

# Counseling Points™

Enhancing care through better communication.

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## Enhancing Medication Interest and Medication Follow-through in the Treatment of Schizophrenia

*A 3-Part Series*

### Improving Medication Adherence in Schizophrenia Through Innovations in Medication Follow-through and Antipsychotic Design

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# Counseling Points™

## Enhancing Medication Interest and Medication

## Follow-through in the Treatment of Schizophrenia

## Improving Medication Adherence in Schizophrenia Through

## Innovations in Medication Follow-through and Antipsychotic Design

## Continuing Education Information

### Target Audience

This activity has been designed to meet the educational needs of practicing psychiatrists involved in the management of patients with schizophrenia.

### Statement of Need/Program Overview

Psychiatrists caring for patients with schizophrenia are challenged by medication nonadherence, which plays a significant role in precipitating relapses of illness. Although all relapses cannot be prevented, appropriate pharmacologic and psychosocial strategies can be implemented to enhance medication interest and follow-through. This *Counseling Points*™ CME program is designed to educate psychiatrists about the latest interviewing, motivational, and management strategies in this area of medicine.

### Educational Objectives

*After completing this activity, the participant should be better able to:*

- Choose strategies for engaging and garnering support from family members (or significant others) for helping a relative use medication as prescribed.
- Describe three different strategies for helping a client modify his/her environment in order to facilitate medication follow-through.
- Explain the benefits and risks of long-term antipsychotic drug treatment in schizophrenia.
- Review appropriate monitoring strategies for assessing efficacy, adverse effects, and adherence associated with long-term pharmacotherapy.

### Accreditation Statement

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# Enhancing Medication Interest and Medication Follow-through in the Treatment of Schizophrenia

## Improving Medication Adherence in Schizophrenia Through Innovations in Medication Follow-through and Antipsychotic Design

### Introduction

As seen in the first two issues of this three-part *Counseling Points*<sup>™</sup> series, the Medication Interest Model (MIM) provides an avenue for understanding medication nonadherence as related to two major issues: 1) low patient interest in taking antipsychotics, and 2) external situational obstacles that prevent a patient from following through with taking a medication once the patient has decided to do so.<sup>2</sup>

Recognizing the importance of the patient being actively involved in the decision to take medication, establishing a strong therapeutic alliance that places a premium on honesty and respects the individual's independence, and exploring how medication may help to achieve desired changes are all critical to fostering the patient's intention to take medication. The MIM provides both a conceptual framework—the Choice Triad—for better understanding these issues as well as a host of behaviorally operationalized interviewing techniques for doing so. However, even after an individual has made the decision to take medication, numerous factors can conspire to interfere with his or her ability to follow through on that choice, leading to nonadherence.

In the concluding issue of this series, strategies for addressing these external situational factors and maximizing the follow-through of patients to take prescribed medication are explored. In addition, developments in antipsychotic design that may impact both patient choice and follow-through will be examined.

### Transforming Situational Barriers to Medication Follow-through

Any situational factor that can interfere with a patient's

*“Physicians are confronted by the particular souls of the individuals and families before them. It is likely that much noncompliance is an oppositional expression of an individual's wish to be consulted and heard....”<sup>1</sup>*

Robert Shuman  
from *The Psychology of Chronic Illness:  
The Healing Work of Patients, Therapists  
& Families*

resolve to follow through on taking medication can be conceptualized as “external” to that person's best intentions. Strategies for overcoming these external roadblocks can be divided into three broad types: 1) skills for illness self-management, 2) strategies for facilitating family support (or that of other significant persons), and 3) approaches for case management.

### Improving Illness Self-Management

Patients with schizophrenia were once viewed as passive participants in their treatment. It is now firmly established that patients can and need to be active participants in their own treatment. Lack of interest in initiating recommended treatments or subsequently following through with them is all too often the price paid for failing to take a collaborative approach.

A successful collaborative approach to coping with schizophrenia, reflected by a high interest in taking medications, often relies upon the sparking of hope. From this hope, a genuine interest in medications as agents of change may more readily arise. One strategy for accomplishing this vital task is to introduce and explore the concept of “recovery” with the patient.<sup>3</sup> Although recovery is conventionally thought of in terms of an individual no longer having any symptoms or impairments related to a disease, in recent years there has been a movement towards defining recovery in more individualized and hopeful ways.<sup>4-7</sup> From this perspective, recovery can be conceptualized as personally meaningful changes in areas such as social relationships, returning to work or school, independent living, or control over personal finances.

Consistent with the principles of the MIM, specific

interviewing techniques can play a critical role in capitalizing on the recovery concept by igniting hope for change and interest in medications as agents of change. The clinician can initiate a discussion about recovery by using the *Recovery Inquiry Question*: “Recovery is a word that means many different things to many different people, what does recovery mean to you?” This question can be followed-up by providing specific examples of what recovery means to other patients in specific areas of living, and exploring whether it has a similar meaning to the patient. For example, “For some people, recovery means having good, close relationships, such as with family members, friends, or an intimate partner, such as boyfriend, girlfriend, or spouse. How about for you? Is having good relationships part of how you would define recovery?” This discussion often leads to a reawakening of the patient’s dreams and the potential role of medication in achieving them.

As the need for a collaborative approach has become widely accepted, illness self-management programs have been developed to teach patients basic information about their illness, treatment options, and strategies for the shared management of the disorder.<sup>8-14</sup> For example, two standardized and empirically supported illness self-management programs that have been developed for people with severe psychiatric disorders are the Illness Management and Recovery program ([www.mentalhealth.samhsa.gov/cmhs/communitysupport/toolkits/default.asp](http://www.mentalhealth.samhsa.gov/cmhs/communitysupport/toolkits/default.asp)) and the Medication Self-Management and Symptom Self-Management modules of the UCLA Skills for Independent Living program ([www.psychrehab.com](http://www.psychrehab.com)).<sup>15-18</sup>

### Pillboxes and Prompts

The most common reason people don’t take medication they intend to take is that they simply forget. This problem is compounded by the memory difficulties experienced by many patients with schizophrenia.<sup>19</sup> Furthermore, complex medication regimens are more difficult for people with schizophrenia to follow because of other cognitive problems, such as conceptual disorganization or an inability to plan ahead.<sup>20,21</sup> One approach to overcoming these problems is to teach patients how to use devices to help take their medication in an orderly fashion. A wide range of pill-organizing boxes is available for storing medications in separate compartments based on the day and time-of-day they are supposed to be taken. Pill organizers may contain the pills for a single day (which can be easily carried around in a purse or pocket), a week, or a

month. When a prescription is filled, the patient, nurse, or pharmacy fills the pill organizer so that all of the pills that need to be taken at a particular time of day are stored together.

