Schizophrenia for Primary Care Providers: How to Contribute to the Care of a Vulnerable Patient Population

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ABSTRACT

Patients with schizophrenia represent a vulnerable population with high medical needs that are often missed or undertreated. Primary care providers have the potential to reduce health disparities experienced by this population and make a substantial difference in the overall health of these patients. This review provides primary care providers with a general understanding of the psychiatric and medical issues specific to patients with schizophrenia and a clinically practical framework for engaging and assessing this vulnerable patient population and assisting them in achieving optimal health. Initial steps in this framework include conducting a focused medical evaluation of psychosis and connecting patients with untreated psychosis to psychiatric care as promptly as possible. Given the significant contribution of cardiovascular disease to morbidity and mortality in schizophrenia, a top priority of primary care for patients with schizophrenia should be cardiovascular disease prevention and treatment through regular risk factor screening, appropriate lifestyle interventions, and other indicated therapies.

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Schizophrenia is the most common psychotic illness, with approximately 7 in 1000 people developing the disorder in their lifetime.1 Schizophrenia is considered a “serious mental illness” because of its chronic course and often poor long-term outcomes in social and vocational realms.2 People with schizophrenia have higher rates of medical illness and mortality than the general population,3 underscoring the crucial role that primary care providers can play in managing patients with this disorder. Some 50% to 90% of people with serious mental illness have 1 or more chronic medical illnesses.4 On average, adults with serious mental illness in the United States die 25 years earlier than adults in the general population; the major contributor to these premature deaths is cardiovascular disease.5 Primary care that is integrated with specialty mental health care has the potential to reduce this dramatic disparity. To deliver effective medical care to those with schizophrenia, the authors do not think that primary care providers must be experts in the diagnosis of schizophrenia, because this task is best achieved in collaboration with a psychiatrist. Rather, primary care providers should have a working knowledge of the illness, its treatment, and the treatment challenges and health risks unique to this population. The aim of this review is to provide primary care providers with a clinically practical framework for engaging and assessing this vulnerable patient population and assisting them in achieving optimal health.

WHAT IS SCHIZOPHRENIA?

Differential Diagnosis

“Psychosis” is not a diagnosis but rather a term that describes certain symptoms, with the most narrow definition including delusions or hallucinations, and more broad def-
initiations including disorganization of speech (thought disorder) and behavior. Although psychotic symptoms may be a prominent part of schizophrenia, not all psychosis is indicative of a primary psychiatric disorder such as schizophrenia. Instead, a broad differential diagnosis of psychosis must be entertained. Psychosis can be “primary” (psychiatric) or “secondary” (organic) in origin. Secondary causes must be ruled out first; these include intoxication or withdrawal from alcohol or drugs and a number of medical illnesses, often as part of delirium. Although uncommon as causes of psychosis, infections, endocrinopathies, electrolyte and metabolic abnormalities, and neurologic processes, such as seizures, demyelinating diseases, or space-occupying brain lesions, can all cause psychosis. A routine history and physical examination with a focused neurologic assessment and basic laboratory testing that includes a urine drug screen provide a useful initial medical assessment of patients presenting with psychosis (Table 1).7

Characteristics of Schizophrenia

Schizophrenia, according to diagnostic criteria, consists of characteristic symptoms (delusions, hallucinations, disorganized speech, and “negative symptoms,” discussed below), lasting for 1 month or more and causing social or occupational dysfunction.6,8 In a broader sense, schizophrenia can be thought of as a disorder with 6 common symptom clusters (Figure 1), some not specifically mentioned in diagnostic criteria, and some more prominent than others in particular patients.9

