

# 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.<sup>1</sup> Schizophrenia is considered a “serious mental illness” because of its chronic course and often poor long-term outcomes in social and vocational realms.<sup>2</sup> People with schizophrenia have higher rates of medical illness and mortality than the general population,<sup>3</sup> 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.<sup>4</sup> 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.<sup>5</sup> 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-

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initions including disorganization of speech (thought disorder) and behavior.<sup>6</sup> 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).<sup>7</sup>

## 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 occupa-

tional dysfunction.<sup>6,8</sup> 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.<sup>9</sup>

Negative symptoms include amotivation, decreased emotional expression (“affective blunting or flattening”), decreased social interaction, and poverty of speech.<sup>10</sup> 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.<sup>11</sup> Motor system abnormalities, such as tremor, bradykinesia, catatonia (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.<sup>12</sup> 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.<sup>9</sup> Therefore, it is important that primary care providers familiarize themselves with questions that effectively elicit the presence of psychotic symptoms (Table 2)<sup>13-15</sup> 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

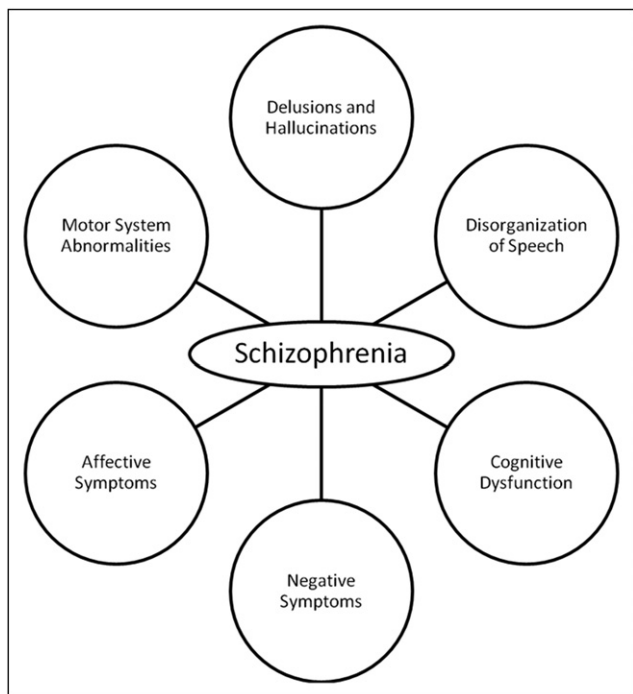
### CLINICAL SIGNIFICANCE

- Patients with schizophrenia die earlier than the general population, mostly from preventable and treatable medical illnesses.
- Higher rates of cardiovascular, infectious, respiratory, endocrine, and gastrointestinal disease are seen in patients with schizophrenia.
- Certain antipsychotic medications contribute to metabolic abnormalities more than others.
- Routine physical health monitoring and targeted interventions, especially for cardiovascular disease and its risk factors, are key considerations when caring for this patient population.

**Table 1** Suggested Medical Assessment to Rule Out Organic Causes of Psychosis<sup>7</sup>

Medical and family history
Physical examination, with focused neurologic examination
Complete blood count
Electrolytes, including calcium
Blood urea nitrogen and creatinine
Liver function tests
Thyroid function tests
Vitamin B <sub>12</sub>
HIV test
Fluorescent treponemal antibody absorption test
Urine drug screen
Head imaging (MRI preferred) – low yield
Additional testing, if clinically indicated:
Electroencephalogram
Ceruloplasmin
Chest radiograph
Lumbar puncture

HIV = human immunodeficiency virus; MRI = magnetic resonance imaging.



**Figure 1** Six common symptom clusters of schizophrenia.<sup>9</sup>

such symptoms. Blockade of D<sub>2</sub> 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.<sup>16</sup>

The original, older antipsychotics are known as first-generation or “typical” antipsychotics and are grouped by

**Table 2** Screening for Psychosis<sup>13-15</sup>

A lead-in statement helps to normalize the experience for the patient and reduces the potential shame and embarrassment of this sensitive topic, for example, “Sometimes when people are [under stress/feeling anxious/feeling depressed], they can have strange experiences such as trouble with their thinking or seeing or hearing things that others don’t.” Affirmative responses to the questions below should be followed by “Tell me more about that.”

**Questions to elicit delusional thinking**

- Have you had any strange or odd experiences lately that are difficult to explain or that others would find hard to believe?
- Have you felt like people are watching or following you or that they want to harass or hurt you?
- Have you felt like others can hear your thoughts or that you can hear another person’s thoughts?