Pill organizers are useful for keeping track of what medications need to be taken when, but they often don’t address the problem of people forgetting to take their medication. Many patients find alarms are effective at serving this function. Some pill organizers also contain alarms or reminder chimes that can be set to prompt people to take medication. Other patients may find it more convenient to set a reminder alarm on something they frequently carry with them, such as a wrist watch, cell phone, MP3 player, or electronic scheduler.

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*Behavioral tailoring involves developing natural prompts by fitting the taking of medication into each person’s usual routine.*

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### Behavioral Tailoring

Behavioral tailoring is a somewhat different approach to helping patients remember to take their medication. Rather than relying on alarms to prompt individuals to take medication at designated times, behavioral tailoring involves developing natural prompts by fitting the taking of medication into each person’s usual routine. For example, someone who is prescribed medication for the morning and evening could incorporate taking medication into his daily routine of brushing teeth at those times by placing the medication right next to his toothbrush, or—for an even more foolproof method—attaching his toothbrush to the pill box with a rubber band. Whenever the person goes to brush his teeth, he is naturally reminded to take his medication. Alternatively, someone who watches an afternoon TV show on a regular basis that coincides with when she is supposed to take her medication could attach the pill box to the remote control. Controlled research has shown that behavioral tailoring is effective at improving adherence to medication in people with severe mental illness.<sup>22-25</sup>

### Dosage Simplification

Reducing the complexity of patients’ medication regimens can further facilitate follow-through, as the more complicated the regimen, the greater the difficulty adhering to it.<sup>26,27</sup> The complexity of a regimen is

determined by a combination of the number of different medications that need to be taken on a daily basis, the number of pills, and the number of times throughout the day that pills must be taken. Simplifying the regimen by reducing the number of medications and/or the frequency of dosing (e.g., taken all at night rather than two or three times per day) can improve adherence.<sup>28</sup>

### Social Skills Training

Managing a complex disorder such as schizophrenia is not a solitary affair. Successful illness self-management requires the ability to communicate effectively with treatment providers, including, at times, self-advocacy. Patients with schizophrenia often lack effective social skills for getting their needs met, including skills for addressing concerns they may have about medication.<sup>29</sup> For example, patients may not understand the purpose of a medication, may be troubled by a side effect, or feel that distressing symptoms are not sufficiently addressed.<sup>30</sup> Rather than voicing their concerns, patients may keep them to themselves.

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*Patients with schizophrenia often lack effective social skills for getting their needs met, including skills for addressing concerns they may have about medication.*

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Social skills training can equip patients with the skills needed for collaborating with their treatment team.<sup>31,32</sup> Skills training programs emphasize the use of frequent modeling and practice, with a focus on the nuances of social behavior critical to success. Even in the absence of formal skills training programs, treatment providers can help patients improve their social skills for discussing medication by encouraging specific behaviors, such as:

- maintaining good eye contact;
- using a firm, loud voice tone;
- clearly stating questions or concerns about medication;
- repeating back or paraphrasing answers to ensure comprehension;
- persisting in requesting more information or additional help when concerns remain; and
- thanking people for their time and help.

Patients sometimes feel flustered when meeting with

their doctor and forget to use even their most practiced skills. These missed opportunities can be averted by teaching patients to write down their concerns in advance and subsequently share them during the meeting. Providers can be sensitive to the difficulties some patients experience communicating their concerns about medication by gently probing about common questions and concerns, and following up on previously discussed issues.

### Harnessing Family Support

Family members and other significant people play an important part in the lives of most people. The role of family (and other caring individuals—hereafter referred to as “family” or “relatives” for the sake of simplicity) is especially crucial in the management of chronic medical conditions, including psychiatric disorders. Lack of family support can undermine the patient’s interest and desire to follow through with taking medication.<sup>33</sup> The involvement and support of family members in the patient’s treatment can facilitate his or her ability to follow through on plans to take medication.<sup>34</sup>

Sometimes the relationship between the treatment provider and family members develops before the relationship with the patient, such as when relatives bring a loved one in for treatment. In many other situations, however, a relationship is first established with the patient. Collaboration with family members is a process that takes time. The steps of developing a working relationship with family members are:

1. Motivate the patient to involve his or her family in treatment.
2. Provide information to the family about the psychiatric disorder and its treatment.
3. Discuss and agree upon medication follow-through strategies.
4. Develop a relapse prevention plan.
5. Establish mechanisms for maintaining an ongoing, collaborative relationship with the family.

Clinicians should not assume that all patients are motivated to have their family involved in their treatment. While some patients are readily open to the idea, others may have reservations, and addressing their concerns is critical to success. The following principles may help:

- Present family involvement in a matter-of-fact manner and explain that it is standard practice for any serious medical condition.

