

# BEST PRACTICES IN: The Treatment of Adults With Schizophrenia: Managing Schizophrenia and Overall Health



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## Introduction

Over the last two decades, the pharmacologic agents available for the treatment of adults with schizophrenia have undergone a dramatic refinement. Whereas first-generation antipsychotic agents generally targeted dopamine, second-generation agents, or atypical antipsychotics, target specific receptor subtypes in the brain. First-generation antipsychotic medications reduced the symptoms of schizophrenia but, frequently induced neurological side effects such as acute dystonic reactions, akathisia, parkinsonism, and tardive dyskinesia, among others, that often limited the usefulness of these treatments.<sup>1</sup>

Second-generation antipsychotic medications have a different receptor binding profile and occupy a variety of specific receptor subtypes such as dopamine D<sub>2</sub>, serotonin 5HT<sub>2A</sub> and 5HT<sub>1A</sub>, histamine H<sub>1</sub>, muscarinic M<sub>1</sub>, and adrenergic  $\alpha_{1b}$  and  $\alpha_2$ . This binding profile is thought to have a different effect on the neurological complications seen with first-generation agents. However, second-generation agents can be associated with a variety of metabolic side effects that may influence patient adherence and overall health. Thus, the contemporary management of schizophrenia requires psychiatrists to consider a patient's psychiatric illness, as well as a patient's general health, presentation, and lifestyle, and how medications and their potential side effects interact with these variables.

## Presentation

Schizophrenia has a prevalence of approximately 1% both in the US and worldwide. Although the popular public perception of schizophrenia is one of homeless men, it actually occurs about equally in men and women. However, there is a marked difference in the age of disease onset between genders, and this difference has an important impact on when, where, and how patients present and the types of medical and social support services available to them.

The average age of symptom onset among men is 18 years, with a typical range of 15 to 25 years.<sup>2</sup> These are transient years during which many male patients may be living independently for the first time, enrolled in college, working a first job, or unemployed, and they are often unmarried and uninsured. Male patients may lack the life skills, financial resources, and social support network to recognize symptoms and proactively seek treatment. Consequently, men are more likely to initially present (or be taken) to and receive treatment from public institutions and to eventually become homeless.<sup>3-5</sup>

Conversely, symptoms of schizophrenia among women begin later—typically after 30 years of age—which is a potentially more stable period of life.<sup>2</sup> At this age, female patients are more likely to have finished college, to have families, employment, health insurance, and social support networks. This combination of factors may positively influence women's health care-seeking behaviors and their willingness and ability to adhere to psychiatric medications. The social and financial stability also suggests that women may be more likely to present to private practices rather than being "taken" to public institutions.

The age of onset and associated life circumstances present a unique set of challenges when treating patients with schizophrenia. For example, a 30-year-old mother of two may be highly motivated to maintain long-term medical therapy, whereas an 18-year-old symptomatic homeless man may be unmotivated and incapable of maintaining a medication regimen. There are many other challenges, as well.

## Challenges in Treating Schizophrenia

In addition to life circumstances, numerous other factors affect medication adherence, the first and foremost of which is convincing a patient that he or she is suffering from a chronic and progressive neurological illness requiring sustained pharmacotherapy. One of the characteristics of schizophrenia is a lack of insight into the disease, and patients may be unwilling to accept or believe that they are sick or experiencing symptoms of schizophrenia.

Even after convincing patients of a pressing need for treatment, the medical therapy, although effective at reducing symptoms, may not completely eliminate them, and patients with persistent or breakthrough symptoms often discontinue therapy. This is especially problematic in the context of the side effect burden of second-generation antipsychotic medications. Side effects such as weight gain, sexual dysfunction, and sedation—side effects that may adversely affect patients' quality of life—especially in the presence of persistent symptoms, often discourage them from continuing treatment.<sup>6</sup> And patients' repeated discontinuation of therapy or unresponsiveness despite sustained treatment often leads to discouragement among physicians. In the face of stagnant clinical improvement, physicians will sometimes reduce treatment to essential minimums and focus only on whether patients are agitated, disruptive, or violent rather than attempting to improve their overall mental and physical health.