**Questions to elicit hallucinations**

- Have your eyes or ears ever played tricks on you?
- Have there been times when you heard or saw things that other people could not?

**Table 3** Common Members of a Mental Health Treatment Team for a Patient with Schizophrenia

**Psychiatrist**

Physician responsible for psychiatric assessment and diagnosis and initial and ongoing treatment planning  
 Prescribes psychotropic medications  
 Serves as the medical expert, ensuring the medical safety and health of the patient in collaboration with a PCP  
 Meets with the patient for an initial hour-long evaluation and subsequent 15-20-min meetings, approximately monthly, but possibly more or less frequently, depending on clinical need  
 Specially trained nurse practitioners or physician’s assistants may function in a similar role, under the general term “prescriber”

**Therapist**

May be a social worker, psychologist, or licensed counselor  
 Works with the patient around stressors in a supportive way or uses more structured psychotherapies, such as cognitive behavioral therapy, to help patients develop coping strategies and approaches for limiting the impact of negative symptoms or psychosis, which may persist despite optimal medication management  
 Additional therapists may be involved, each focusing on a specific area, such as vocational, educational, or addiction issues

**Case Manager**

Coordinates the many services a patient may be receiving  
 Attempts to keep the treatment team on the same page by having and conveying an overall understanding of the treatment plan

**Outreach Worker**

Interacts with the patient, often outside of traditional treatment settings, to ensure important parts of the treatment plan are accomplished  
 May help the patient keep appointments or pick up prescriptions  
 May have limited formal mental health training or experience

**Visiting Nurse**

Provides assistance to patients with complex medication regimens or medical needs (eg, insulin injections)

**Residential (“group home”) Staff Member**

Has daily contact with the patient and is often a good source of collateral information regarding the patient’s day-to-day functioning  
 Advocates for the patient and serves as ally in ensuring the implementation of treatment plans  
 May have limited formal mental health training or experience

**Legal Guardian**

A court-appointed individual who helps with medical decisions by acting in the patient’s best interest when the patient’s illness affects his/her decision-making ability

PCP = primary care provider.

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

**Table 4** Relative Likelihood of Metabolic Abnormalities of Selected Antipsychotic Medications<sup>18,19</sup>

Medication	Weight Gain	Glucose Dysregulation	Lipid Abnormalities
FGAs			
Haloperidol	+/-	+/-	-
Perphenazine	+/-	+/-	-
SGAs			
Clozapine	++++	++++	++++
Olanzapine	++++	++++	++++
Quetiapine	+++	+++	++++
Risperidone	++	+	+
Aripiprazole	-	-	-
Ziprasidone	-	-	-

FGA = first-generation antipsychotic; SGA = second-generation antipsychotic; + = increased likelihood; - = lower likelihood.

symptoms and prolactin elevation. Medium-potency agents, such as perphenazine, fall somewhere in between with respect to the aforementioned side effects. The second-generation antipsychotics or “atypicals,” such as clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole (a D<sub>2</sub> partial agonist), share 5-HT<sub>2</sub> and D<sub>2</sub> antagonism and a lower liability for extrapyramidal symptoms. Some of these medications have the potential for troubling weight gain and disturbances in glucose and lipid metabolism, although they exhibit differential liabilities for these side effects (Table 4).<sup>17-19</sup> Several new second-generation antipsychotics are available (paliperidone, asenapine, iloperidone, and lurasidone) but do not seem to have significant advantages over other second-generation antipsychotics.<sup>20-23</sup>

Most antipsychotics have similar efficacy with respect to the amelioration of psychosis and may not fully eliminate a patient's symptoms despite adequate dosages.<sup>24</sup> Clozapine may be more effective than other antipsychotics in refractory cases of schizophrenia,<sup>25</sup> but it carries the burden of additional side effects and, because of the risk of agranulocytosis, requires routine blood monitoring and enrollment of the patient in a monitoring registry. Antipsychotics are often discontinued or switched because of limited efficacy or bothersome side effects.<sup>24</sup> Because of the similar efficacy of most antipsychotics, the choice of a medication is often guided by patient preference and side effect profile.

### Treatment of an Initial Presentation of Psychosis in the Primary Care Setting

A patient experiencing a first episode of psychosis may initially present to a primary care practice. Primary care providers also may encounter patients with long-standing psychotic illness who are not actively engaged in psychiatric care. In both instances, after an appropriate medical evaluation, the primary care provider should obtain psychiatric consultation for the patient.