- Discuss how involving family members can help the

- Explain that family collaboration is intended to improve the lives of everyone involved, and not just the patient's life.
- Describe the nature of family collaboration (education, sharing perspectives, treatment planning) and emphasize that it is not stressful and can often reduce stress and conflict in the family.
- Address concerns about confidentiality, including what will and won't be shared.<sup>35</sup>

A variety of interviewing techniques have been developed to help transform these powerful principles into readily utilized interviewing techniques and strategies.<sup>2</sup> An outstanding article entitled "Practical Interviewing Strategies for Building an Alliance with the Families of Patients Who Have Severe Mental Illness" describes interviewing techniques for effectively working with families in both outpatient and inpatient settings.<sup>36</sup> Two techniques are particularly germane to our discussion.<sup>37</sup> With the first technique, *Acknowledging Family Expertise*, the clinician openly recognizes the immense value of the family member's first-hand knowledge of the patient and his or her care:

*"One of the things I want to emphasize early on is how important your input and background information is in our helping John. There is no one in the world who knows him better than you. We are dependent on your input. I also really want to know what you think has worked and what you think hasn't."*

A common fear of parents is that the "new psychiatrist" is going to "screw around with the meds." These fears are often not ungrounded, as previous experiences

### Recommended Books for Families

- Amador X, Johnson A-L. *I'm Not Sick, I Don't Need Help! Helping the Seriously Mentally Ill Accept Treatment: A Practical Guide for Families and Therapists*. Peconic, NY: Vida Press. 2000.
- Beard JJ, Gillespie P. *Nothing to Hide: Mental Illness in the Family*. New York, NY, New Press. 2002.
- Mueser KT, Gingerich S. *The Complete Family Guide to Schizophrenia: Helping Your Loved One Get the Most Out of Life*. New York, NY: Guilford Press. 2006.
- Torrey EF. *Surviving Schizophrenia: A Manual for Families, Consumers and Providers, 5<sup>th</sup> edition*. New York, NY: HarperTrade. 2006
- Woolis R. *When Someone You Love Has a Mental Illness, revised edition*. New York, NY: Jeremy P. Tarcher/Penguin Books. 2003.

patient achieve his or her personal goals.

with unwarranted medication changes have often had painful effects on both the patient and family members. This concern can be addressed with the second interviewing technique called the *No Need to Fret Statement*. Although the urgency of the presenting symptoms may necessitate that prescribers make immediate major medication changes, this situation (in an outpatient setting) is not typical. With this interviewing technique, the clinician emphasizes that although new medications may be tried—and could prove to be quite helpful—nothing is going to be done hastily. Moreover, the clinician highlights that the ongoing input of the family (if allowed by the patient) will be sought first:

*“One of the most foolish things a physician can do is to change the medications before talking with parents and the patient about what is working. Your input is vital. Who knows? We may find some really useful new medications to try, or we may find that his current meds are the best. No matter what, I have no intention of changing anything until I learn more from you on what has and has not worked. By the way, if your son agrees, in the future I would like to talk with you and get your thoughts about any potential major medication changes. At this point in time, what is your opinion about the medications that (consumer’s name) is on?”*

When the patient has agreed to involve his or her family in treatment, educating family members about the patient’s psychiatric disorder and care is an excellent way of developing a working relationship. A variety of psychoeducational resources are available.<sup>35,38-42</sup> Providing family members with information about medications and correcting misconceptions about them is critical to getting their “buy-in” with regard to the treatment plan.

A discussion about schizophrenia with family members, the patient, and a professional can be used to correct common stereotypes, such as the belief that people with schizophrenia can’t work, contribute to society, or lead rewarding and productive lives. Many families benefit from several sessions devoted to psychoeducation, and ongoing support is often pivotal to medication follow-through. Family psychoeducation can be supplemented with educational handouts, books for families, and referrals to local chapters of the National Alliance on Mental Illness (NAMI). Some recommended books for families about schizophrenia are summarized in the box below.

Teaching patients how to develop a relapse preven-

tion plan, either alone or in collaboration with their families, can have a powerful effect on reducing rehospitalizations for schizophrenia.<sup>43,44</sup> Developing a relapse prevention plan draws attention to the importance of medication, both as a primary prevention strategy and as an intervention for fending off the early warning signs of a relapse. The core elements of developing a relapse prevention plan include:

- Explaining that symptom relapses usually occur gradually over several days or weeks and are usually preceded by early warning signs (i.e., subtle changes in mood, thinking, or behavior), and that a rapid response to these signs can prevent a full-blown relapse.
- Discussing the past one or two relapses to identify several of the patient’s early warning signs.
- Reviewing situations that have triggered relapses in the past, including discontinuing medication.
- Agreeing on how family members and the patient should respond to the early warning signs of a relapse (e.g., by contacting the doctor to evaluate the need for a temporary increase in medication).
- Agreeing on a plan for monitoring early warning signs of a relapse.
- Writing down the whole plan and giving copies to everyone involved (e.g., patient, family members, treatment team).<sup>45</sup>

Family members may benefit from using a standard relapse prevention plan form, such as the one in Mueser and Gingerich’s *Complete Family Guide to Schizophrenia*, a book which addresses all of the above points in depth (**Table 1**).<sup>45</sup>

## Case Management

Case managers or other members of the patient’s treatment team (e.g., nurses) can play a valuable role in helping patients follow through on overcoming barriers to taking medication. Many patients are capable of learning how to organize their medications with pill boxes, but require considerable practice before they are able to safely do it on their own. A case manager can demonstrate, observe the patient, and guide him or her towards competence at this skill. When changes in the regimen take place, the clinician can work with the patient to ensure that the changes are incorporated into the individual’s medication organizer. Some patients may not be capable of learning how to organize their medications on their own, but can take them safely as directed once they have been organized for

## Table 1. Relapse Prevention Plan

**Step 1.** Who should participate in a family meeting if early warning signs are a concern? List below:

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**Step 2.** What are your relative's early warning signs (e.g., mood shifts back and forth, energy level is high or low, has lost interest in doing things, feels discouraged about the future, feels lonely, is bothered by thoughts he/she can't get rid of, etc.)? Talk about past relapses and list 2-5 early warning signs of a relapse:

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**Step 3.** If your relative is experiencing early warning signs, evaluate whether he/she is taking his/her medication regularly:

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**Step 4.** If your relative is not taking medication regularly, make a plan for helping him/her to resume doing so:

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**Step 5.** Evaluate whether your relative is abusing alcohol or drugs:

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**Step 6.** If your relative is abusing alcohol or drugs, make a plan for helping him/her to reduce or discontinue the substance abuse:

