

Balancing Therapeutic Safety and Efficacy to Improve Clinical and Economic Outcomes in Schizophrenia: A Managed Care Perspective

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Abstract

Schizophrenia is a serious mental disorder associated with high morbidity and mortality, reduced life expectancy, and increased economic burden. Antipsychotic agents used for the management of schizophrenia are often associated with undesirable adverse effects, such as weight gain and metabolic abnormalities, contributing to elevated risk of cardiovascular disease, diabetes, and mortality. Contributors to the growing economic burden of schizophrenia include direct (eg, medical care and hospitalization) and indirect costs (eg, lost productivity and mortality). Strategies to reduce these expenditures include the use of generic medications, improving treatment adherence, avoidance of switching antipsychotic therapies, reducing disease relapses, and appropriate management of cardiometabolic disease. Arguably, while pharmacy benefit and managed care strategies (eg, prior authorization, prescription caps, copayments and patient cost-sharing strategies, tiered formulary pricing, and gap coverage) are designed and implemented to reduce healthcare costs, they may have the unintended result of creating barriers to treatment access and thereby contribute to further adverse patient outcomes. Managed care professionals should be cognizant of the drivers of cost and the need for cardiometabolic monitoring to individualize care for patients with schizophrenia. Further, comprehensive disease management plans should be developed that include the monitoring of disease progression and treatment adherence, while factoring in medication and healthcare administration costs.

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For author information and disclosures, see end of text.

The Burden of Disease in Schizophrenia

Despite the ongoing medical research into schizophrenia and the increasing amount of literature that is published every decade, the mental disorder continues to be incompletely understood. The annual incidence of schizophrenia ranges from 8 to 40 cases per 100,000 individuals, or 1 in 10,000 adults, with a relatively similar rate across all continents. In urban areas, the documented incidence of the mental disorder appears to be higher than in non-urban areas, with an overall lifetime risk of developing schizophrenia of approximately 0.7%.^{1,2} Although the cardinal features of positive (ie, impaired reality) and negative (ie, loss of range of affect, impulse, desire, volition, and striving) symptoms are central to schizophrenia, it has become further recognized that the psychotic phase of schizophrenia is preceded by a premorbid phase (ie, cognitive, motor, or social deficits) and a prodromal phase (ie, attenuated positive symptoms and/or functional decline).³ After the psychotic phase of excessive (ie, florid) positive symptoms, the patient enters a stable phase in which negative symptoms occur, with continuing cognitive, social, and functional decline. Following each psychotic episode, there are variable degrees of recovery to the patient's baseline state of well-being. Consequently, disease control in the early stage of treatment is essential.³ In addition, schizophrenia is linked to at least a 1.9-fold increased rate of mortality, relative to healthy individuals, which is not entirely explained by disease-specific factors, such as an expected increased rate of suicide.⁴ One study published in 2008 demonstrated that when comparing their survival with the general population, patients with schizophrenia or schizoaffective disorder 30 years after initial diagnosis had a significantly higher mortality rate. Median survival following diagnosis was 35.9 years for people with schizophrenia and 39.3 years for patients with schizoaffective disorder. The leading causes of death among those patients were cardiovascular disease (CVD) (29%), neoplastic disease (19%), and pulmonary disease (17%).⁵

CVD is very prevalent among patients with schizophrenia. Compared with non-schizophrenia controls in a population-

