

# Schizophrenia: A Review

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Schizophrenia is a debilitating mental illness that affects 1 percent of the population in all cultures. It affects equal numbers of men and women, but the onset is often later in women than in men. Schizophrenia is characterized by positive and negative symptoms. Positive symptoms include hallucinations, voices that converse with or about the patient, and delusions that are often paranoid. Negative symptoms include flattened affect, loss of a sense of pleasure, loss of will or drive, and social withdrawal. Both types of symptoms affect patients' families; therefore, it is important for physicians to provide guidance to all persons affected by the disease. Psychosocial and family interventions can improve outcomes. Medications can control symptoms, but virtually all antipsychotics have neurologic or physical side effects (e.g., weight gain, hypercholesterolemia, diabetes). There is a 10 percent lifetime risk of suicide in patients with schizophrenia. (*Am Fam Physician* 2007;75:1821-9, 1830. Copyright © 2007 American Academy of Family Physicians.)

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► **Patient information:** A handout on helping a family member with schizophrenia, written by the authors of this article, is provided on page 1830.

Schizophrenia is a devastating mental illness that impairs mental and social functioning and often leads to the development of comorbid diseases. These changes disrupt the lives of patients as well as their families and friends. Family physicians can play an important role in the effective treatment of schizophrenia; they are in a position to recognize the early signs of illness, make referrals to appropriate mental health professionals, help patients and their families cope with the devastating effects of schizophrenia, and encourage a multidisciplinary approach to address all dimensions of the illness.

## Risk Factors, Etiology, and Pathophysiology

Schizophrenia has a prevalence of 1 percent in all cultures and is equally common in men and women.<sup>1</sup> Men typically present with the disease in their late teenage years or early 20s, whereas women generally present in their late 20s or early 30s.

A family history of schizophrenia is the most significant risk factor (*Table 1*).<sup>3</sup> Other hypothetical risk factors include season and location of birth, socioeconomic status, and maternal infections. However, data supporting these ideas are inconclusive.<sup>3,4</sup>

Schizophrenia appears to be a polygenic disorder with environmental and developmental factors mediating a person's

likelihood of becoming schizophrenic.<sup>2</sup> It is unknown if the range of severity and clinical manifestations reflect problems in different brain regions, in different causalities, or in different diseases that share some phenotypic features.<sup>2</sup>

The Finnish Adoptive Family Study of Schizophrenia has confirmed that genetics plays a major role in the development of schizophrenia.<sup>5-8</sup> It also found that persons with a genetic risk of schizophrenia are especially sensitive to the emotional climate of their family environment. A child-rearing environment with infrequent criticism and clear, straightforward communication appears to be protective against the symptomatic expression of this genetic risk.<sup>6</sup>

The neurotransmitter dopamine also plays an important role. For example, drugs that cause psychoses similar to the positive symptoms of schizophrenia increase dopaminergic neurotransmission, and almost all antipsychotics decrease dopaminergic neurotransmission.<sup>9</sup> Still, dopaminergic pathways cannot entirely explain the pathophysiology of schizophrenia, and the roles of other neurotransmitters are being investigated.<sup>9</sup>

Researchers have examined the possibility of preventive treatment or premorbid screenings for schizophrenia. Currently, no studies have attempted treatment before the

**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Antipsychotic therapy should be initiated when schizophrenia is diagnosed; delaying treatment may worsen long-term outcomes.	B	19, 20
Weight should be monitored in patients taking first- or second-generation antipsychotics.	C	22, 24
Blood sugar and lipids levels should be monitored in patients taking second-generation antipsychotics.	C	22, 24
Family interventions are recommended to reduce relapse of schizophrenia and to improve symptoms, medication adherence, and function.	B	29, 30, 35

*A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1754 or <http://www.aafp.org/afpsort.xml>.*

onset of definitive symptoms. The risk of false-positive screening results is high, and screening is not yet accurate enough to warrant the cost and harms associated with misdiagnosis.<sup>10,11</sup>

**Diagnosis**

Schizophrenia is characterized by positive and negative symptoms that can influence a patient’s thoughts, perceptions, speech, affect, and behaviors (*Table 2*<sup>1</sup>). Positive symptoms include hallucinations, voices that converse with or about the patient, and delusions that are often paranoid. Negative symptoms include flattened affect, loss of a sense of pleasure, loss of will or drive, and social withdrawal.

