

Diagnosis, Treatment Options, and Costs of Schizophrenia

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Summary

Schizophrenia is a chronic mental disorder that causes functional impairment in work, interpersonal relationships, and self-care. Both the direct and indirect costs of this disease are significant. Managed care can implement various interventions to improve patient outcomes and manage costs.

Key Points

- Schizophrenia is a costly disease both from a direct and indirect cost perspective.
- Medication nonadherence has a significant impact on costs.
- The costs of schizophrenia treatment can be managed by using available resources more effectively.
- Strong evidence for effectiveness exists for antipsychotic medications, family education, community atreatment teams, supported employment and housing, psychosocial remedial therapies, and case management.
- Managed care can improve outcomes in patients with schizophrenia by utilizing community treatment teams, case management, disease management programs, schizophrenia treatment algorithms, provider partnerships, specialty mental and behavioral health organizations, and Community Mental Health Centers.

SCHIZOPHRENIA IS A PERSISTENT, OFTEN chronic, and usually serious mental disorder affecting a variety of aspects of behavior, thinking, and emotion. Patients with delusions or hallucinations may be described as psychotic. Thinking may be disconnected and illogical. Peculiar behaviors may be associated with social withdrawal and disinterest.

While the word for schizophrenia is less than 100 years old, Kraepelin concretely identified the disease in 1887. Bleuler coined the term we know today based on the Greek words schizo (split) and phrene (mind), and also was the first to describe symptoms in terms of positive and negative. Evidence that schizophrenia is biologically based has accumulated in the past 20 years; genetic advancements offer even more promise of understanding this illness.

About 1 percent of the population develops this disorder. There are both positive and negative symptoms. Positive symptoms are those such as hearing voices and negative symptoms include lack of motivation. There also are cognitive deficits, disorganization, and mood symptoms. About 10 percent of patients with schizophrenia commit suicide during the course of their illness. Compared with someone

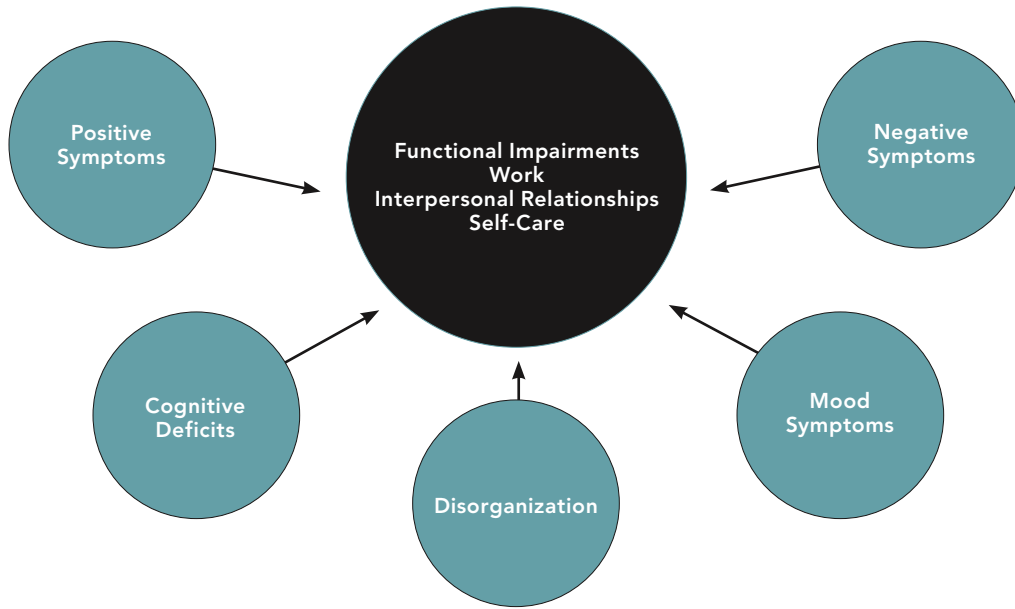
without the disease, these patients have a decreased life expectancy of about 25 years. This has actually worsened over the past 20 years. All of the symptoms of schizophrenia cause functional impairment in work, interpersonal relationships, and self-care (Exhibit 1).¹

The diagnostic criteria for schizophrenia are listed in Exhibit 2.² The differential diagnosis includes schizoid personality, schizophreniform disorder, schizotypal personality, bipolar disorder, and Asperger's Syndrome. Bipolar disorder is frequently misdiagnosed as schizophrenia and the other way around.