based study, patients with schizophrenia demonstrated higher rates of CVD (27% vs 17%, odds ratio [OR] 1.76; 95% CI 1.72-1.81) and diabetes (males aged 30 to 39 years, adjusted OR 1.57; 95% CI 1.3-1.91; females age 30 to 39 years, adjusted OR 1.72; 95% CI 1.44-2.04), and were more likely to be of older age and lower socioeconomic status.⁶ The increased risk of CVD associated with schizophrenia is further linked to a reduction in average life expectancy, relative to non-schizophrenic patients, of approximately 20% from 76 years (72 years in men, 80 years in women) to 61 years (57 years in men, 65 years in women). Two-thirds of patients with schizophrenia versus only half of patients without schizophrenia will eventually die of coronary heart disease (CHD).⁷ An examination of the predicted risk of CHD from the large-scale Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, compared with National Health and Nutrition Examination Survey III data, demonstrated a higher 10-year CHD risk in males (9.4% vs 7%; $P = .0001$) and females (6.3% vs 4.2%; $P = .0001$), higher smoking rates (68% vs 35%; $P < .001$), rates of diabetes (13% vs 3%; $P < .001$), and hypertension (27% vs 17%; $P < .001$), and lower high-density lipoprotein (HDL) cholesterol levels (43.7 vs 49.3 mg/dL; $P < .001$).^{8,9}

Evidence has linked weight gain to the observed impaired glucose tolerance, higher rates of diabetes and hypertension, and increased mortality.¹⁰ One study from 2001 estimated that a mean weight gain of 2.5 kg per person would result in 366 additional diabetics and 1833 hypertensive patients per 100,000 people over 10 years, and similarly, a weight gain of 12.5 kg per person would result in an additional 2505 diabetic and 9169 hypertensive patients per 100,000 people. Further, the study linked a 2.5-kg and 12.5-kg weight gain per person to an additional 30 and 751 deaths per 100,000 people over 10 years, respectively.¹⁰ It is well documented that many of the antipsychotic medications typically used to treat schizophrenia are associated with the adverse effect of weight gain.¹¹⁻¹³ To put the impact of medication-induced weight gain into perspective, Fontaine et al found that while clozapine would prevent 492 potential suicide deaths per 100,000 patients with schizophrenia, the weight gain associated with the use of clozapine would also result in 416 additional deaths over the same time period.¹⁰ Despite the clear link between these medications and weight gain, hypertension, and diabetes, it should be noted that patients with schizophrenia have also been reported to have impaired glucose tolerance prior to treatment with antipsychotic medications, suggesting a potential

genetic linkage or susceptibility.^{14,15} All of these factors together highlight the significant burden of disease that is associated with the nonpsychiatric consequences of schizophrenia.

The Cost of Schizophrenia Treatment

Schizophrenia is a complex psychiatric disease that is very challenging to manage appropriately, and treatments are often associated with a high risk of nonpsychiatric morbidity and mortality, including CVD and diabetes. To achieve the delicate balance between efficacy and safety, it is important to examine the cost factors associated with the disease.

The direct and indirect costs associated with schizophrenia are summarized in [Table 1](#).¹⁶⁻¹⁸ Direct medical costs include the expenses associated with treatment, such as psychotherapy, medication, and hospitalization, and the cost of managing complications, such as CVD and diabetes. Direct nonmedical costs include society's cost of managing patients with schizophrenia in the community. CVD is the leading cause of death in the United States and accounts for 17% of all healthcare expenditures in the country. Between 2010 and 2030, the total direct cost (in 2008 dollars) resulting from CVD is projected to triple, from \$273 billion to \$818 billion. During that time, the indirect cost of CVD is also estimated to increase by 61%, from \$172 billion to \$276 billion.¹⁹ The estimated cost of diabetes in the United States was \$245 billion in 2012, including \$176 billion resulting from direct medical costs and \$69 billion from indirect costs, a 47% increase from 2007.²⁰ The overall economic burden of schizophrenia in 2002 was estimated to be \$62.7 billion, with \$22.7 billion in direct healthcare costs, \$7.6 billion in direct non-healthcare costs, and \$32.4 billion in indirect costs.¹⁶

Indirect costs associated with schizophrenia include the loss of productivity and the loss of life. While lost productivity has been shown to have the highest overall impact on the cost of schizophrenia, the direct healthcare expenditures associated with drug therapy, hospitalization, physician/psychiatric treatment, and long-term/day care are also major drivers of the economic burden tied to schizophrenia.¹⁶⁻¹⁸ Relapse of psychotic symptoms and hospital admissions and readmissions are also important, potentially preventable drivers of cost in schizophrenia. According to a study published in 2013, patients with a relapse within the past 6 months increased the cost of care 4-fold relative to patients without a relapse.²¹ Adherence to antipsychotic medi-

