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# 7-point checkup

Defuse cardiovascular and psychiatric risks in schizophrenia outpatients

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**Routine maintenance includes optimizing medication, offering psychosocial interventions, and monitoring physical health and well-being.**

**M**r. K, age 34, has been hospitalized 4 times in 5 years for acute exacerbations of schizophrenia caused by medication nonadherence. This time he reports he discontinued antipsychotic therapy because he was “tired of taking medications every day.”

He spent 2 weeks in the acute inpatient psychiatric unit and restarted olanzapine—titrated to 15 mg/d—to which he responded well. When he presented to our outpatient clinic for follow-up, Mr. K reported adhering to his medications and denied positive symptoms. He complained of mild daytime sedation but no other side effects.

Schizophrenia patients spend most of their lives stable, rather than hospitalized for acute psychotic episodes. While stable, they continue to require close attention, and medical issues are particularly important during this time. Outpatient maintenance—such as optimizing antipsychotic therapy, offering psychosocial interventions, and monitoring physical health and well-being—provides opportunities to improve the course of illness for patients such as Mr. K.

continued



## 7-point checklist

Table 1

### 7-point checklist for assessing the stable schizophrenia patient

1. **Evaluate** positive, negative, and cognitive symptoms
2. **Monitor** level of adherence
3. **Evaluate** weight, cardiovascular risk factors, and other medical parameters
4. **Examine** for extrapyramidal symptoms or tardive dyskinesia
5. **Evaluate** for comorbid mood symptoms and substance use
6. **Look** for prodromal symptoms that may signal relapse
7. **Evaluate** psychosocial interventions

Table 2

### Schizophrenia's 4 symptom clusters\*

<b>Positive symptoms</b>	Delusions, hallucinations, disorganization
<b>Negative symptoms</b>	Blunted affect, alogia, avolition, anhedonia
<b>Cognitive symptoms</b>	Attention, memory, executive functions (such as abstraction)
<b>Affective symptoms</b>	Dysphoria, suicidality, hopelessness

\* Interaction of symptoms contributes to social and occupational dysfunction and adversely affects work and interpersonal relationships and self-care.

This article describes a 7-point checklist to keep schizophrenia outpatients stable. It can help you maintain or improve patients' function, prevent relapse, and monitor for adverse effects (*Table 1*).

#### ✓ 1. SYMPTOM CLUSTERS

For several years, Mr. K worked as a research technician in a university lab, maintained an apartment, and attended to activities of daily living while taking olanzapine, 15 mg nightly. After discontinuing his medication, he reported auditory hallucinations,

paranoid delusions, ideas of reference, and grossly disorganized thinking and behavior. He also was using marijuana daily, which exacerbated his psychotic symptoms and paranoia.

Addressing schizophrenia's symptom clusters (*Table 2*) is key to improving patients' social and occupational function and quality of life. Mr. K no longer has hallucinations, delusions, or disorganized thinking or behavior, but our evaluation shows his improvements are limited to schizophrenia's positive symptoms.

**Negative symptoms.** Mr. K exhibits blunted affect, avolition, amotivation, and anhedonia. He finds it difficult to go to work and often leaves stacks of unopened mail on his kitchen table.

**Cognitive symptoms.** Mr. K's concentration, attention, and memory are impaired, which interferes with his work. His ability to abstract is not impaired.

**Affective symptoms.** Mr. K denies signs or symptoms of depression, mania, hopelessness, or thoughts of wanting to hurt himself or anyone else.

Because antipsychotics do not adequately treat negative and cognitive symptoms, we will address these symptom clusters with psychosocial interventions (discussed below).

#### ✓ 2. ADHERENCE

Nonadherence to medication is the most common cause of relapse and rehospitalization for patients

with schizophrenia.<sup>1</sup> We find the following strategies helpful when encouraging, maintaining, and monitoring adherence to medications.

**Normalize adherence** and enlist patient participation. We inform Mr. K that most patients have trouble taking medications every day and ask how he remembers. Brainstorming with patients on ways to remember to take medications increases their likelihood of participating.

**Try alternate strategies.** Recommend pillboxes, alarms, and other aids. Consider enlisting family members to help patients remember to take their medications every day.