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**Step 7.** What situations have triggered relapses in the past or does your relative find stressful? Note these situations below:

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**Step 8.** If your relative is experiencing stress or is in a situation that has triggered relapses in the past, make a plan to reduce the stress or deal with the situation:

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**Step 9.** List treatment providers (and other supportive people or agencies) to contact if early warning signs persist for more than a few days. Names and phone numbers:

1. Psychiatrist: \_\_\_\_\_
  2. Nurse: \_\_\_\_\_
  3. Case manager: \_\_\_\_\_
  4. Social worker: \_\_\_\_\_
  5. Therapist or counselor: \_\_\_\_\_
  6. Other: \_\_\_\_\_
- 

**Step 10.** Set a date for a family meeting to follow up: \_\_\_\_\_. At the follow-up meeting, evaluate whether the early warning signs are still a problem. Make a new plan and set a date for additional follow-up as necessary.

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Adapted with permission from Mueser KT, Gingerich S. *The Complete Family Guide to Schizophrenia*. New York, NY: Guilford Press. 2006. Pages 204-205. Copyright 2006 The Guilford Press.

them by the case manager.

Behavioral tailoring to natural prompts such as brushing one's teeth is often most effectively implemented when a case manager can make one or two home visits. A home visit provides valuable information about the environment in which the patient lives, having the advantage of cueing the case manager about possible obstacles to implementing the behavioral tailoring plan. If the patient wants to take medications when he prepares his coffee in the morning but his kitchen counter is extremely cluttered, the case manager can first help the patient organize the counter and coffee supplies and then help the patient decide where to put his medications on the counter. Follow-up visits could check on whether the counter organization and behavioral tailoring plan have been maintained.

A final consideration for helping patients with severe symptoms or cognitive difficulties follow through with their medications is to use more frequent home visits. Assertive Community Treatment (ACT) is an approach to providing services to patients with very severe mental illness who have difficulty accessing mental-health-center-based services on their own.<sup>46,47</sup> ACT differs from traditional case management along several dimensions, including the provision of the majority of the services in the community (rather than at the clinic), a lower caseload of patients per clinician (average 1:10 in ACT compared with 1:20 or more in standard case management), shared caseloads between team members (rather than individual caseloads), 24-hour team responsibility for patients (rather than office hours only), and direct provision of most services (rather than brokering of services to other providers).<sup>48,49</sup> Supervision of medication follow-through and close monitoring of symptoms are common activities of ACT teams. Such teams are cost-effective and have been shown to reduce rehospitalizations and symptom severity, stabilize housing, and improve quality of life.<sup>48,49</sup>

## Advances in Antipsychotic Design: A Quest that Bridges both Medication Interest and Medication Follow-through

From the perspective of the MIM, improvements in antipsychotic design clearly represent external factors, which can powerfully impact on the second consideration of the MIM (the patient's medication follow-through). For example, as seen with the development of long-acting injectables, ease of administration, as

well as consistency of blood levels, can be improved. The research question is clear: Can laboratory science develop medications that are both more effective in relieving the symptoms of schizophrenia while also being less likely to create side effects? Improved antipsychotic design also bridges with the first step of the MIM (patient interest and choice), for the effectiveness of any given antipsychotic to better relieve symptoms and produce fewer side effects can play a pivotal role in the third step of the Choice Triad—the weighing of the pro and cons by the patient (see issues 1 and 2 in this *Counseling Points*<sup>™</sup> series available at [www.counselingpoints.com](http://www.counselingpoints.com)).

## The Search for Improved Effectiveness and Better Side Effect Profiles

Schizophrenia is a complex illness affecting numerous aspects of thought, behavior, affect, and cognition. The illness is generally divided into three major domains: positive symptoms (delusions, hallucinations, and suspiciousness); negative symptoms (affective flattening, avolition, and anhedonia); and cognitive dysfunction (impaired attention, memory, and executive function).<sup>50,51</sup> Patients with schizophrenia also have a high frequency of comorbid conditions such as anxiety, depression, and/or substance abuse.<sup>50,51</sup>

## First-Generation Antipsychotics: Breakthroughs in Treatment and Side Effect Limitations

Antipsychotic medications were introduced in the 1950s and were found to be extremely helpful in controlling many facets of the illness, particularly in the positive symptom domain.<sup>51</sup> Improvements were, however, also observed in some aspects of negative symptoms and cognitive dysfunction.<sup>51</sup> In addition, it became apparent that these medications could play an important role in reducing the risk of psychotic relapse as well as dramatically diminishing the need for chronic institutionalization.<sup>51</sup>

The first generation of antipsychotic medications included such agents as chlorpromazine, thioridazine, and haloperidol. From the beginning, it was recognized that neurologic side effects, particularly drug-induced parkinsonism and akathisia, were frequent adverse effects.<sup>51</sup> The majority of patients experienced varying degrees of these side effects with some (e.g., acute dystonic reactions) being extremely distressing.

Many clinicians prescribed prophylactic antiparkinsonism medication in order to prevent the occurrence of these so called “extrapyramidal” side effects, while

**Table 2. Typical Versus Atypical Antipsychotics**

<b>"Typical" or First-Generation Antipsychotics</b>	<b>"Atypical" or Second-Generation Antipsychotics</b>
Chlorpromazine (Thorazine <sup>®</sup> )	Aripiprazole (Abilify <sup>®</sup> )
Fluphenazine (Prolixin <sup>®</sup> )	Clozapine (Clozaril <sup>®</sup> )
Haloperidol (Haldol <sup>®</sup> )	Olanzapine (Zyprexa <sup>®</sup> )**
Molindone (Moban <sup>®</sup> )	Paliperidone (Invega <sup>®</sup> )**
Perphenazine (Trilafon <sup>®</sup> )	Quetiapine (Seroquel <sup>®</sup> )
Thiothixene (Navane <sup>®</sup> )	Risperidone (Risperdal <sup>®</sup> )*
	Ziprasidone (Geodon <sup>®</sup> )

\*Depot version available.