Table 1. Breakdown of Cost Factors and Their Relative Contributions to Overall Cost in Schizophrenia¹⁶⁻¹⁸

Cost Factors	Percent of Total	Percent of Category
Direct Medical Costs	36.3	
Drug treatment		22.0-35.9
Outpatient care/professional fees		22.9-30.5
Hospitalization		12.0-27.1
Long-term care or full-day programs		27.9-35.1
Lab and diagnostic tests		1.5
Nurse home visits		2.4
Direct Nonmedical Costs	14.9	
Law enforcement		28.3
Research and training		3.1
Homeless shelters		68.6
Direct Cost Offsets	-2.8	
Living in a home or jail which decreases cost of living		(100.0)
Indirect Costs	51.6	
Unemployment		49.3-66.8
Reduced productivity at work		5.4-23.3
Premature mortality		3.4
Caregiver productivity		8.7-24.4

cation therapy is a critical component of preventing relapse in patients with schizophrenia, because monthly relapse occurs in approximately 3.5% of patients who are maintained on neuroleptics versus 11% for patients who have discontinued their antipsychotic medication.²² Treatment nonadherence is estimated to occur in 7.6% of patients per month in the community setting, and approximately 40% of hospital readmissions for patients with schizophrenia are attributed to nonadherence, with 60% owing to the loss of neuroleptic efficacy.²² A study on factors associated with high schizophrenia-related costs published in 2013 demonstrated that patients with poor perceived health status were more likely to be in the high-cost treatment group, whereas patients who were older or who had a spouse were less likely to be in that high-cost group.²³ Further, in comparison with older patients, younger patients, African Americans, patients with private insurance, or patients in the northeastern United States had higher relative schizophrenia-related direct medical costs, providing intriguing insight into potential drivers of cost for this complicated disease.²³

In addition to the cost of medications, appropriate medication selection is an important cost driver because, depending on the patient, the choice of medication may affect treatment adherence, relapse rate, and hospital

readmission.²⁴ Goals of medication management are to achieve symptomatic remission, functional remission (eg, improved productivity), and an adequate level of subjective well-being, measured by a valid tool, such as the Subjective Well Being Under Neuroleptic Treatment Scale Short Form.²⁴ Despite advances in psychosocial and pharmacologic treatment of schizophrenia, a study published in 2006 revealed that 90% of patients with the disease were unable to achieve the combined triple end point (symptomatic and functional remission with improved well-being) over at least 6 months of treatment.²⁴ “Real-world” studies, which were intended to imitate practice more closely than a typical clinical trial, such as CATIE, the Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1), and the European First-Episode Schizophrenia Trial (EUFEST), compared the less expensive first-generation antipsychotics (FGAs) with second-generation antipsychotics (SGAs) in an effort to establish a superior treatment.^{8,25-28} Unfortunately, the resulting data failed to demonstrate a clear preference for any 1 antipsychotic agent, and instead sparked controversy.²⁹⁻³¹ FGAs have also been compared with SGAs in pharmacoeconomic studies that focused on lower acquisition costs.^{32,33} CATIE demonstrated that perphenazine, in the setting of similar

■ **Table 2.** Relative Comparison of Antipsychotic Medications^{8,12,33,41-43}

Drug	Antipsychotic Efficacy	Weight Gain	Diabetes	Extrapyramidal Symptoms
Second-generation antipsychotic				
Aripiprazole	+	+/-	-	+
Clozapine	+++	+++	+	+/-
Olanzapine	++	+++	+	+/-
Quetiapine	+	++	+/-	+
Risperidone	++	++	+/-	+
Ziprasidone	+	+/-	-	+
First-generation antipsychotic				
Haloperidol	++	+/-	-	++
Low-potency agent	++	++/+++	+/-	+