Schizophrenia is also characterized by disorganized thought, which is manifested in speech and behavior. Disorganized speech may range from loose associations and moving quickly through multiple topics to speech that is so muddled that it resembles schizophasia (commonly referred to as “word salad”). Schizophasia is speech that is confused and repetitive, and that uses words that have no apparent meaning or relationship to one another. Disorganized behavior may lead to difficulties in performing daily living activities, such as preparing a meal or maintaining hygiene. It also can

manifest as childlike silliness or outbursts of unpredictable agitation.<sup>1</sup>

No single sign or symptom is pathognomonic of schizophrenia. To make a definitive diagnosis, signs and symptoms must be present for a significant portion of one month (or a shorter period if successfully treated), and some must be present for at least six months. These symptoms also must be associated with marked social and occupational dysfunction.

There are five types of schizophrenia: paranoid, disorganized, catatonic, undifferentiated, and residual.<sup>1</sup> Paranoid type is characterized by a preoccupation with one or more delusions or frequent auditory hallucinations; cognitive function and affect remain relatively well preserved.<sup>1</sup> Disorganized type is characterized by disorganized speech and behavior, as well as flat or inappropriate affect.<sup>1</sup> Catatonic type has at least two of the following features: immobility (as evidenced by stupor or catalepsy); excessive, purposeless motor activity; extreme negativism (e.g., resistance to all instructions, maintenance of rigid posture, mutism); or peculiarities of voluntary movement (e.g., posturing, prominent mannerisms, grimacing).<sup>1</sup> A patient is said to have undifferentiated schizophrenia if none of the criteria for paranoid, disorganized, or catatonic types are met.<sup>1</sup> Residual type

is characterized by the continued presence of negative symptoms (e.g., flat affects, poverty of speech) and at least two attenuated positive symptoms (e.g., eccentric behavior, mildly disorganized speech, odd beliefs). A patient is diagnosed with residual type if he or she has no significant positive psychotic features.<sup>1</sup>

Of note, this classic typing of schizophrenia can be limiting because patients often are difficult to classify. For that reason, an alternative three-factor dimensional model is given. The three factors are psychotic, disorganized, and negative (deficit). The symptoms are categorized as absent, mild, moderate, or severe.<sup>1</sup>

**Table 1. Family History and Schizophrenia**

<i>Family history</i>	<i>Approximate lifetime incidence (%)</i>
None (e.g., general population)	1
Third-degree relative (e.g., first cousin)	2
Second-degree relative (e.g., niece or nephew)	2 to 6
First-degree relative (e.g., parent, child, sibling)	6 to 17
Dizygotic twin	17
Monozygotic twin	50

*Information from reference 2.*

**Table 2. Diagnostic Criteria for Schizophrenia**

A. Characteristic symptoms	Two or more of the following,* each present for a significant portion of time during a one-month period (or less if successfully treated): <ul style="list-style-type: none"><li>• Delusions</li><li>• Hallucinations</li><li>• Disorganized speech (e.g., frequent derailment or incoherence)</li><li>• Grossly disorganized or catatonic behavior</li><li>• Negative symptoms (i.e., affective flattening, alogia, or avolition)</li></ul>
B. Social/occupational dysfunction	For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning, such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).
C. Duration	Continuous signs of disturbance persist for at least six months. This six-month period must include at least one month of symptoms (or less if successfully treated) that meet criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).
D. Schizoaffective and mood disorder exclusions	Schizoaffective disorder and mood disorder with psychotic features have been ruled out because either (1) no major depressive, manic, or mixed episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during the active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.
E. Substance/general medical condition exclusion	The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.
F. Relationship to a pervasive developmental disorder	If there is a history of autistic disorder or another pervasive developmental disorder, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

\*—Only one criterion A symptom is required if delusions are bizarre or hallucinations consist of keeping a running commentary on the person's behaviors or thoughts, or two or more voices conversing with each other.