\*\*Depot version in development.

others waited until they emerged before doing so.<sup>52</sup> These side effects were not only distressing but also contributed to functional impairment and stigma. To complicate matters further, some extrapyramidal side effects could easily be confused with clinical manifestations of the schizophrenia, making detection and appropriate management even more challenging. For example, akathisia, an objective and/or subjective experience of restlessness, could be mistaken for anxiety or psychotic agitation.<sup>53-55</sup> Akinesia could easily be mistaken for negative symptoms or depression.<sup>56,57</sup> As a result, these adverse effects often were missed or inappropriately treated.

A few years after the introduction of antipsychotic medications, another neurologic syndrome known as "tardive dyskinesia" (TD) was reported. This syndrome involved abnormal movements of the mouth, face, tongue, trunk, and/or extremities, and occurred in about 5% of patients with each year of cumulative antipsychotic drug exposure.<sup>58</sup> Although most cases were mild and reversible, a small proportion could be severe, persistent, and disabling. Even mild cases potentially added to the stigma associated with antipsychotic medications.

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*The overall results from large-scale, controlled trials demonstrated the importance of continuous pharmacotherapy.*

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The occurrence of TD led to reevaluation of the benefit-to-risk ratio of antipsychotics, particularly long-term administration. However, numerous place-

bo-controlled, double-blind studies continued to demonstrate the value of continued pharmacotherapy in the prevention of relapse.<sup>51</sup> A number of strategies were explored to potentially reduce the incidence of TD, including the use of low doses of medication or "intermittent" or "targeted" treatment, which involved discontinuing medication in stable patients and only reinstating it when the patients showed signs of early relapse. Both of these strategies were intended to reduce the side effect burden of these drugs by reducing cumulative exposure. However, the overall results from large-scale, controlled trials demonstrated the importance of continuous pharmacotherapy.<sup>51,59</sup>

### 2nd-Generation Antipsychotics: New Breakthroughs and Fewer Neurologic Side Effects

Clozapine was the first antipsychotic medication to provide comparable, if not superior, efficacy to conventional antipsychotics without the usual propensity to cause neurologic side effects.<sup>51</sup> Clozapine demonstrated that one could separate antipsychotic efficacy from the neurologic side effects traditionally associated with conventional antipsychotics. Since the term "neuroleptic" had become associated with these neurologic side effects, other terms such as "atypical" and "second generation" were introduced to describe clozapine's characteristics. In addition to a substantially lower propensity to cause neurologic side effects, clozapine demonstrated superior efficacy compared with other medications among those individuals considered to be resistant to treatment.<sup>60</sup>

Although the reasons for clozapine's superiority have not been fully elucidated, considerable effort was undertaken to develop medications that might share some of clozapine's "novel" properties. The resulting class of atypical or second-generation medications are to a large extent the result (**Table 2**). However, clozapine continues to remain the gold standard in the treatment of patients identified as poorly responsive to other agents.

The second-generation medications did result in a substantial reduction in the risk of neurologic side effects.<sup>51</sup> Although some questions have been raised regarding this apparent superiority, attributing it to the use of higher than necessary doses of high-potency comparator agents (e.g., haloperidol), the advantages of second-generation antipsychotics are evident even in comparison to doses of haloperidol as low as 4 mg in

**Table 3. Features and Differential Diagnoses of Acute and Tardive Movement Syndromes<sup>65</sup>**

Feature	Acute Akathisia	Dystonia	Extrapyramidal Symptoms	Restless Legs Syndrome	Tardive Dsykinesia	Tardive Akathisia
<b>Onset of Symptoms</b>	Acute—hours to days after initiation of dosage increase	Acute—usually 24-48 hours (but up to 7 days) after drug initiation or dosage increases	Acute—several days to weeks after drug initiation or dosage increase of continuous antipsychotic medication	Often unrelated to antipsychotic medication use	Delayed onset, typically not earlier than 3 months after drug initiation or dosage increase	Delayed onset unrelated to drug initiation or dosage increase, can be unmasked by drug withdrawal
<b>Symptoms</b>	Inner feelings of restlessness; anxiety; irritability or dysphoria; urge to move to relieve symptoms; symptoms persist throughout day, no circadian pattern (although symptoms may improve on sleeping)	Sudden inability to relax involved muscle group (e.g., return neck to midline, center gaze, etc.); discomfort and pain in affected muscle group	Depression; subjective feelings of being slowed or unable to move	Internal urge to move limbs (must include legs) when resting, sleeping, or relaxed; symptoms not present when stationary but alert; discomfort relieved by movement; symptoms typically have circadian pattern (worse at night)	Awareness of abnormal movements is highly variable across patients	Inner feelings of restlessness; anxiety; irritability or dysphoria; urge to move to relieve symptoms; symptoms persist throughout day, no circadian pattern (although symptoms may improve on sleeping)
<b>Signs</b>	Pacing; rocking while sitting or standing; marching in place; crossing and uncrossing legs; fidgeting or other purposeless repetitive action	Fixed and abnormal posturing of the neck, limbs, trunk; fixed deviation of gaze (oculogyric crisis); fixed protrusion of tongue; fixed contraction of jaw (trismus); contractions can last seconds to hours but relax quickly with anticholinergic treatment	Tremor (low-frequency, resting, “pill-rolling” quality); rigidity of the limbs and/or trunk (can be asymmetrical, often cogwheel rigidity); bradykinesia (reduction in spontaneous movement or activity, reduced facial expressions, softening of voice, decreased ability to initiate or arrest movement)	Unlike akathisia, which is often evident during office visits, patients with restless legs syndrome are typically alert and therefore asymptomatic during appointments	Choreic movements of the tongue, trunk, upper and lower extremities, especially fingers and toes (piano playing movements); lip smacking, pouting, chewing; facial grimacing, rapid or exaggerated eye blinking	Same as signs of acute akathisia, sometimes associated with choreoathetoid limb dyskinesias and orofacial dyskinesias
<b>Differential Diagnosis</b>	Primary anxiety; psychotic agitation; tardive dyskinesia; tardive akathisia; restless legs syndrome	Malingering; seizures; conversion reaction	Parkinson’s disease; tardive dyskinesia; dystonia	Drug-induced akathisia; restless insomnia; peripheral neuropathy and vascular insufficiency	Extrapyramidal symptoms; akathisia; dystonia; idiopathic dyskinesias; hereditary and metabolic dyskinesias	Primary anxiety; psychotic agitation; tardive dyskinesia; acute akathisia; restless legs syndrome

Reproduced with permission from Bratti IM. Chronic restlessness with antipsychotics. *Am J Psychiatry*. 2007;164:1648-1654.