+ indicates mild increased efficacy or risk; ++, moderate increased efficacy or risk; +++, high increased efficacy or risk; +/- variable effects on risk; -, no increased risk.
Adapted from American Diabetes Association; American Psychiatric Association; American Association of Clinical Endocrinologists; North American Association for the Study of Obesity. *Diabetes Care*. 2004;27(2):596-601.

overall efficacy and safety, was less costly than SGAs due to lower acquisition cost; however, this result has been questioned, because the patients who tolerated the FGA were selected for comparison with the SGA (ie, patients who were initially on an FGA were crossed over to treatment with an SGA).³² A similar conclusion, that the FGA was less expensive and outcomes were similar, was reached when olanzapine (ie, an SGA) was compared with haloperidol (ie, an FGA) in another study published in 2003 by Rosenheck et al.³³ Pharmacoeconomic studies have also compared the SGAs to one another,^{34,40} and several of these studies demonstrated that increased cost containment may occur with improved adherence and/or prevention of relapse/readmission.^{21,34,36} Other studies took a more global approach and evaluated the total cost of treating a patient, including adverse effects, such as the development of weight gain, diabetes, and CVD, and found that these factors contribute significantly to long-term patient outcomes and cost.³⁷⁻⁴⁰ **Table 2**^{8,12,33,41-43} highlights several important differences between antipsychotic agents that affect short- and long-term costs, with the general findings indicating that SGAs are associated with reduced extrapyramidal symptoms but more weight gain than FGAs.

Accounting for the increased risk of developing diabetes and CVD, one of the biggest points of discussion surrounding the optimal management of schizophrenia is whether antipsychotic agents save lives or cost lives.⁴⁴ Selecting the appropriate treatment for patients with schizophrenia is often a practice of balancing risk and benefit; however, it should be noted that patient mortality is generally reduced with pharmacologic treatment.^{44,45}

A study published in 2009 demonstrated that long-term cumulative exposure to antipsychotic medication for 7 to 11 years was associated with a 19% reduction in mortality, and the risk of mortality varied by agents, as shown in the **Figure**.⁴⁵ Another study from 2007 evaluated cardiovascular- and cancer-related mortality in patients receiving antipsychotic medications and found that while the risk of developing non-respiratory cancer was not increased, patients on the highest prescribed doses of antipsychotics had a 1.4- to 4-fold increase in CHD mortality and twice the risk of death from stroke.⁴⁶

Lastly, there are differences in tolerability and efficacy between the various antipsychotics that may lead to frequent medication switches, which is another important cost driver. These therapeutic switches are associated with increased resource utilization, and a study published in 2009 identified a 25% increase in annual total health-care costs per patient who had switched medications.^{47,48} Furthermore, rates of discontinuation can be very high in practice; for instance, 74% by 18 months in the CATIE trial.⁸

Managed Care Implications

Despite studies like CATIE and CUtLASS-1, which supported FGAs as a means to provide cost-effective care, there has been a dramatic rise in SGA prescriptions,^{8,25,49} resulting in concerns of increased medication costs and negative consequences to cardiovascular health.⁴⁹ Health plans, pharmacy benefit managers, and managed care organizations have developed strategies to control these costs, including strategies such as step therapy, prior authorization, tiered formulary pricing,

Figure. Risk of Death During Current Monotherapy, Relative to Perphenazine^{45,a}