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### TYPICAL PRESENTATION

The onset of schizophrenia can be abrupt or insidious. Most patients undergo a prodromal phase marked by a slow and gradual development of symptoms, such as social withdrawal, loss of interest in school or work, deterioration in hygiene and grooming, unusual behavior, or outbursts of anger. Family members can find this behavior disturbing and difficult to interpret. They may assume that the person is just “going through a phase.” Eventually, the appearance of active-phase symptoms (e.g., psychosis) marks the disturbance as schizophrenia.<sup>1</sup>

### DIFFERENTIAL DIAGNOSIS

Table 3 outlines common diagnoses that produce symptoms similar to schizophrenia. Because substance abuse can mimic many signs and symptoms of schizophrenia, diagnosis should not be made if the patient is actively using illicit drugs. Patients who present with psychotic features should receive a drug screening as part of their initial evaluation. Those with severe depression or bipolar disorder also may present with psychotic features; however, the diagnosis of a mood disorder always takes precedence over the diagnosis of schizophrenia.

Despite the stability of the diagnostic criteria for schizophrenia, diagnosis often changes over time. In a study of 936 inpatients over seven years, 21.9 percent of those who were initially diagnosed with schizophrenia had their diagnosis changed during subsequent hospitalizations, and 32.8 percent of those who were initially diagnosed with another illness were later diagnosed with schizophrenia. Most diagnostic changes from schizophrenia were to either bipolar disorder or organic disorders. Organic disorders, psychotic disorders, and major depression were the diagnoses most commonly changed to schizophrenia.<sup>12</sup>

Delirium can have features that are similar to the active symptoms of schizophrenia (e.g., hallucinations, delusions). The etiology of delirium is extensive. The crucial difference between schizophrenia and delirium is the timing; signs and symptoms of schizophrenia generally develop over weeks to months, whereas delirium usually has a much more rapid onset. Because many medical illnesses can cause delirium, the diagnosis of new-onset schizophrenia should be made cautiously in patients who have an existing serious medical illness.

**Table 3. Differential Diagnosis of Schizophrenia**

<i>Alternative diagnosis</i>	<i>Distinguishing features</i>
Brief psychotic disorder	Presence of delusions, hallucinations, disorganized speech, or grossly disorganized or catatonic behavior lasting at least one day but less than one month
Delirium	Multiple underlying etiologies; symptoms often similar to positive symptoms of schizophrenia but with a much shorter course
Delusional disorder	Delusions are not bizarre, and there are no other characteristics of schizophrenia
Medical illnesses	Illnesses that may cause schizophrenia-like symptoms include hepatic encephalopathy, hypoglycemia, electrolyte abnormalities (e.g., hyponatremia, hypercalcemia, hypocalcemia, hypomagnesemia), and sepsis; symptoms resolve with treatment of underlying condition
Medication-induced disorder	Medications that may cause schizophrenia-like symptoms include anticholinergics, anxiolytics, digoxin, phenytoin (Dilantin), steroids, narcotics, and cimetidine (Tagamet); symptoms resolve with discontinuation of medication
Mood disorders with psychotic features	No major depressive, manic, or mixed episodes have occurred concurrently with active phase symptoms; or, if they have occurred, their total duration has been brief relative to the duration of the active and residual symptoms
Pervasive developmental disorder	Recognized during infancy or early childhood; absence of delusions and hallucinations
Psychotic disorder NOS	This diagnosis is made if there is insufficient information available to choose between schizophrenia and other psychotic disorders
Schizophreniform disorder	Lasts one to six months; diagnosis does not require a decline in functioning
Schizotypal personality disorder	Pervasive patterns of social and interpersonal deficits beginning in early adulthood; accompanied by eccentric behavior and cognitive or perceptual distortions
Substance abuse	Multiple substances (e.g., hallucinogens, narcotics, alcohol) and withdrawal from these substances can cause delusions and hallucinations

NOS = not otherwise specified.