**Table 4. Consensus Statement on Antipsychotic Drugs, Obesity, and Diabetes: Monitoring Protocol for Patients on Second-Generation Antipsychotics<sup>66\*</sup>**

	Short-Term				Long-Term		
	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually*	Every 5 Years
Personal/Family History	✓					✓	
Weight (BMI)	✓	✓	✓	✓	✓		
Waist Circumference	✓					✓	
Blood Pressure	✓			✓		✓	
Fasting Plasma Glucose	✓			✓		✓	
Fasting Lipid Profile	✓			✓		✓	← [✓]

\*More frequent assessments may be warranted based on clinical status.

BMI=body mass index.

Adapted with permission from American Diabetes Association. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care*. 2004;27:596-601.

chronic patients and in comparison to low-potency antipsychotics.<sup>61,62</sup> In the CATIE trial, which has been cited as evidence of a lack of superiority for second-generation medications with regard to neurologic side effects, significantly more patients assigned to the conventional antipsychotic perphenazine discontinued their initial medication due to extrapyramidal side effects in comparison to the atypical medications.<sup>63</sup>

With regard to TD, a review of the literature by Correll, Leucht, and Kane involving prospective studies lasting at least 1 year provided data on the incidence of TD and suggested that the newer medications are associated with 1/5 the risk of TD that had been observed with older, conventional antipsychotics.<sup>64</sup> Therefore, the data overall suggest substantially less risk for neurologic adverse effects associated with the newer medications. It is important to recognize that neurologic side effects can still occur with these medications, and that patients must continue to be monitored for their potential occurrence. Recommendations for monitoring are provided in **Table 3**.<sup>65</sup> It is also important to recognize that the first-generation medications vary in their side effect profiles and that the distinctions we make in terms of medication class do not mean that these medications are interchangeable in terms of efficacy or adverse effects.

Similarly, the second-generation medications also vary in their tolerability profiles and though in general they are associated with fewer neurologic side effects, there will be differences among these agents in their

specific receptor binding profiles and, in turn, their propensity to cause adverse effects associated with dopaminergic, histaminergic, cholinergic, or adrenergic antagonism.<sup>51</sup>

### Atypical Antipsychotics: A New Set of Side Effects Emerges

Some second-generation medications have been associated with significant, and sometimes serious, metabolic adverse effects, particularly clozapine and olanzapine.<sup>66</sup> All of these medications have labeling that warns against the risks of increases in weight, glucose dysregulation, and dyslipidemia, and suggest ongoing monitoring. The American Diabetes Association has published recommendations for monitoring individuals receiving antipsychotic medications (**Table 4**).<sup>66</sup>

With regard to nonpsychiatric illness, it is important

**Table 5. Advantages of Long-acting Injectable Medications**

- Assure reliable medication delivery
- Offer convenient regimen and freedom from daily medication
- Provide immediate awareness of nonadherence
- Avoid first-pass metabolism\*
- Have predictable and stable plasma levels
- Do not result in abrupt loss of efficacy if a dose is missed
- Are preferred by many patients

\*Use lowest effective dose.

to remember that in addition to metabolic syndromes caused by antipsychotics, patients with schizophrenia have a number of risk factors associated with cardiovascular mortality, including high rates of smoking, obesity, and insufficient exercise. Estimates suggest that individuals with schizophrenia have substantially reduced expected lifespans, largely due to increases in cardiovascular mortality as well as suicide.<sup>67</sup> It is critical that patients with this illness receive appropriate primary medical care to insure that comorbid medical conditions are prevented or managed in an optimal fashion. When we discuss both medication interest and follow-through, it is also important to keep in mind that patients might need to take antidiabetic, antihypertensive, or lipid-lowering agents along with their psychotropic medications. Strategies to enhance interest and follow-through with these treatments are also important.

### Long-acting Injectables: Potential Advantages in Both Medication Interest and Follow-Through

The introduction of long-acting injectable antipsychotics marked an important advance in helping patients to benefit from continuous medication without having to rely on taking oral medication on a daily basis. The long-acting injectable medications are formulations involving drugs that have been widely used in their oral forms. Therefore, their side effect profile is well known. In general, long-acting injections are not associated with any different side effects than their oral counterparts, except those side effects associated with the injection process itself (e.g., pain, swelling, bleeding, or inadvertent intravascular injection). Glazer and Kane have systematically reviewed the relative rates of adverse effects with long-acting injectables as opposed to oral medications and found that, when dosing is controlled for, there are no substantial differences.<sup>68</sup>

Long-acting injectable medications have a number of important advantages (**Table 5**). These formulations can provide consistent delivery of medication without having to rely on daily pill-taking. Estimates suggest that the majority of patients have considerable difficulty reliably taking medications, yet both patients and clinicians tend to overestimate the degree with which patients are following through with medication use.<sup>69</sup> Poor medication follow-through is immediately detected if a patient fails to receive an injection and steps can be initiated (calling the patient or the family, doing a home visit, etc.) to reengage the patient. In addition, there is no abrupt loss of efficacy. With oral

medications, nonadherence can be covert and the medication leaves the system fairly quickly after missed doses. Long-acting injectable medications also overcome the considerable inter-individual differences in absorption and bioavailability allowing for a better and more consistent correlation between dosage administered and actual blood level achieved.