Negative symptoms include amotivation, decreased emotional expression (“affective blunting or flattening”), decreased social interaction, and poverty of speech.10 These symptoms may be mistaken by clinicians or family members as a depressive disorder or even “laziness.” Cognitive dysfunction is both common and impairing in schizophrenia, affecting aspects of memory, processing speed, and executive function.11 Motor system abnormalities, such as tremor, bradykinesia, catalepsy (generalized motoric inhibition or purposeless and excessive activity), akathisia (inner restlessness characterized by inability to remain still), and abnormal involuntary movements are not uncommon and can be related to the illness or its treatment with antipsychotic medication.12 Finally, many patients with schizophrenia present with affective symptoms during the course of illness, including demoralization, major depression, or periods of manic-like behaviors, such as increased energy, excitement, irritability, and disinhibition.9 Therefore, it is important that primary care providers familiarize themselves with questions that effectively elicit the presence of psychotic symptoms (Table 2)13-15 and routinely screen for them in all patients presenting with psychiatric symptoms, because other symptoms might overshadow the presence of psychosis.

TREATMENT OF SCHIZOPHRENIA

General Principles

The complexity and chronicity of schizophrenia, as well as the functional disruption it can cause, usually necessitate the involvement of a multidisciplinary mental health treatment team to provide effective and comprehensive psychiatric care. Understanding the team structure and basic roles of the various team members (Table 3) allows for targeted and effective collaboration between primary care providers and mental health professionals.

Medication Management

A mainstay of treatment for schizophrenia is maintenance antipsychotic medication, which is effective in controlling acute exacerbations of psychosis and preventing relapse of

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**Table 1** Suggested Medical Assessment to Rule Out Organic Causes of Psychosis7

<table>
<thead>
<tr>
<th>Medical and family history</th>
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</thead>
<tbody>
<tr>
<td>Physical examination, with focused neurologic examination</td>
</tr>
<tr>
<td>Complete blood count</td>
</tr>
<tr>
<td>Electrolytes, including calcium</td>
</tr>
<tr>
<td>Blood urea nitrogen and creatinine</td>
</tr>
<tr>
<td>Liver function tests</td>
</tr>
<tr>
<td>Thyroid function tests</td>
</tr>
<tr>
<td>Vitamin B12</td>
</tr>
<tr>
<td>HIV test</td>
</tr>
<tr>
<td>Fluorescent treponemal antibody absorption test</td>
</tr>
<tr>
<td>Urine drug screen</td>
</tr>
<tr>
<td>Head imaging (MRI preferred) – low yield</td>
</tr>
<tr>
<td>Additional testing, if clinically indicated:</td>
</tr>
<tr>
<td>Electroencephalogram</td>
</tr>
<tr>
<td>Ceruloplasmin</td>
</tr>
<tr>
<td>Chest radiograph</td>
</tr>
<tr>
<td>Lumbar puncture</td>
</tr>
</tbody>
</table>

HIV = human immunodeficiency virus; MRI = magnetic resonance imaging.
such symptoms. Blockade of D2 dopamine receptors in the brain is a property shared by all antipsychotic medications. Antipsychotics are most helpful for positive symptoms of schizophrenia and show limited, if any, efficacy for negative or cognitive symptoms.16

The original, older antipsychotics are known as first-generation or “typical” antipsychotics and are grouped by potency (the dose needed to produce desired effect). Low-potency agents such as chlorpromazine (the first antipsychotic) are more likely to produce sedation, orthostasis, and anticholinergic side effects. High-potency agents, such as haloperidol, are more likely to produce extrapyramidal
Psychosis in and of itself is not necessarily an indication for emergency evaluation or hospitalization. In outpatient situations where timely psychiatric referral or consultation is not readily available and no acute safety concerns exist, the primary care provider may elect to start an antipsychotic medication after ruling out medical causes for the presentation and while awaiting definitive psychiatric assessment and treatment. If the patient has experience with antipsychotic medications, asking about those that have been tolerated and helpful in the past can assist in choosing a medication; restarting that medication at the lower end of the recommended dose range will likely be of benefit.