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.<sup>26</sup> 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.<sup>27</sup> This elevated risk of death is due to higher rates of mortality from suicide and injuries, as well as multiple categories of medical illness.<sup>28,29</sup> Approximately 5% of people with schizophrenia will commit suicide,<sup>30</sup> and the risk of death from suicide is approximately 13 times greater than the risk in the general population.<sup>28</sup> Many patients who commit suicide make contact with their primary care provider before the act,<sup>31</sup> 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

and resource limitations, primary care providers should be familiar with basic suicide risk assessments<sup>32</sup> 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.<sup>4</sup> 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×).<sup>33</sup> 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.<sup>3</sup> After patients with serious mental illness are diagnosed with cardiovascular disease, they die sooner than those with cardiovascular disease but without serious mental illness.<sup>34</sup>

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.<sup>26</sup> In a large cohort of chronic schizophrenia patients, 41% had the metabolic syndrome.<sup>35</sup> Antipsychotic medication, particularly second-generation antipsychotics, can exacerbate many of these metabolic parameters, although the risk varies by agent (**Table 4**). 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.<sup>3</sup>

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<sup>36</sup> 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 (**Table 5**).<sup>19,26,37-39</sup> 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.<sup>40</sup> 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.<sup>41</sup> 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%,<sup>26</sup> patients are motivated to quit,<sup>42</sup> and effective treatments (including counseling and pharmacotherapy) with minimal risk of psychiatric destabilization exist.<sup>43</sup> Lifestyle interventions focusing on improving diet and exercise, which are often suboptimal in patients with schizophrenia,<sup>44</sup> also have been found to be helpful for reducing weight and other metabolic syndrome risk factors.<sup>45</sup> 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.<sup>46</sup>

## 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.<sup>3</sup> 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.<sup>47</sup> 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,<sup>48</sup> which can interfere with treatment adherence and efficacy and increase the burden of medical illness substantially.<sup>49</sup>

In some instances, primary care providers may feel uncomfortable treating patients with schizophrenia because of limited experience or resources.<sup>50,51</sup> Stigmatization of schizophrenia is common among the general public and healthcare providers.<sup>52</sup> In addition, providers’ inaccurate attribution of a patient’s physical symptoms to his or her mental illness, known as “diagnostic overshadowing,”<sup>53</sup> can

**Table 5** Physical Health Monitoring in Schizophrenia<sup>19,26,37-39</sup>

Assessment	Rationale	Frequency
Personal and family history of obesity, diabetes, dyslipidemia, HTN, or CVD	High rates of CVD and CVD risk factors	Baseline, annually
Smoking status	High rates of smoking	Each visit
Weight (BMI)	Weight gain common with many psychiatric medications	Before initiation or switching of antipsychotic, then monthly for 3 mo, then quarterly if stable
Waist circumference	Weight gain common with many psychiatric medications	Baseline, annually
Blood pressure	High rates of HTN	Baseline, 3 mo, then at least annually
Fasting plasma glucose	Elevated risk of diabetes in schizophrenia and with use of antipsychotics	Before initiation or switching of antipsychotic, then at 3 mo, then annually if normal
Fasting lipid panel	Certain antipsychotics are associated with hyperlipidemia	Before initiation or changing of antipsychotic, then at 3 mo, then annually if normal
ECG	Antipsychotics may prolong QTc	No clear consensus. Consider before initiation of any antipsychotic. Thioridazine 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).
Neurologic examination (for dyskinesias or rigidity)	Increased risk of movement disorders (parkinsonism and tardive dyskinesia), particularly with FGAs	Every 6 mo (FGAs) or annually (SGAs)
Prolactin level	Antipsychotics can increase prolactin	When indicated by symptoms of hyperprolactinemia (decreased libido, erectile dysfunction, galactorrhea, menstrual disturbances)
Eye examination	Chlorpromazine and quetiapine have been associated with cataracts	Every 2 y in those aged < 40 y; annually if aged > 40 y

BMI = body mass index; CVD = cardiovascular disease; ECG = electrocardiogram; FGA = first-generation antipsychotic; HTN = hypertension; SGA = second-generation antipsychotic.

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.<sup>54</sup>

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.<sup>3,36</sup> 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.<sup>55</sup> 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.<sup>56</sup> Fragmentation of care across the mental health and primary care systems makes communication and care coordination particularly challenging.<sup>57</sup> A range of integrated healthcare delivery models are being developed and tested with this hope of addressing this long-standing and significant issue.<sup>58</sup>

## 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

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.

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