There also are racial disparities in the diagnosis of schizophrenia. For example, black persons are more likely than other racial groups to have symptoms attributed to schizophrenia,<sup>13</sup> and Hispanics are more likely to be diagnosed with major depression when presenting with psychotic symptoms.<sup>14</sup>

A complete history chronicling the development of signs and symptoms is crucial when diagnosing schizophrenia. Because the patient may have altered perceptions, obtaining a comprehensive history from at least one family member or close friend is essential to provide another perspective of the disease course.

### Drug Treatment

Effective pharmacologic treatment of schizophrenia has been available since the 1950s. In the early 1950s, the term “neuroleptic” was introduced to denote the effects of chlorpromazine (Thorazine; brand no longer available in the United States) and reserpine on laboratory animals. It was intended to distinguish their effects from those of sedatives and other central nervous system depressants.<sup>15</sup> Although “neuroleptic” is still used synonymously with “antipsychotic,” the term now usually refers to first-generation antipsychotics that confer an increased risk of extrapyramidal side effects, such as dystonic reactions (e.g., fixed upper gaze, neck twisting, facial muscle spasms), parkinsonian symptoms

(e.g., rigidity, bradykinesia, shuffling gait, tremor), and akathisia (e.g., inability to sit still, restlessness, tapping of feet). Tardive dyskinesia, which is a chronic disorder of the nervous system characterized by involuntary jerking movements (primarily of the face, tongue, and jaw), often is considered an extrapyramidal side effect. However, it is actually a separate and mechanistically different phenomenon.

The term “atypical antipsychotic” refers to newer antipsychotics that confer less risk of extrapyramidal side effects than traditional antipsychotics. *Table 4* lists antipsychotic agents currently available in the United States.

Nonadherence to medications is a significant problem; in a recent study, 74 percent of patients discontinued their medication within 18 months.<sup>16</sup> Nonadherence often leads to relapse of symptoms. Atypical antipsychotics were initially thought to help with adherence because of their lower rate of neurologic side effects. However, meta-analyses have found that drop-out rates and relapse prevention are no better with atypical antipsychotics than with neuroleptics.<sup>17,18</sup> Meta-analyses also have found that in terms of symptom scores and drop-out rates, atypical antipsychotics are better than high dosages (i.e., more than 12 mg per day) of haloperidol (Haldol); there was no advantage when the dosage of haloperidol was less than 12 mg per day.<sup>17</sup> In other words, many of the perceived benefits of atypical antipsychotics actually were a result

