available options.

Clinical Points

- Antipsychotic medication is critical in the prevention of relapse and rehospitalization.
- Rates of nonadherence are enormously high among patients taking antipsychotic medication.
- Long-acting formulations can be a very powerful strategy in helping to ensure that patients get the benefit of the medication they have been prescribed.
- Patients should be offered the option of LAI antipsychotic treatment and should understand the logistics and the potential benefits of the regimen.
- Communication strategies can be used to improve clinicians' dialogue with patients about LAI treatment

Discussion of Case Practice Questions

Case 1: **Preferred response is a.**

Clinicians may not communicate effectively with patients about LAI options, especially if they harbor negative opinions of the treatment modality or of patients' willingness to try LAIs. John's clinical team should use nonjudgmental questions and objective tools to assess whether John has a problem with adherence and, if so, offer education and patient-tailored interventions. He may be more willing to try an LAI now if his treatment team describes it in a positive way, answers his questions, and helps him understand that it might help him to avoid relapses and achieve his own, personalized goals.

Case 2: **Preferred response is c.** *See explanation below.*

Case 3: **Preferred response is d.**

Guidelines now suggest considering the use of LAIs following the first episode of schizophrenia to reduce the risk of relapse (as in Case 2). Studies have also indicated benefits of LAIs versus oral treatment among patients who have substance abuse and contact with the legal system (as in Case 3).

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Disclosure of off-label usage: The chair has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

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For the CME Posttest, see next page.

Posttest

To obtain credit, go to PSYCHIATRIST.COM (Keyword: **October CME**) to complete the Posttest and Evaluation.

1. **You have been treating Jen for schizophrenia since her first episode 4 years ago, when she was 18 years old. She lives with her parents and has a goal of finishing community college so that she can get at least a part-time job. Jen has been missing classes, and her mother brought her to see you because she's worried about signs of a relapse. As you assess Jen's treatment adherence, which would be the *least* helpful strategy?**
   a. Use a tool like the Medication Adherence Rating Scale
   b. Ask Jen if she's taking her pills every day
   c. Ask Jen if she thinks her medication helps her and when she usually takes it
   d. Ask Jen if she's ever decided to skip her pills and, if so, what led to that decision

2. **Evidence indicates that all of the following statements about relapse risk in patients with schizophrenia are true *except*:**
   a. A medication gap of 1–10 days roughly doubles the risk of hospitalization among patients with schizophrenia, and a gap over 30 days roughly quadruples it.
   b. Long-acting injectable (LAI) antipsychotics are associated with a lower relapse rate than oral agents among patients with first-episode schizophrenia.
   c. LAI antipsychotics are associated with the same rate of relapse as oral agents among patients with schizophrenia and comorbid substance use disorder.
   d. Patients with schizophrenia and a history of homelessness or incarceration have a lower rate of treatment failure (eg, hospitalization) with oral antipsychotics than with LAI formulations.

3. **According to research, all of the following statements about morbidity and mortality in patients with schizophrenia are true *except*:**
   a. A 30-year study found that their mean age at death has decreased over time.
   b. A 30-year study found that deaths from cardiovascular disease and cancer increased over time.
   c. Low-density lipoprotein cholesterol should be monitored among patients taking antipsychotics (oral and LAI).
   d. The risk of mortality is decreased with LAIs compared with oral antipsychotic treatment.

4. **Which one of the following is not included in the GAIN model for discussing LAI antipsychotics with patients?**
   a. Goal setting
   b. Assessing adherence
   c. Initiating treatment
   d. Nurturing motivation