The use of these formulations can also reduce family burden and negative interactions. Since family members are often the first to recognize an exacerbation and must cope with its painful consequences, they can become extremely concerned about missed doses. This anxiety can prove to be a source of considerable tension in family interactions.

Despite the potential advantages of these formulations, which can have a dramatic impact on relapse rates, they are not widely utilized. Interestingly, utilization varies considerably from one clinic to another, one hospital to another, and one country to another, suggesting that differences in training, attitudes, and practice patterns as well as logistical and reimbursement factors may play a greater role than patient attitude or acceptance.<sup>70</sup>

### Conclusion: Reflections on Decision-making, Future Research, and Training

Several factors, such as measurement-based decision-making, related to successfully creating a generation of clinicians competent in applying the principles we have outlined are worth emphasizing. Clinicians take such evidence-based decision-making for granted when evaluating weight gain, type 2 diabetes, or dyslipidemia, as the identification of these problems depends on objective measurement. In contrast, when assessing the management and prevention of exacerbations in psychopathology, as well as the presence of side effects, clinicians tend to rely heavily on subjective impressions. Greater utilization of quantitative assessment measures could be helpful in evidence-based decision-making as well as discussing target symptoms for medication intervention, collaborative goals, and the pros and cons of medications with patients and families (e.g., the remission criteria proposed by Andreasen et al 2005).<sup>71</sup>

When transferred to the realm of education, the above principles point toward the utility of training psychiatric residents and other clinicians in evidence-based assessment tools for evaluating symptoms (e.g.,

the Brief Psychiatric Rating Scale, the Folstein Mini-Mental State Exam, the Montreal Cognitive Assessment [MoCA]) and side effects (e.g., the Abnormal Involuntary Movement Scale) to help patients and family members better weigh the pros and cons of taking medication.<sup>72,73</sup>

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*Improving medication interest and follow-through is a complex challenge, particularly in an illness such as schizophrenia where problems in cognition, insight, judgment, motivation, and trust influence medication-taking.*

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A complete program and curriculum (emphasizing direct mentoring) for teaching clinical interviewing to psychiatric residents has been described that integrates interviewing techniques for more objectively uncovering the phenomenology of psychopathology with training in collaborative approaches to improving medication interest.<sup>74</sup> Weiden and Rao have elegantly delineated the need for specific course-work and training regarding medication interest and follow-through, including an outline of a five-session course dedicated to the topic.<sup>75</sup> Moreover, in order to more effectively provide guidance to patients as they weigh the pros and cons of medications, clinicians should be trained to effectively read the evidence base presented in the clinical literature.

With regard to research design, the MIM (with its emphasis upon delineating interviewing techniques that are behaviorally well-defined) was designed specifically to provide a conceptual platform for future quantitative studies regarding interviewing techniques and their impact upon medication adherence rates.<sup>76</sup> Such evidence-based research can hopefully provide concrete direction on which interviewing techniques are most effective and can be effectively taught (and subsequently tested to competence) in medical and nursing schools as well as in residencies from family practice to psychiatry.<sup>77</sup>

In conclusion, improving medication interest and follow-through is a complex challenge, particularly in an illness such as schizophrenia where problems in cognition, insight, judgment, motivation, and trust influence medication-taking. It is our hope that the principles described in this three-issue *Counseling Points*<sup>™</sup> series, from the advances in antipsychotic design to the innovations in how we collaboratively

discuss medications and enhance the likelihood of follow-through, offer fresh hope for both our patients suffering from schizophrenia and the family members who love them.

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# Counseling Points™

## **Improving Medication Adherence in Schizophrenia Through Innovations in Medication Follow-through and Antipsychotic Design**

- Even after an individual has made the decision to take medication, numerous factors can conspire to interfere with his or her ability to follow through on that choice, leading to nonadherence and the negative outcomes associated with it.
- It is now firmly established that patients can and need to be active participants in their own treatment.
- Medication follow-through can be improved through the use of various illness self-management strategies such as pillboxes and prompts, behavioral tailoring, dosage simplification, and social skills training.
- It is also important to develop a collaborative relationship with the family of the patient to encourage the patient's interest and desire to follow through with taking medication.
- Developing a relapse prevention plan draws attention to the importance of medication, both as a primary prevention strategy and as an intervention for fending off the early warning signs of a relapse.
- Case managers or other members of the patient's treatment team (e.g., nurses) can play a valuable role in helping patients follow through on overcoming barriers to taking medication.
- Improvements in antipsychotic design can powerfully impact on a patient's medication follow-through.
- Second-generation antipsychotic medications have resulted in a substantial reduction in the risk of neurologic side effects for patients with schizophrenia.
- Some second-generation medications, particularly clozapine and olanzapine, have been associated with significant, and sometimes serious, metabolic adverse effects.
- It is critical that patients with schizophrenia receive appropriate primary care to insure that comorbid medical conditions are prevented or managed in an optimal fashion.

# Counseling Points™

## Improving Medication Adherence in Schizophrenia Through Innovations in Medication Follow-through and Antipsychotic Design Continuing Medical Education Posttest

If you wish to receive acknowledgment for completing this activity, please complete the posttest by selecting the best answer to each question, complete the evaluation verification of participation, and **fax to: (303) 790-4876**. You may also complete the posttest online at [www.cmeuniversity.com](http://www.cmeuniversity.com). On the navigation menu, click on “Find Posttests by Course” and search by project ID 5793. Upon successfully completing the posttest and evaluation, your certificate will be made available immediately to print online.