Exhibit 3 shows the progression of the course of schizophrenia.³ Like bipolar disorder and major depression, there is a kindling model with schizophrenia, which suggests that the more episodes one has the harder treatment is and the more brain damage that occurs. Current practice is to treat schizophrenia early and for life to limit deterioration of function.

The direct and indirect costs of treating schizophrenia are significant. Inpatient costs have decreased since 1991 while outpatient expenses have increased (Exhibit 4).⁴ This particular direct cost analysis used a direct cost offset to take out the av-

Exhibit 1: Features of Schizophrenia¹



erage cost of regular housing. The bulk of indirect costs come from unemployment (Exhibit 5).⁴

Medication nonadherence, which is a common problem in schizophrenia treatment, has a significant impact on costs. The degree of medication adherence varies over the course of an individual's illness. Overall, about 50 percent of patients are not compliant with their medications. Only 20 to 30 percent of patients will relapse within one year with consistent use of medication whereas 60 to 80 percent will relapse without medication consistency.^{5,6} Because of the increased relapse rate, medication nonadherence increases the risk of hospitalization. In one study of acute care inpatient admissions and hospital days for Medicaid schizophrenia patients attributable to nonadherence, 10,686 acute care hospital admissions occurred due to gaps in treatment. This resulted in 121,838 inpatient days and an approximate cost of \$106 million.⁷ The financial burden of relapse was estimated at \$300 million per year in 1995.⁸ Extrapolating to 2008 dollars the total cost is greater than \$420 million.

Components of schizophrenia treatment that have strong evidence for effectiveness are antipsychotic medications, family education, community treatment teams, supported employment and housing, psychosocial remedial therapies (organized peer support network, clubhouses, etc.), and case management. The costs of schizophrenia treatment can be managed by using available resources more effectively. This includes using protocols for proper administration and timing of psychotherapeutic

agents, using expert consensus guidelines, holding providers accountable for improving patient outcomes, facilitating measurement-based clinical decision making, and utilizing case management and disease management programs.

There are a number of antipsychotics available for use (Exhibit 6). Some of these are available in injectable long acting formulations (depot). The goal of using long acting agents is to improve adherence and prevent relapse. The long acting agents are injected every two weeks [fluphenazine (Prolixin) and risperidone (Risperdal)] or four weeks [haloperidol (Haldol)]. These were widely used in the past but have not been commonly used in the past 10 years because of the introduction of the atypical agents. A meta-analysis of six studies showed significantly lower relapse rates in patients taking depot versus oral antipsychotics ($P < 0.0002$).⁹ Encouraging the use of depot agents is one strategy that managed care can use to improve adherence rates and contain costs.

Refractory symptoms are a common occurrence with schizophrenia. A poor treatment response occurs in 30 percent of patients. An incomplete treatment response occurs in an additional 30 percent or more. Clozapine is the treatment of choice for treatment-resistant schizophrenia. Use of clozapine produces a consistent 30 percent response rate in severely ill, treatment-resistant patients versus four percent with chlorpromazine.¹⁰

The adverse effects of the antipsychotic agents have to be balanced against their efficacy. As a class, the first generation antipsychotics (FGAs) have the

Exhibit 2: DSM IV Diagnostic criteria for Schizophrenia²

A. Characteristic Symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

- (1) Delusions
- (2) Hallucinations
- (3) Disorganized speech (e.g., frequent derailment or incoherence)
- (4) Grossly disorganized or catatonic behavior
- (5) Negative Symptoms, i.e., Affect Flattening, Alogia or Avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other.