A. Risk of death from any cause

	Number of Deaths	Person-Years	Mortality	Crude Rate Ratio (95% CI)	Adjusted HR (95% CI)
Clozapine	182	32,000	5.69	0.53 (0.43-0.65)	0.74 (0.60-0.91)
Perphenazine	193	17,930	10.77	1.00	1.00
Polypharmacy	1481	132,320	11.19	1.04 (0.89-1.21)	1.08 (0.92-1.26)
Olanzapine	264	25,130	10.50	0.98 (0.81-1.17)	1.13 (0.93-1.36)
Thioridazine	227	18,420	12.32	1.14 (0.94-1.39)	1.14 (0.93-1.38)
Risperidone	295	19,410	15.20	1.41 (1.18-1.69)	1.34 (1.12-1.62)
Haloperidol	135	7040	19.19	1.78 (1.43-2.22)	1.37 (1.10-1.72)
Quetiapine	89	5360	16.60	1.54 (1.20-1.98)	1.41 (1.09-1.82)
Other	1234	70,520	17.50	1.63 (1.40-1.89)	1.45 (1.24-1.69)

B. Risk of death from suicide

	Number of Deaths	Person-Years	Mortality	Crude Rate Ratio (95% CI)	Adjusted HR (95% CI)
Clozapine	27	32,000	0.84	0.46 (0.28-0.76)	0.34 (0.20-0.57)
Haloperidol	7	7040	1.00	0.54 (0.24-1.22)	0.61 (0.27-1.37)
Polypharmacy	226	132,320	1.71	0.93 (0.64-1.34)	0.86 (0.59-1.24)
Thioridazine	27	18,420	1.47	0.80 (0.48-1.32)	0.93 (0.56-1.55)
Olanzapine	57	25,130	2.27	1.23 (0.80-1.89)	0.94 (0.61-1.45)
Perphenazine	33	17,930	1.84	1.00	1.00
Risperidone	47	19,410	2.42	1.32 (0.84-2.05)	1.12 (0.72-1.76)
Other	194	70,520	2.75	1.49 (1.03-2.16)	1.55 (1.07-2.25)
Quetiapine	19	5360	3.54	1.93 (1.09-3.39)	1.58 (0.89-2.79)

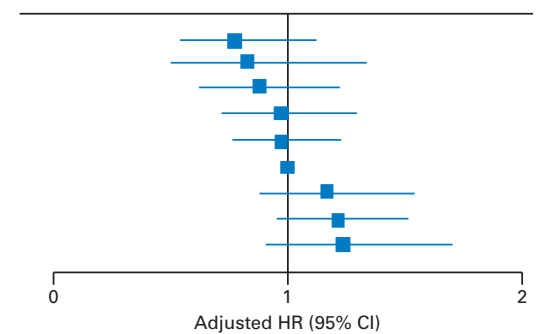
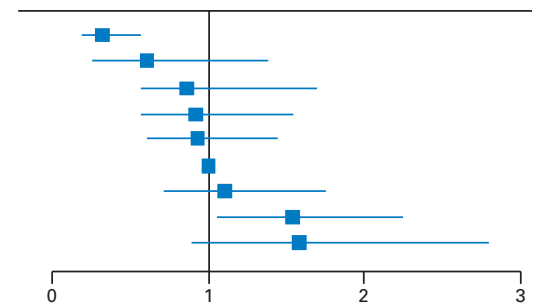
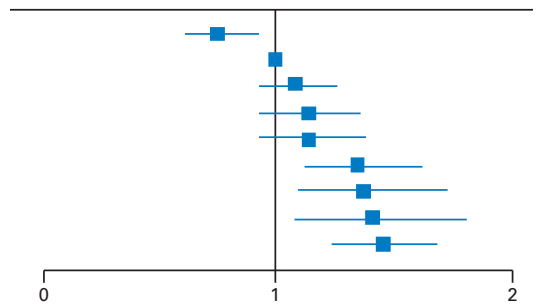
C. Risk of death from ischemic heart disease