- 1. Strategies for overcoming situational roadblocks to medication adherence include all BUT which of the following?**
  - A. Illness self-management skills
  - B. Use of antianxiety agents
  - C. Strategies for facilitating family support
  - D. Case management approaches
- 2. Behavioral tailoring is an approach that:**
  - A. can be used to help patients remember to take their medications
  - B. involves natural prompts by fitting the taking of medication into the person’s usual routine
  - C. has been shown to be effective at improving adherence to medications in people with severe mental illness, including schizophrenia
  - D. all of the above
- 3. Social skills training programs emphasize the use of frequent modeling and practice, with a focus on the nuances of social behavior critical to success.**
  - A. True
  - B. False
- 4. The core elements of developing a relapse prevention plan include:**
  - A. explaining that relapse symptoms usually occur gradually and are preceded by early warning signs
  - B. discussing the past one or two relapses to identify several of the patient’s early warning signs
  - C. both A and B
  - D. neither A or B
- 5. Assertive Community Treatment (ACT) differs from traditional case management approaches in that ACT:**
  - A. involves individual caseloads as high as 20-30 patients
  - B. involves provision of most services in the community rather than in the clinic
  - C. limits services and outreach to a 9 am-5 pm time frame
  - D. all of the above
- 6. Tardive dyskinesia is an infrequent side effect of administration of first-generation antipsychotics.**
  - A. True
  - B. False
- 7. Which of the following atypical antipsychotics was the first to provide comparable, if not superior, efficacy to conventional antipsychotics without the usual propensity to cause neurologic side effects?**
  - A. Aripiprazole
  - B. Clozapine
  - C. Quetiapine
  - D. Risperidone
- 8. Patients with schizophrenia:**
  - A. have a high number of risk factors associated with cardiovascular mortality
  - B. are at risk for metabolic syndromes caused by antipsychotic agents
  - C. have substantially reduced expected lifespans, largely due to increases in cardiovascular mortality and suicide
  - D. all of the above
- 9. Long-acting injectable antipsychotic agents:**
  - A. quickly lose efficacy if a dose is missed
  - B. are only indicated for patients who refuse to take oral medications
  - C. provide predictable and stable plasma levels
  - D. all of the above
- 10. Improving medication interest and follow-through is a complex challenge, particularly in an illness such as schizophrenia, because medication-taking is influenced by:**
  - A. patient problems in cognition, insight, and judgment
  - B. patient problems in motivation and trust
  - C. both A and B
  - D. neither A nor B

# EVALUATION FORM

## Counseling Points™: Improving Medication Adherence in Schizophrenia Through Innovations in Medication Follow-through and Antipsychotic Design

Project ID: 5793ES38

To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this evaluation form. *You must complete this evaluation form to receive acknowledgment for completing this activity.*

1 = Strongly Disagree    2 = Disagree    3 = Somewhat Disagree    4 = Somewhat Agree    5 = Agree    6 = Strongly Agree

**To what extent do you agree with the following statements?** (Please circle the appropriate number on the scale.)

- Behavioral tailoring is effective in improving adherence to medications in patients with schizophrenia. .... 1 2 3 4 5 6
- Pill organizers alone are not generally effective in improving medication adherence in patients with schizophrenia. .... 1 2 3 4 5 6
- When the schizophrenic patient has non-psychiatric co-morbid conditions, medication adherence strategy planning should include consideration of maintenance medications related to those conditions as well as for the psychotropic medications. .... 1 2 3 4 5 6
- When initiating therapy with a second-generation antipsychotic agent, the patient should be assessed for weight gain monthly for the first 3 months and then at least every 3 months thereafter for as long as on the medication. .... 1 2 3 4 5 6
- I am confident in my ability to develop a relapse prevention plan, involving patient and family in the process. .... 1 2 3 4 5 6

**Extent to Which Program Activities Met the Identified Objectives**

(After completing this activity, I am now better able to:)

- Choose strategies for engaging and garnering support from family members (or significant others) for helping a relative use medication as prescribed. .... 1 2 3 4 5 6
- Describe three different strategies for helping a client modify his/her environment in order to facilitate medication follow-through..... 1 2 3 4 5 6
- Explain the benefits and risks of long-term antipsychotic drug treatment in schizophrenia. .... 1 2 3 4 5 6
- Review appropriate monitoring strategies for assessing efficacy, adverse effects and adherence associated with long-term pharmacotherapy ..... 1 2 3 4 5 6

**Overall Effectiveness of the Activity**

(The content presented:)

- Was timely and will influence how I practice .... 1 2 3 4 5 6
- Enhanced my current knowledge base ..... 1 2 3 4 5 6
- Addressed my most pressing questions ..... 1 2 3 4 5 6
- Provided new ideas or information I expect to use ..... 1 2 3 4 5 6
- Addressed competencies identified by my specialty ..... 1 2 3 4 5 6
- Avoided commercial bias or influence..... 1 2 3 4 5 6

**Impact of the Activity**

Name one thing you intend to change in your practice as a result of completing this activity: \_\_\_\_\_

Please list any topics you would like to see addressed in future educational activities: \_\_\_\_\_

Additional comments about this activity: \_\_\_\_\_

**Follow-up**

As part of our continuous quality improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate if you would be willing to participate in such a survey:

- Yes, I would be interested in participating in a follow-up survey.
- No, I would not be interested in participating in a follow-up survey.

*If you wish to receive acknowledgment for completing this activity, please complete the posttest by selecting the best answer to each question, complete this evaluation verification of participation, and fax to: (303) 790-4876. You may also complete the posttest online at [www.cmeuniversity.com](http://www.cmeuniversity.com). On the navigation menu, click on "Find Posttests by Course" and search by project ID 5793. Upon successfully completing the posttest and evaluation, your certificate will be made available immediately to print online.*

<b>Posttest Answer Key</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>

**Request for Credit**

Name \_\_\_\_\_ Type of Degree \_\_\_\_\_  
 Type of Practice \_\_\_\_\_ Est. Number of Patients Seen Weekly \_\_\_\_\_  
 Organization \_\_\_\_\_ Specialty \_\_\_\_\_  
 Address \_\_\_\_\_  
 City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_  
 Phone \_\_\_\_\_ Fax \_\_\_\_\_ E-mail \_\_\_\_\_  
 Signature \_\_\_\_\_ Date \_\_\_\_\_

**For Physicians Only**

I certify my actual time spent to complete this educational activity to be:

- I participated in the entire activity and claim 1 credit.
- I participated in only part of the activity and claim \_\_\_\_\_ credits.

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