**Table 4. Antipsychotics Currently Available in the United States**

Medication class	Medication	Year approved by the FDA*	Usual effective dosage	Monthly cost†
Dopamine D <sub>2</sub> antagonists (high-potency)	Perphenazine (Trilafon‡)	1957	16 mg twice daily	\$83 to \$93
	Trifluoperazine (Stelazine‡)	1959	6 mg twice daily	\$150 to \$234
	Fluphenazine (Prolixin‡)	1960	2.5 mg twice daily	\$45 to \$54
	Haloperidol (Haldol)	1967	5 mg three times daily	\$9 to \$88
	Thiothixene (Navane)	1967	10 mg three times daily	\$148 (brand); \$37 to \$60 (generic)
	Fluphenazine decanoate (Prolixin Decanoate‡)	1972	25 mg IM every three weeks	\$5 to \$15
Dopamine D <sub>2</sub> antagonists (mid-potency)	Haloperidol decanoate (Haldol Decanoate)	1986	100 mg IM every four weeks	\$86 (brand); \$19 to \$53 (generic)
	Molindone (Moban)	1974	25 mg three times daily	\$271
Dopamine D <sub>2</sub> antagonists (low-potency)	Loxapine (Loxitane)	1975	50 mg twice daily	\$242 (brand); \$154 (generic)
	Chlorpromazine (Thorazine‡)	1957	100 mg three times daily	\$6 to \$103
Atypical (mixed neuroreceptor antagonists [low-affinity D <sub>2</sub> antagonists, high-affinity 5HT <sub>2A</sub> antagonists])	Thioridazine (Mellaril‡)	1962	100 mg three times daily	\$15 to \$62
	Clozapine (Clozaril)	1989	125 mg twice daily	\$407 (brand); \$266 to \$284 (generic)
	Risperidone (Risperdal)	1993	4 mg once daily	\$317
	Olanzapine (Zyprexa)	1996	10 mg once daily	\$353
	Quetiapine (Seroquel)	1997	200 mg twice daily	\$397
	Ziprasidone (Geodon)	2001	40 mg twice daily	\$315
	Aripiprazole (Abilify)	2002	20 mg once daily	\$490

FDA = U.S. Food and Drug Administration; IM = intramuscular.

\*—Information from <http://www.accessdata.fda.gov>.

†—Estimated cost to the pharmacist based on average wholesale prices (rounded to the nearest dollar) in Red Book. Montvale, N.J.: Medical Economics Data, 2006. Cost to the patient will be higher, depending on prescription filling fee.

‡—Brand no longer available in the United States

of the excessive doses of first-generation antipsychotics that were used for comparison in randomized trials.<sup>17</sup>

Evidence suggests that delays in initiating therapy with antipsychotics may result in a lifetime deleterious effect on psychotic episodes and social adjustment.<sup>19,20</sup> If initiation of antipsychotic therapy is delayed because of limited psychiatric resources, family physicians should consider starting medications instead.

#### ADVERSE EFFECTS

Prescribers should be aware of the potential adverse effects of antipsychotics and when the effects are likely to occur. The most concerning side effects of first-generation antipsychotics are neurologic (Table 5<sup>15</sup>). The Abnormal Involuntary Movement Scale can be used to help monitor the development of involuntary movements associated with neurologic side effects.<sup>21</sup>

Although newer atypical antipsychotics are associated with fewer neurologic side effects, they confer a higher risk of metabolic side effects such as diabetes, hypercholesterolemia, and weight gain. The comparative risk of diabetes-related side effects of several of the most

common antipsychotics (atypical and conventional) are shown in Table 6.<sup>22</sup>

Although atypical antipsychotics can cause weight gain, this effect is independent from the development of diabetes; the exact mechanism by which atypical agents might cause diabetes is unknown.<sup>22,23</sup> In one retrospective cohort study of 3,015 patients comparing olanzapine (Zyprexa) with risperidone (Risperdal), both were associated with gaining weight in the first year but only olanzapine was shown to be associated with the development of diabetes.<sup>23</sup> The diabetogenic potential of antipsychotics appears to be reversible if the medication is discontinued.

There have been no controlled trials on the effectiveness of long-term monitoring of biomedical markers (e.g., weight, blood sugar and cholesterol levels) in patients taking atypical antipsychotics, but the risk of metabolic side effects is high enough that regular monitoring is recommended by several consensus panels (Table 7<sup>24</sup>).<sup>22,24</sup> There are few or no data on the relative frequency that these tests should be performed, and no data to show that monitoring affects disease-specific or all-cause mortality rates.