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 the disturbance persist for at least 6 months. This 6-month period must include at least 1 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 exclusion: 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 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 Autism 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).

potential to cause sedation, dizziness, anticholinergic effects, extrapyramidal symptoms, agranulocytosis, cardiovascular events, and depression. All of them have at least one “boxed” warning in the FDA approved package labeling. The second-generation antipsychotics (SGAs) have a wide variety of different side effects. These also have at least one “boxed” warning in the package labeling. As a class, most of the SGAs all cause significant weight gain and metabolic syndrome. Ziprasidone (Geodon[®]) and aripiprazole (Abilify[®]) are the two SGAs that do not appear to cause these problems.

After evaluating the available evidence, the Schizophrenia Patient Outcomes Research Team recommended SGAs (other than clozapine) as first choice medications.¹¹ These recommendations do note that weight gain and metabolic effects of the SGAs may alter the choice in an individual patient and are more expensive. The recommendations made no clear statement of preference of SGAs over FGAs in acute or maintenance treatment. Clozapine is recommended for treatment-refractory positive symptoms, hostility, and suicidality. Long-acting injectable antipsychotics are recommended for individuals who do not adhere to oral medication regimens.

When the SGAs first were introduced, many practitioners considered it almost malpractice not to use them over the FGAs because of the reduced incidence of long-term adverse effects such as tardive dyskinesia and benefit for negative symptoms. This assumption has been turned around by the findings from one large, well-designed trial (CATIE).¹² This study compared several SGAs (olanzapine, quetiapine, risperidone, ziprasidone) with perphenazine, a FGA, over 18 months. The medications were similarly effective. Fewer people discontinued olanzapine but it caused significantly more weight gain and metabolic problems. Perphenazine did not cause more EPS than the other medications and was just as effective as three of the four medications. There was no advantage of the newer medications on negative symptoms or cognitive functioning and perphenazine was the most cost effective. Unfortunately, with a relatively short-term study, the difference in rates of tardive dyskinesias was not answered.

Because of the CATIE trial and a similar study from the United Kingdom, the World Psychiatric Association did a comparison of all the available trials.¹³ This analysis stated that antipsychotic treatment needs to be individually tailored to promote optimal recovery. It noted that medications are very

Exhibit 3: Schematic Model of Course of Schizophrenia³

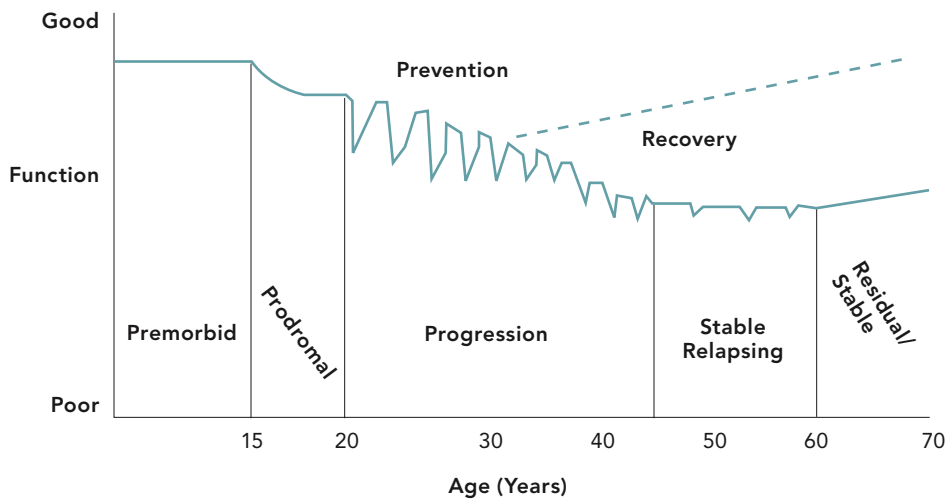
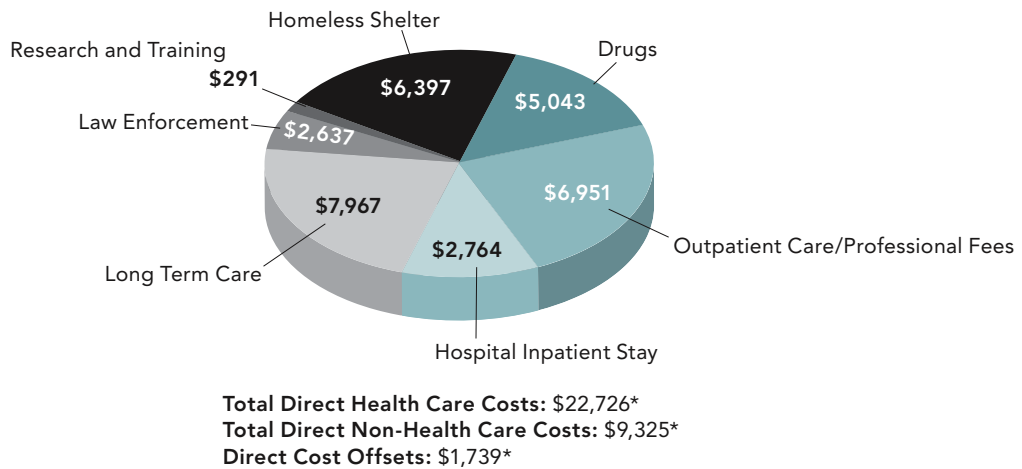