**Monitor prescriptions.** We limit Mr. K's prescription to 1 month so that we can assess the timeliness and consistency of refills.

**Educate.** Emphasize the link between adherence and wellness, and nonadherence and relapse—which Mr. K has clearly demonstrated. We repeat this lesson on multiple visits and counsel any involved family members as well, so that everyone understands the importance of adherence to the patient's continued well-being.

**Look for signs of nonadherence.** Because Mr. K discontinued his medications without telling his physician, we remain vigilant for signs of nonadherence—such as reemergence of hallucinations, delusions, paranoia, or ideas of reference—or sudden disappearance of a side effect—such as daytime sedation, which he has consistently reported with olanzapine.

Discontinuation rates in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) suggest that many stable schizophrenia

outpatients are dissatisfied with their medications. Most patients in all treatment groups changed their medications during the 18-month National Institute of Mental Health-sponsored trial.<sup>2</sup>

**SGAs versus FGAs.** Schizophrenia patients may be more likely to tolerate second-generation antipsychotics (SGAs) than first-generation antipsychotics (FGAs) because of FGAs' higher risk of movement side effects such as akathisia. Some data suggest that patients find SGAs more tolerable overall, leading to lower discontinuation rates.<sup>3</sup>

Recent evidence, however, has cast doubt on the idea that SGAs are clinically superior to FGAs. The CUtLASS trial,<sup>4</sup> for example, found no quality-of-life differences in patients using either class. Both FGAs and SGAs reduce the risk of relapse in stable patients, although SGAs may have an advantage over FGAs in preventing relapse. An analysis by Leucht et al<sup>5</sup> found lower relapse/treatment failure rates in 6 placebo-controlled SGA trials (total 983 patients), compared with 11 FGA trials (total 2,032 patients).

Although the data comparing SGAs with FGAs are controversial, SGAs seem to have lower

Table 3

### Does your patient have metabolic syndrome?

Metabolic syndrome is defined as having any 3 of these findings:

<b>Abdominal obesity</b>	Waist circumference >102 cm (40 in) in men >88 cm (35 in) in women
<b>Elevated triglycerides</b>	≥150 mg/dL
<b>Low HDL</b>	<40 mg/dL in men <50 mg/dL in women
<b>Hypertension</b>	≥130/85 mm/Hg
<b>Hyperglycemia</b>	Fasting blood glucose ≥110 mg/dL

Source: National Cholesterol Education Program Adult Treatment Panel III guidelines, reference 10





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Table 4

### Monitoring protocol for patients taking second-generation antipsychotics\*

	Short-term				Long-term		
	Baseline	4 wk	8 wk	12 wk	Quarterly	Annually	Every 5 yrs
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

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

BMI: body mass index

Source: Reference 12

EPS potential. Regardless of the type of antipsychotic, however, studies have shown that patients who relapse while taking antipsychotics have less-severe episodes than those who relapse after discontinuing their medications.

For patients who frequently forget or incorrectly take oral medications, long-acting depot antipsychotics may increase adherence and decrease relapse rates during the stable phase.<sup>6</sup>



### 3. WEIGHT GAIN, CARDIOVASCULAR RISK

Cardiovascular disease is the leading cause of death among persons with schizophrenia,<sup>7,8</sup> whose life span is 10 to 20 years shorter than the population at large.<sup>9</sup> Schizophrenia patients may be genetically predisposed to cardiovascular disease and metabolic syndrome (*Table 3, page 23*),<sup>10</sup> exacerbated by typically sedentary lifestyles, high smoking rates, and poor diets. Certain SGAs add to the risk of weight gain and metabolic abnormalities.<sup>11</sup>

**Metabolic syndrome.** Being familiar with the 2004 consensus report of the American Diabetes Association/American Psychiatric Association (ADA/APA)<sup>12</sup> can help differentiate SGAs' rela-

tive risks of causing weight gain, type 2 diabetes, and hyperlipidemia. The report recommends monitoring blood pressure, weight, and lipid and fasting glucose levels when antipsychotics are initiated and at least yearly thereafter (*Table 4*).