If the patient is naive to antipsychotic medication, reasonable first-line choices are risperidone or perphenazine. Risperidone has the advantages of being relatively easy to dose, being available as a generic medication, and having low rates of extrapyramidal symptoms and moderate metabolic side effects. Starting doses are generally 1 to 2 mg/d, often divided into 2 daily doses. The typical daily dose range for risperidone is 2 to 4 mg for patients with a first episode and 4 to 8 mg for patients with chronic episodes. The first-generation antipsychotic perphenazine also is an off-patent medication and has a similar or better metabolic profile than risperidone but an increased risk of extrapyramidal symptoms, including acute dystonia and tardive dyskinesia.20 Starting doses are 4 to 8 mg twice per day, and the maximum suggested total daily dose is 64 mg.

The choice and dose of medication can be a complicated process of trial and error and should be guided by patient preference, side effect profile, and pertinent medical history. When possible, efforts should be made to avoid antipsychotics with a poor metabolic profile in patients with obesity or diabetes. Baseline metabolic measures as described below should be obtained at the time of antipsychotic medication initiation, and patients should be educated about general lifestyle interventions, such as diet and exercise, that may help mitigate antipsychotic-induced weight gain.

### MEDICAL CARE OF PATIENTS WITH SCHIZOPHRENIA

The basic treatment goals of people with schizophrenia are similar to those of any other patient population: stay alive and stay healthy. Primary care providers are well positioned to have a positive impact on both these domains.

The mortality rate in schizophrenia is 2 to 3 times higher than in the general population.27 This elevated risk of death is due to higher rates of mortality from suicide and injuries, as well as multiple categories of medical illness.28,29 Approximately 5% of people with schizophrenia will commit suicide,30 and the risk of death from suicide is approximately 13 times greater than the risk in the general population.29 Many patients who commit suicide make contact with their primary care provider before the act,31 so routine risk assessment is a necessary part of the clinical encounter. Although comprehensive suicide risk assessments are likely beyond the scope of the primary care setting because of time

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**Table 4 Relative Likelihood of Metabolic Abnormalities of Selected Antipsychotic Medications**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Weight Gain</th>
<th>Glucose Dysregulation</th>
<th>Lipid Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>+/−</td>
<td>+/−</td>
<td>−</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>+/−</td>
<td>+/−</td>
<td>−</td>
</tr>
<tr>
<td>SGA</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Clozapine</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Risperidone</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

FGA = first-generation antipsychotic; SGA = second-generation antipsychotic; + = increased likelihood; − = lower likelihood.
and resource limitations, primary care providers should be familiar with basic suicide risk assessments and have a protocol for referral to mental health crisis services if further evaluation or a higher level of care is needed.

Medical illness is highly prevalent in patients with serious mental illness, with 50% to 90% of patients having at least 1 chronic medical condition. In patients with schizophrenia, rates of mortality from medical illnesses are elevated in comparison with the general population across a number of disease categories, including infectious (3.4 times higher), respiratory (3.2×), endocrine (2.7×), gastrointestinal (2.5×), and cardiovascular (2.3×). Most concerning is the high risk of death from cardiovascular disease, which may account for 50% to 60% of the premature mortality from medical illness seen in patients with serious mental illness. After patients with serious mental illness are diagnosed with cardiovascular disease, they die sooner than those with cardiovascular disease but without serious mental illness.

Contributing to the increased risk of cardiovascular disease are the higher rates of cardiovascular disease risk factors seen in patients with schizophrenia. Obesity, smoking, diabetes, hypertension, dyslipidemia, and metabolic syndrome are present at rates 1.5 to 5 times greater than in the general population. In a large cohort of chronic schizophrenia patients, 41% had the metabolic syndrome. Anti-psychotic medication, particularly second-generation antipsychotics, can exacerbate many of these metabolic parameters, although the risk varies by agent. Further compounding this issue are low rates of general health screening and preventive care obtained by patients with serious mental illness and evidence that some of the care received by those with serious mental illness may be of lower quality in certain situations.