Exhibit 4: Direct Costs of Schizophrenia⁴



*In millions

heterogeneous with substantial differences in side effect profiles. SGAs were found to be inconsistently more efficacious than FGAs with a lower likelihood to cause EPS but associated with more metabolic events. Consistent with other evidence, clozapine was found to be most efficacious in treatment-resistant schizophrenia.

Numerous strategies can be used to improve the outcomes in patients with schizophrenia. One of these is assertive community treatment (ACT). This uses a 24/7 community-based treatment and rehabilitation model. Multidisciplinary teams provide ongoing continuous service, assertive outreach, and support services. Care teams have small, manageable caseloads and provide all key services

to patients. The team adapts itself and the environment to patients' needs. An example would be providing services where the patient lives rather than expecting them to show up for appointments. ACT programs have reduced hospitalizations for severely mentally ill patients by approximately 40 percent.¹⁴ Unfortunately, the ACT model is difficult to replicate successfully.

In one evaluation of schizophrenics with substance abuse receiving ACT versus standard case management (SCM), both groups showed significant reductions in substance use over time.¹⁵ ACT and SCM were not significantly different in cost-effectiveness over three years. SCM was more effective than ACT in the first two years, but ACT became more effi-

Exhibit 5: Indirect Costs⁴

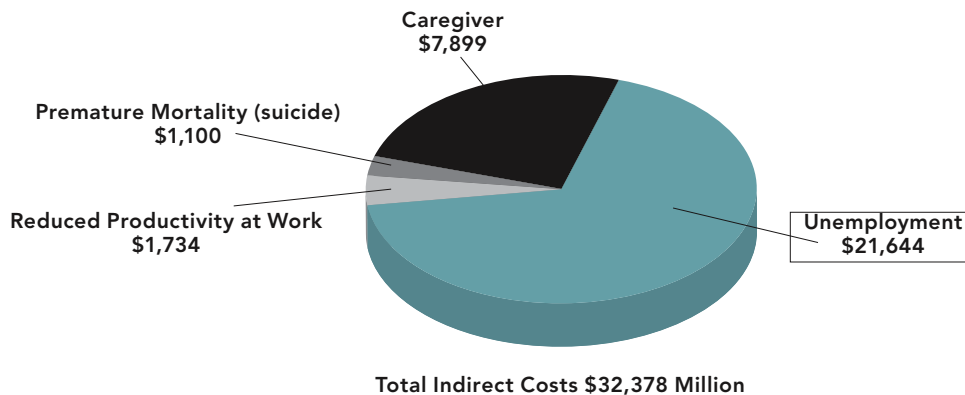


Exhibit 6: Available Antipsychotic Agents

"Typical" Antipsychotics (first-generation or FGAs)	"Atypical" Antipsychotics (second-generation or SGAs)
Chlorpromazine (Thorazine)	Clozapine (Clozaril)
Perphenazine (Trilafon)	Risperidone (Risperdal)*
Molindone (Moban)	Olanzapine (Zyprexa)**
Thiothixene (Navane)	Quetiapine (Seroquel)
Fluphenazine (Prolixin)*	Ziprasidone (Geodon)
Haloperidol (Haldol)*	Aripiprazole (Abilify)
	Paliperidone (Invega)**

*Depot version available
 **Depot version in development

cient during the final year. The SCM program costs were about one-half of ACT costs, but subjects in the SCM group used more mental health center services. Standard case management can be replicated easier over a wide area and group of patients.