**Table 5. Neurologic Side Effects of Antipsychotics**

Side effect	Features	Time of maximal risk	Proposed mechanism	Treatment
Acute dystonia	Muscle spasms of the tongue, face, neck, and back; may mimic seizures; not hysteria	One to five days	Unknown	Antiparkinsonian agents are diagnostic and curative*
Akathisia	Motor restlessness; not anxiety or agitation	Five to 60 days	Unknown	Reduce dose or change drug; antiparkinsonian agents (benzodiazepines or propranolol [Inderal])† may help
Parkinsonism	Bradykinesia, rigidity, variable tremor, mask facies, shuffling gait	Five to 30 days (can recur even after a single dose)	Antagonism of dopamine	Antiparkinsonian agents helpful
Neuroleptic malignant syndrome	Catatonia, stupor, fever, unstable blood pressure, myoglobinemia; can be fatal	One or more weeks (can persist for days after stopping medication)	Antagonism of dopamine may contribute	Stop medication immediately; dantrolene (Dantrium) or bromocriptine (Parlodel)‡ may be helpful; antiparkinsonian agents not effective
Perioral tremor (i.e., rabbit syndrome)	Perioral tremor (may be a late variant of parkinsonism)	After months or years	Unknown	Antiparkinsonian agents often helpful
Tardive dyskinesia	Oral facial dyskinesia; widespread choreoathetosis or dystonia	After months or years (worse on withdrawal)	Excess function of dopamine hypothesized	Prevention crucial; treatment unsatisfactory

\*—Many drugs have claimed to be helpful for acute dystonia. The most commonly employed treatments are diphenhydramine (Benadryl) 25 or 50 mg intramuscularly; or bethanechol (Duvoid) 1 or 2 mg intramuscularly or slowly intravenously, followed by oral medication with the same agent for a period of days to perhaps several weeks.

†—Propranolol often is effective in relatively low dosages (20 to 80 mg per day). Selective beta<sub>1</sub>-adrenergic receptor antagonists are less effective.

‡—Despite the response to dantrolene, there is no evidence of an abnormality of Ca<sup>2+</sup> transport in skeletal muscle; with lingering neuroleptic effects, bromocriptine may be tolerated in large dosages (10 to 40 mg per day).

Adapted with permission from Goodman LS, Gilman A, Hardman JG, Limbird LE. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York, N.Y.: McGraw-Hill, 2001:501.

Tardive dyskinesia is a common late side effect of prolonged treatment with antipsychotics. Stopping the causal antipsychotic does not diminish the chronicity and severity.<sup>25-28</sup>

To help manage side effects of drug treatment, family physicians should inquire about positive and negative symptoms at every patient visit, and they should regularly communicate with patients' mental health professionals about changes in symptoms, new lab results, and prescribing and monitoring roles.

### Psychosocial Treatments

Individual, group, and family treatments have been developed as therapies for persons with schizophrenia. Family interventions include therapy with individual families, psychoeducation with groups of families, and family group therapy.<sup>29</sup> These interventions offer support, education about the illness, and options for reducing critical and emotionally overinvolved attitudes and behaviors toward the patients.

Family treatments have the most empiric support for improving symptoms and reducing hospitalizations.<sup>30</sup> These treatments are based on early findings that family environments that were high in "expressed emotion" (either critical and rejecting or emotionally overinvolved) were associated with relapse in patients with schizophrenia.<sup>31-34</sup> Multiple studies have shown that family interventions reduce relapse rates and improve symptoms, adherence to medications, and functioning.<sup>30</sup> However, a recent review suggested that there are weaknesses in many family intervention studies, and that there is a need for additional investigation.<sup>35</sup>

There are several psychosocial rehabilitative interventions that have been shown to be effective in improving the quality of life in patients with schizophrenia. The Intensive Psychiatric Rehabilitation Treatment, which is a program that teaches living, job, and social skills to patients, has resulted in improvements in functioning.<sup>36</sup> Social skills training has improved independent living skills<sup>37-40</sup>; supported employment programs have shown

**Table 6. Ranking of Antipsychotics According to Risk of Diabetes-Related Conditions\***

Condition	Clozapine (Clozaril)	Olanzapine (Zyprexa)	Risperidone (Risperdal)	Conventional antipsychotics
Diabetes (prevalence)	4	3	1	2
Hyperglycemia (fasting)	4	3	2	1
Hyperinsulinemia (fasting)	3	4	2	1
Elevated total cholesterol levels	4	2	1	3
Elevated triglyceride levels	4	3	1	2
Elevated BMI	3	4	2	1
Elevated plasma uric acid levels	4	2	3	1
<b>Sum of ranks†</b>	<b>26</b>	<b>21</b>	<b>12</b>	<b>11</b>

NOTE: 1 = lowest risk; 4 = highest risk.