Because of schizophrenia patients' risk of metabolic abnormalities, consider:

- using treatments that do not increase the risk for cardiovascular disease
- switching to agents with less weight gain liability if a patient's weight increases >7% or his or her body mass index (BMI) increases 1 unit during antipsychotic therapy.

Mr. K smokes a pack a day and shows no interest in cutting down or quitting. He is African-American (which increases his cardiovascular risk), sedentary, and has a family history of heart disease. Thus, monitoring these risk factors and referring him for primary care are priorities in his treatment plan.

Mr. K remained stable on olanzapine for several years, but his blood glucose, cholesterol, and triglycerides have risen dramatically and he has gained 40 lbs. Although we were concerned that he might not

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Table 5

### Differential risks of weight gain and metabolic abnormalities with SGAs

Risk	Antipsychotics
Highest	Clozapine, olanzapine
Intermediate/low	Risperidone, quetiapine
Lowest	Aripiprazole, ziprasidone

SGAs: Second-generation antipsychotics

respond as well to another SGA, we reviewed the risks and benefits with specific concern about his cardiovascular health. As a result, we switched him to aripiprazole, 15 mg/d, with close monitoring and supervision for signs of relapse.

**SGAs' heterogeneity.** The ADA/APA statement and multiple clinical trials support differential risks of weight gain and metabolic abnormalities with SGAs (*Table 5*). Patients in CATIE phase 1 who were randomly assigned to olanzapine experienced greater total weight gain and monthly weight gain (mean +2 lb/month) than patients taking any other antipsychotic.<sup>13</sup> In an analysis of change from baseline to last observation, 30% of patients in the olanzapine group gained >7% of their baseline weight, compared with 7% to 16% of patients taking other antipsychotics.

Patients in the CATIE trial tended to stay on olanzapine longer than on any of the other antipsychotics, however. Average time to discontinuation for any cause was 9.2 months, versus 3.5, 4.6, 4.8, and 5.6 months for ziprasidone, quetiapine, risperidone, and perphenazine, respectively. Thus, in clinical practice, it is important to balance longer duration of treatment against increased risk of weight gain.<sup>14,15</sup>

Mr. K remains free of positive symptoms after taking aripiprazole for several months. He complains

less of daytime sedation and has lost >10 lbs. We are awaiting repeat glucose, cholesterol, and triglyceride serum levels. We will continue to monitor his weight and metabolic values and ensure that he receives primary care follow-up.



#### 4. EPS AND TARDIVE DYSKINESIA

Compared with FGAs, SGAs may be associated with a lower incidence of tardive dyskinesia (TD) and extrapyramidal symptoms (EPS). Even so, routine screening for

EPS and TD remains necessary, according to the Mount Sinai consensus conference on physical health monitoring of patients with schizophrenia.<sup>16</sup> At every visit, we observe Mr. K for:

- facial movements (excessive blinking, puckering, lip smacking, sucking, or grimacing)
- decreased arm swing while walking or choreoathetoid-like or writhing limb or trunk movements.

We also ask him about subjective feelings of rigidity, restlessness, or changes in voluntary or involuntary movements. Every 6 months we do a more thorough assessment—such as the Assessment for Involuntary Movement Scale (AIMS)—regardless of the antipsychotic he is taking. We test his limbs for rigidity or cogwheeling, observe him for changes in arm swing and gait, and check his mouth for tongue fasciculations. Patients at higher risk for TD, such as the elderly, should be examined more often.

In addition to screening for metabolic syndrome, EPS, and movement disorders, the Mount Sinai consensus conference<sup>16</sup> offers guidelines for monitoring prolactin, cardiac, and ocular changes in patients taking antipsychotics.



#### 5. MOOD DISORDERS, SUBSTANCE ABUSE

**Screen schizophrenia outpatients** for signs of anxiety, depression, mania, and substance abuse at every visit. An antidepressant trial is recommend-

ed for depressive episodes even if antipsychotic therapy has adequately reduced positive psychotic symptoms.<sup>17</sup> This strategy can prevent depressive relapses and might help prevent psychotic relapse as well.<sup>18</sup> Also consider adjunctive therapy such as:

- mood stabilizers for affective instability
- benzodiazepines for short-term anxiety or agitation
- tricyclics or selective serotonin reuptake inhibitors for comorbid anxiety disorders such as obsessive-compulsive or panic disorder.<sup>19</sup>

As part of Mr. K's routine mental status exam, we ask him about his mood, sleep, appetite, energy, anxiety level, and thoughts of hurting himself or others. If mood symptoms are present, we question him further to determine if he meets criteria for a coexisting affective illness.