On the basis of the high prevalence of cardiometabolic risk factors, cardiovascular disease, and early mortality from cardiovascular disease in patients with serious mental illness, Morden and colleagues questioned whether serious mental illness should, like diabetes, be considered a “risk equivalent” for cardiovascular disease. This would put patients with serious mental illness in a risk category in which more intensive prevention, screening, and treatment goals would be recommended. Even without receiving a formal designation as a risk equivalent, serious mental illness represents a condition in which the diagnosis and treatment of cardiovascular risk factors and cardiovascular disease should be aggressively pursued.

Medical screening guidelines for patients with schizophrenia exist, and they are often more intensive than screening guidelines for similar parameters in the general population. Such screening efforts may be led by psychiatrists in certain systems of care, but for optimal management of identified abnormalities, effective communication and coordination with primary care are essential. Indeed, because of resource constraints in mental health settings, primary care providers may be in a better position to undertake certain medical screening, such as electrocardiograms.

For patients who develop or experience worsening of metabolic parameters while taking an antipsychotic medication, switching to an antipsychotic medication with lower risk of metabolic problems may represent an effective strategy for targeting these risk factors. Such a change should be undertaken only with communication with the psychiatric treatment team because some patients may require a certain medication, despite its negative metabolic consequences, because they have not responded to others in the past. Other patients may have a course of illness where the potential for psychiatric decompensation during a medication switch poses too great a risk to the patient or others. In these cases, antipsychotic medication may be an “unmodifiable” risk factor, and efforts at intervention should be directed toward lifestyle modification or other indicated treatments.

Other risk factors may be more amenable to intervention. Although rates of smoking in schizophrenia are between 50% and 80%, patients are motivated to quit, and effective treatments (including counseling and pharmacotherapy) with minimal risk of psychiatric destabilization exist. Lifestyle interventions focusing on improving diet and exercise, which are often suboptimal in patients with schizophrenia, also have been found to be helpful for reducing weight and other metabolic syndrome risk factors. Pharmacologic interventions such as metformin seem to have potential for reducing metabolic risks for patients taking antipsychotics, but more data are needed before these strategies can be broadly recommended.

CHALLENGES TO EFFECTIVE CARE

Certain patient, provider, and healthcare system factors present important challenges to providing primary care to people with schizophrenia. Symptoms of the illness may disrupt the process of engagement with a provider or clinic. Paranoia may make it difficult for the patient to feel comfortable with a provider or sitting in a crowded waiting room. Thought disorder and cognitive impairment can obscure the patient’s accounting of his or her chief symptom or medical history, potentially making the use of collateral sources of information imperative. Negative symptoms such as amotivation may present an obstacle to the successful attendance of appointments or adherence to treatment plans. Up to one half of people with schizophrenia have a substance use disorder, which can interfere with treatment adherence and efficacy and increase the burden of medical illness substantially.

In some instances, primary care providers may feel uncomfortable treating patients with schizophrenia because of limited experience or resources. Stigmatization of schizophrenia is common among the general public and healthcare providers. In addition, providers’ inaccurate attribution of a patient’s physical symptoms to his or her mental illness, known as “diagnostic overshadowing,” can
interfere with patients receiving appropriate diagnosis and treatment for medical illness. Patients may feel that their physician takes their physical symptoms less seriously once they reveal their psychiatric diagnosis.54

Another barrier to effective care is a provider’s underestimation of patients as capable partners in their own care. Such an outlook may lead to “therapeutic nihilism,” where effective preventive measures or treatments are not offered to patients.3,36 In situations where a treatment regimen is unavoidably complex or a condition requires close monitoring and there are questions about the patient’s ability to manage the situation independently, family members or members of the psychiatric treatment team should be enlisted as appropriate to help ensure favorable outcomes.