BMI = body mass index.

\*—Adjusted for diagnosis, duration of antipsychotic treatment, other medications, family history of diabetes, ethnicity, and smoking status.

†—The parameters are not equivalent in their contribution to the pathology of diabetes or its cardiovascular complications; no attempt has been made to weight the sums of rank orders. Low rank order equals low prevalence or risk.

Adapted with permission from Lean ME, Pajonk FG. Patients on atypical antipsychotic drugs: another high-risk group for type 2 diabetes. *Diabetes Care* 2003;26:1599.

**Table 7. Physical Health Monitoring for Patients Taking Antipsychotics**

Disease process	Antipsychotics	Monitoring
Obesity	First- and second-generation	Calculate BMI at initiation of medication and every six months; encourage patients to monitor their weight; recommend weight-management program for patients with more than a 1-unit increase in BMI
Diabetes	Second-generation	Perform baseline plasma glucose before initiation of medication; measure A1C four months after initiation of medication; inquire about polyuria and polydipsia at each visit
Hyperlipidemia	Second-generation	Perform a lipid screening at initiation of medication; repeat lipid screening every six months if abnormal and every two years if normal; follow NCEP recommendations for lipid management

BMI = body mass index; NCEP = National Cholesterol Education Program.

Information from reference 24.

improvements in the number of hours worked and total wages earned<sup>41</sup>; and in-home crisis intervention demonstrates promise by reducing treatment drop-out rates.<sup>42</sup> Studies have shown that individual cognitive behavior therapy for schizophrenia reduces positive and negative symptoms,<sup>43</sup> but currently there is no evidence that it reduces relapse rates.<sup>44</sup>

### Prognosis

Understanding the potential course of disease can help guide treatment. Patients with schizophrenia have a high rate of substance abuse, and those with substance abuse have their first hospitalizations at earlier ages, have more frequent hospitalizations, and have more interpersonal and family discord.<sup>45</sup> The strength of patients' commitment to their delusions is directly proportional

to their likelihood of rehospitalization.<sup>46</sup> Patients with poor executive functioning (i.e., skills involving problem solving, setting and attaining future goals, and decision making) use outpatient services at a higher rate and therefore may require increased support to maintain their independence.<sup>47</sup>

Patients with severe psychotic disturbances have a higher likelihood of aggressive behavior than those with fewer psychotic symptoms.<sup>48</sup> Patients with schizophrenia also have a low marital rate and high divorce rate.<sup>49-52</sup>

Accelerated heart disease is the most common cause of death in patients with schizophrenia; the risk of dying from cardiovascular disease is two to three times higher than in the general population.<sup>22</sup> This risk is accelerated because their rate of cigarette smoking is two to four times higher than that of the general population.

# Schizophrenia

Persons with schizophrenia also smoke more than patients with other mental disorders. In several studies, 90 percent of hospitalized patients with schizophrenia smoked.<sup>53,54</sup> Nicotine has a possible positive effect on cognitive functioning in patients with schizophrenia, which may explain the high rate of smoking.<sup>53,55</sup>

Suicide also is a common cause of death in patients with schizophrenia; it has a 10 percent lifetime risk.<sup>2,56</sup> The risk of suicide is strongly associated with depression, previous suicide attempts, drug abuse, agitation or motor restlessness, fear of mental disintegration, poor adherence to treatment, and recent loss.<sup>57</sup> Overdose of treatment medications as a method of suicide is not common because antipsychotics have a high therapeutic index (i.e., lethal doses are much higher than the dosages that produce a therapeutic effect).

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