Frustration and discouragement may be overcome with effective communication between physicians and patients, provided that physicians recognize that patients perceive side effects differently. Whereas physicians tend to value objective measurements of lipids, blood sugar levels, and symptom control, patients tend to place more importance on subjective measures such as weight gain, sedation, and sexual dysfunction (Table). When talking to patients, it is important that physicians bear in mind that objective measures of a good treatment response and general health are not synonymous with patient satisfaction.

### Antipsychotic Medication Side Effects: Patients' Versus Health Care Providers' Perceptions

Physician Perception	Patient Perception
Lipids	Weight gain
Blood sugar	Hungry
Prolactin	Sexual dysfunction
Calm	Tired
Symptom control	Flat

## Individualized Treatment

Patients with schizophrenia are diverse, as are the disease's underlying causes. Multiple genes that may increase the risk of developing specific symptoms of schizophrenia have been identified. No two patients will present with the same combination of symptoms, symptom severity, or underlying genetic profile. Patients may be paranoid, withdrawn, agitated, or hallucinating or have some combination thereof, and different antipsychotics control different symptoms with varying degrees of efficacy.

Treatments are also selected based on side effect profiles, and managing treatment-related comorbidities—especially cardiovascular comorbidities—is an increasingly important component of treatment. Patients with schizophrenia have a 15 to 25-year shorter life expectancy than the general population, and the leading cause of death among patients with schizophrenia is heart disease.<sup>7,8</sup>

Partnering with primary care physicians to monitor lipids, weight gain, glucose, blood pressure, and other metabolic parameters is now a standard of care, as are controlling and changing modifiable risk factors. Among patients with schizophrenia, modifiable risk factors include

smoking, substance abuse, hypertension, hyperglycemia, obesity, dyslipidemia, and lack of physical fitness.<sup>8</sup> Controlling cardiovascular risk factors has the potential to prolong and improve the health and quality of life of patients with schizophrenia, and exercise may reduce symptoms.

A recent study evaluated the effect of aerobic exercise training (cycling) on the brain in healthy volunteers and patients with schizophrenia.<sup>9</sup> As compared to controls, exercise was associated with increased hippocampal volume and aerobic fitness among patients with and without schizophrenia. Among patients with schizophrenia, the increase in hippocampal volume was also associated with a 35% increase in the *N*-acetylaspartate to creatine ratio, a marker of neuronal integrity in the hippocampus.

Social isolation is another common modifiable risk factor among patients with schizophrenia. Encouraging patients to visit day clinics, support groups, or any social activity or contact can help improve health and quality of life.

These factors all contribute to the ultimate goal of schizophrenia therapy: symptom control and improving overall quality of life. Enabling people to work, develop and maintain relationships, and care for families and themselves—the basics of daily life—are possible with long-term consistent and sustained treatment, avoiding social isolation, and maintaining general physical health and fitness.

Among the largest hurdles to achieving these goals is apathy among physicians. Physicians are too often ready to leave patients symptomatic as long as they are not agitated, disruptive, or aggressive, and do not attempt to control or modify the many modifiable factors such as weight gain and sexual dysfunction that discourage patients from using their medications consistently, correctly, and for sustained periods of time. Overcoming apathy requires physicians' continued commitment to uncovering the individualized, underlying causes of what makes each patient with schizophrenia unique.

## Summary

The contemporary management of schizophrenia goes well beyond simply prescribing medications that suppress patient's symptoms. Successful management requires that physicians address and treat both a patient's entire mental and physical health. For this reason it is also important to consider how medication side effects may affect lifestyle and well-being, as well as how these side effects influence patient adherence to treatment.

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