Limitations of the healthcare system also can impede the provision of effective medical care to patients with schizophrenia. Ways of obtaining access to psychiatric outpatient care, including systems for scheduling appointments, can be needlessly complex and difficult for patients (and providers) to navigate.55 Reducing such barriers through the use of care managers may be an effective way to improve the overall quality and effectiveness of primary care for patients with schizophrenia.56 Fragmentation of care across the mental health and primary care systems makes communication and care coordination particularly challenging.57 A range of integrated healthcare delivery models are being developed and tested with this hope of addressing this long-standing and significant issue.58

CONCLUSIONS

Patients with schizophrenia represent a vulnerable population with high medical needs that are often missed or undertreated and lead to premature mortality. As frontline clinicians, primary care providers have the potential to reduce the health disparities experienced by this population. A general understanding of the psychiatric and medical issues common to patients with schizophrenia will assist primary

Table 5  Physical Health Monitoring in Schizophrenia19,26,37-39

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Rationale</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal and family history of obesity, diabetes, dystlipidemia, HTN, or CVD</td>
<td>High rates of CVD and CVD risk factors</td>
<td>Baseline, annually</td>
</tr>
<tr>
<td>Smoking status</td>
<td>High rates of smoking</td>
<td>Each visit</td>
</tr>
<tr>
<td>Weight (BMI)</td>
<td>Weight gain common with many psychiatric medications</td>
<td>Before initiation or switching of antipsychotic, then monthly for 3 mo, then quarterly if stable</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>Weight gain common with many psychiatric medications</td>
<td>Baseline, annually</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>High rates of HTN</td>
<td>Baseline, 3 mo, then at least annually</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>Elevated risk of diabetes in schizophrenia and with use of antipsychotics</td>
<td>Before initiation or switching of antipsychotic, then at 3 mo, then annually if normal</td>
</tr>
<tr>
<td>Fasting lipid panel</td>
<td>Certain antipsychotics are associated with hyperlipidemia</td>
<td>Before initiation or changing of antipsychotic, then at 3 mo, then annually if normal</td>
</tr>
<tr>
<td>ECG</td>
<td>Antipsychotics may prolong QTc</td>
<td>No clear consensus. Consider before initiation of any antipsychotic. Thoridazine and pimozide should be avoided in patients with cardiac risk factors. For anyone taking these 2 medications, obtain baseline ECG and serum potassium. For ziprasidone, if a patient has CVD, congenital long QT, history of syncope, or family history of sudden death, get baseline ECG and serum potassium. For the above patient groups, obtain subsequent ECG with significant dose change of antipsychotic, addition of another QTc prolonging medication, or symptoms suggestive of prolonged QTc (eg, syncope).</td>
</tr>
<tr>
<td>Neurologic examination (for dyskinesias or rigidity)</td>
<td>Increased risk of movement disorders (parkinsonism and tardive dyskinesia), particularly with FGAs</td>
<td>Every 6 mo (FGAs) or annually (SGAs)</td>
</tr>
<tr>
<td>Prolactin level</td>
<td>Antipsychotics can increase prolactin</td>
<td>When indicated by symptoms of hyperprolactinemia (decreased libido, erectile dysfunction, galactorrhea, menstrual disturbances)</td>
</tr>
<tr>
<td>Eye examination</td>
<td>Chlorpromazine and quetiapine have been associated with cataracts</td>
<td>Every 2 y in those aged &lt; 40 y; annually if aged &gt; 40 y</td>
</tr>
</tbody>
</table>

BMI = body mass index; CVD = cardiovascular disease; ECG = electrocardiogram; FGA = first-generation antipsychotic; HTN = hypertension; SGA = second-generation antipsychotic.
care providers in providing necessary and effective medical care within an accommodating and compassionate framework. Initial steps in this framework include conducting a focused medical evaluation of psychosis and promptly connecting patients with untreated psychosis to psychiatric care. Given the increased prevalence of cardiovascular disease and cardiovascular disease risk factors in this population, ongoing primary care for patients with schizophrenia should focus on cardiovascular disease prevention and treatment. Thoughtful and comprehensive primary care for individuals with schizophrenia can be crucial in promoting meaningful engagement in health care and guiding these patients in their journey to lead healthy and fulfilling lives.

References