	Number of Deaths	Person-Years	Mortality	Crude Rate Ratio (95% CI)	Adjusted HR (95% CI)
Clozapine	42	32,000	1.31	0.25 (0.17-0.35)	0.78 (0.54-1.12)
Quetiapine	21	5360	3.92	0.73 (0.46-1.17)	0.83 (0.52-1.34)
Olanzapine	65	25,130	2.59	0.48 (0.35-0.66)	0.88 (0.63-1.21)
Thioridazine	104	18,420	5.65	1.05 (0.80-1.39)	0.97 (0.73-1.29)
Polypharmacy	522	132,320	3.94	0.74 (0.59-0.92)	0.97 (0.77-1.21)
Perphenazine	96	17,930	5.35	1.00	1.00
Risperidone	119	19,410	6.13	1.15 (0.88-1.50)	1.17 (0.89-1.54)
Other	520	70,520	7.37	1.38 (1.11-1.71)	1.21 (0.97-1.51)
Haloperidol	72	7040	10.23	1.91 (1.41-2.59)	1.24 (0.91-1.69)

HR indicates hazard ratio.

^aMortality indicated as unadjusted absolute risk per 1000 person-years.

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and increased education or counter-detailing, where physicians were educated on the benefits of generic medications.⁵⁰ However, notably, the counter-detailing strategy has been found to be ineffective for reducing SGA prescriptions in a Veterans Health Administration setting, with prescribers citing improved efficacy (48.9%), reduced side effects (29.1%), and increased sleep or sedation (34.5%) as the predominant reasons for choosing an SGA.⁵¹ Another study by Soumerai et al evaluated the implementation of a 3-prescription monthly Medicaid cap on psychotropic medication for patients with schizophrenia, which resulted in an immediate 15% to 49%

reduction in the number of prescriptions filled for anti-psychotic drugs, antidepressants, lithium, anxiolytics, and hypnotics ($P < .01$).⁵² This reduction was associated with an increase of 1 to 2 visit(s) (43%-57%; $P < .001$) per patient per month to community mental health centers, and an increase of 1.2 to 1.4 episodes per patient per month for emergency mental health services and partial hospitalization, but not inpatient hospitalization. The use of medications and mental health services reverted to baseline levels when the Medicaid cap was rescinded, and over the remaining course of the 42-month pilot program, the mental healthcare costs per patient then exceeded the

drug savings 17-fold. Medication costs decreased \$5.14 ± 0.67 per patient per month, while the total cost increased \$139 per patient per month due to increased utilization of other resources.⁵² To a similar degree, programs with prior authorizations, donut hole gaps, and copayments may inadvertently create barriers to medication access and reduce medication continuity, which may further lead to increased utilization of other resources, such as inpatient services.⁵³⁻⁵⁶

Evidence has shown the challenges of maintaining continuity in medication therapy when cost is applied to the patient. Unfortunately, recent legislative activity may not improve this situation, with proposed changes to Medicare Part D that will limit the patient's choice of antipsychotic medications, despite the American Psychiatric Association's stance that having a broader selection of antipsychotics to choose from is necessary due to the various unique drug effects and tolerability.⁵⁷ Furthermore, lack of coverage once patients reach the donut hole, where medication costs are patient out-of-pocket (OOP) expenses, in accountable care organization models may lead to an increase in self-rationing of medications by the patients and consequent hospitalizations, because 56% of patients with schizophrenia are expected to hit the gap.^{55,58} In addition, mental health parity rules may actually have the opposite effect by limiting certain benefits, like residential coverage or copayment requirements, resulting in further patient OOP expenses.⁵⁹

Merging Clinical Data and Treatment Pathways to Improve Patient Care

Based on compiled prescription data, patients with schizophrenia are primarily treated by psychiatrists and general practitioners, who prescribe 49% and 37% of antipsychotic prescriptions, respectively.⁶⁰ However, published studies have revealed that guideline compliance is poor in outpatients.^{61,62} There are currently 5 major guidelines/algorithms developed for the treatment of schizophrenia in the United States: the American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia⁶³; the Schizophrenia Patient Outcomes Research Team treatment recommendations⁶⁴; the Texas Medication Algorithm Project antipsychotic algorithm for schizophrenia⁶⁵; the International Psychopharmacology Algorithm Project⁶⁶; and the Expert Consensus Guidelines.⁶⁷ There are also European guidelines, including the recently released National Institute for Health and Clinical Excellence schizophrenia guide-