High-risk, high cost patients with schizophrenia should be identified and placed in intensive case management programs or ACT. Case managers can ensure patients are receiving evidence-based treatment and can assist with provider-to-provider communication, transportation, and other needs.

Disease management programs are another way to improve patient outcomes. These programs have many potential goals such as to build and strengthen support systems, support physician-patient relationships, increase medication adherence, reduce hospitalizations and length of stay, improve patient function and quality of life, and empower the patient and family with education. They also can be used to improve

practice behavior through clinician and staff education and to improve cost effectiveness of treatment. Interventions that may be utilized by disease management programs include evidence-based practice guidelines, case management, self-management education, patient risk stratification, patient satisfaction surveys, outcomes tracking and reporting, specialized software, computerized data warehouse, automated decision support tools, and callback systems.

Schizophrenia treatment algorithms also can be used to improve cost effectiveness and patient outcomes. These algorithms can be developed with input from mental health experts, literature reviews, and data from consensus conferences. The goals of a treatment algorithm include increased effectiveness of drug therapy to reduce symptoms and improve function, and enhanced quality of clinical decision-making and practice. One example is the Texas Medication Algorithm Project. Clinician and patient/family

materials from this program are available at www.dshs.state.tx.us/mhprograms/tmapover.shtm.

Provider partnerships are another way to improve patient outcomes. Providers can work creatively with care managers to get patients into treatment. This may include having weekend appointments, after-hours services, and home visits. Another creative idea is to negotiate rates with providers for in-hospital visits before patients are stepped down to lower levels of care. The patients are then more likely to follow-up with a provider or group with whom they have had prior contact. Managed care should also consider additional negotiated rates for telephone contact and travel time.

Specialty mental and behavioral health organizations (MBHO) offer unique resources and services that are communicated to providers, patients, and families. Their products may include provider education programs, updated schizophrenia treatment guidelines, consumer treatment guides, communication tools (newsletters, online CME, patient/family education), and peer-to-peer support.

Another way to improve patient outcomes is to contract with Community Mental Health Centers. The payer has to initiate contact because the mental health centers will not. This can provide alternative services not typically provided by the MBHO such as housing, employment services, legal services, assertive community treatment teams, and wrap-around services like respite care and in-home intervention.

Transitions from one provider to another are when patients can be lost to follow-up. To ensure success, payers must ensure transition does not disrupt continuity of care, especially for high-risk schizophrenia patients. Payers should cover patients being treated by out of network providers for 6 months to make transitions smoother.

Payer medical directors have a role in improving payer-provider communication. Their role is often stereotyped as “Dr. No” through denying claims. They can introduce changes that improve medical services through quality improvement initiatives, conduct literature reviews to determine best practices, consult academic experts, and communicate with colleagues before making a medical necessity decision. One area where medical directors are underutilized is working directly with providers in the community.

Managed care can take some immediate actions to improve outcomes in patients with schizophrenia. First should be the identification of outlier patients and providers. Various programs can be implemented to manage these subsets of patients and providers such as an intensive case management program. Another immediate intervention would be educa-

tion of outliers on best practices for schizophrenia management. Managed care should partner with community mental health centers for specialty services that they only provide. Lastly, processes, interventions, and outcomes should be tracked through health information technology.

Conclusion

Schizophrenia is a costly disease with significant impact on all areas of patient functioning. Management of this disease requires a multitude of interventions. By efficiently utilizing available community resources and implementing other strategies such as disease management programs, managed care can improve patient outcomes while minimizing costs. **JMCM**

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