Because of Mr. K's history of marijuana abuse, we tell him we will use random urine toxicology screens. We also order urine toxicology if patients behave abnormally or appear impaired. We counsel patients and families about the link between substance use and psychotic decompensation, which Mr. K has demonstrated several times.

We emphasize that the goal of repeated questioning and screening is to ensure Mr. K's well-being. If he is using substances, we will refer him to the help he needs.

## ✓ 6. PRODROMAL SIGNS OF RELAPSE

Mr. K has reported decreased sleep, increased irritability, increased social isolation, and some agitation before his acute psychotic decompensations. These symptoms form his prodrome for relapse, which we routinely assess at follow-up visits.

We question him about sleep, social contacts, irritability, and agitation; assess psychotic symptoms; and observe thought processes and behav-

iors. If a patient endorses or displays prodromal signs of relapse, we consider:

- Is he taking the medication?
- Is he abusing substances?
- Does a change in dosage (actual or a cytochrome P450-mediated drug-drug interaction) explain a decrease in efficacy?
- Is he under stress and need an increased antipsychotic dosage?

• Might psychosocial interventions (support groups, cognitive-behavioral therapy, family involvement, etc.) help him

deal with symptoms, decrease stress, or avoid an exacerbation?

- Has medication been optimized (correct dosing, long enough duration), or does the patient need an increased dosage or a different antipsychotic?

When we detect prodromal symptoms, we see patients more often (every 1 to 2 weeks) until interventions can be tried and patients are stable again.

Detecting and addressing prodromal symptoms early may help avoid hospitalization and minimize potential consequences of relapse.

## ✓ 7. PSYCHOSOCIAL INTERVENTIONS

Combining medications with psychosocial programs is most effective for maintaining remission

A 7-point checklist for managing stable schizophrenia outpatients can help prevent relapse and improve quality of life. When choosing antipsychotics, balance potential benefits with risks of weight gain and metabolic syndrome. Combine medications with psychosocial programs to address needs in negative and cognitive symptom domains.

BottomLine

Prodromal signs of relapse? A drug-drug interaction may explain a decrease in efficacy



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### Related resources

- ▶ Torrey EF. *Surviving schizophrenia: a manual for families, patients, and providers*, 5th ed. New York: Harper Collins; 2006.
- ▶ Mueser KT, Gingerich S. *The complete family guide to schizophrenia: helping your loved one get the most out of life*. New York: The Guilford Press, 2006.
- ▶ National Alliance on Mental Illness. Resources for schizophrenia patients and their families. [www.nami.org](http://www.nami.org).

### DRUG BRAND NAMES

Aripiprazole • Abilify	Quetiapine • Seroquel
Clozapine • Clozaril	Risperidone • Risperdal
Haloperidol • Haldol	Thioridazine • Mellaril
Olanzapine • Zyprexa	Ziprasidone • Geodon
Perphenazine • Trilafon	

### DISCLOSURE

Dr. Arey reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

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and improving patients' social and occupational functioning.<sup>17</sup> For Mr. K we recommend these interventions:

**Social skills training.** Mr. K now meets with other schizophrenia patients and a moderator to set long-term goals and smaller, attainable goals as homework assignments each week. Patients get feedback, positive reinforcement, and the opportunity to practice new skills. Mr. K is working on improving family relationships, furthering his career, and improving his interpersonal skills.

**Family therapy and education.** We have met with Mr. K's mother several times, and she now visits him regularly and speaks with him on the phone at least once a week. She attends Support and Family Education (SAFE) and National Alliance for the Mentally Ill (NAMI) meetings to increase her understanding of her son's illness.

**Alcoholics Anonymous/Marijuana Anonymous.** We refer Mr. K to AA/MA groups; he attends 2 to 3 times per week and has a sponsor. He is not sober yet but has dramatically cut back his substance use and continues to express motivation to quit.

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