line from the United Kingdom, and several others.⁶⁸⁻⁷⁰ It is important to note that each guideline may differ slightly in scope, focus, and goals as a result of using different criteria for its establishment. Although CATIE and CUtLASS-1 supported the first-line use of FGAs, it should be recognized that these studies selected patients who tolerated FGAs to compare with the use of SGAs, and in reality, choosing an appropriate antipsychotic may rely more on patient-specific factors, as outlined earlier in this supplement.^{8,13,25,29,71,72} Unfortunately, current cost-containment strategies may restrict access to an optimal medication therapy based on patient-specific factors, which would actually result in further use of costly healthcare services that might have otherwise been avoided, such as intensive outpatient follow-up or (re)hospitalization.⁵² As mentioned in an article published in 2010, although it is reasonable to attempt the first-line use of an FGA from a cost-effectiveness perspective, "We [practitioners] are forced to acknowledge that [the] choice of antipsychotic is (as it was when we had only FGAs) guided largely by side effects [experienced by the patient]."^{71,72}

Perhaps the most important potential adverse effects to manage when using FGAs or SGAs in patients with schizophrenia are metabolic abnormalities and/or CVD. Although extrapyramidal symptoms and tardive dyskinesia can increase mortality, CVD continues to be the greatest contributor to death in patients with schizophrenia.^{5,7,43} Concordance with guidelines and treatment recommendations to monitor metabolic risk are low, with only 60% to 70% of patients with schizophrenia having their blood pressure and triglycerides monitored, 41% to 48% of patients having their cholesterol, glucose, and weight monitored, and less than 25% of patients having their lipids and glycosylated hemoglobin monitored.⁷³

Consequently, the National Committee for Quality Assurance (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS) 2014 contains 4 new performance measures to increase accountability in healthcare for the benefit of patients with schizophrenia.⁷⁴ HEDIS measures were implemented to establish accountability in healthcare and to aid physicians in quality improvement by measuring quality at the health plan level for purchasers of healthcare.⁷⁴ As mentioned, prior to HEDIS, concordance with guideline recommendations for diabetes and CVD monitoring in schizophrenia was low.⁷¹ The new measures for schizophrenia (Table 3⁷³⁻⁷⁵) were first released in 2013 and are also contained in the 2014 update.⁷⁴ The

Table 3. NCQA HEDIS 2014⁷⁴

- Diabetes screening for people with schizophrenia or bipolar disorder who are using antipsychotic medications
 - o The percentage of patients 18-64 years of age with schizophrenia or bipolar disorder who are not diabetic, but who, during the measurement year, were dispensed an antipsychotic medication and had a diabetes screening test, a glucose test, or a hemoglobin A1c (HbA1c) test, as identified by claim/encounter or automated laboratory data
- Diabetes monitoring for people with diabetes and schizophrenia
 - o The percentage of patients 18-64 years of age with schizophrenia and diabetes who had both an LDL-C test and an HbA1c test during the measurement year
- Cardiovascular monitoring for people with cardiovascular disease and schizophrenia
 - o The percentage of patients 18-64 years of age with schizophrenia who had an LDL-C during the measurement year and selected cardiovascular indicators (acute myocardial infarction, coronary artery bypass graft procedure, or percutaneous coronary intervention) in the measurement year or an acute inpatient or outpatient visit with a diagnosis of ischemic vascular disease in both the measurement year and the year prior
- Adherence to antipsychotic medications for individuals with schizophrenia
 - o The percentage of patients 19-64 years of age during the measurement year with schizophrenia who were dispensed and remained on an antipsychotic medication for at least 80% of their treatment period

HEDIS indicates Healthcare Effectiveness Data and Information Set; LDL-C, low-density lipoprotein cholesterol; NCQA, National Committee for Quality Assurance. Reproduced with permission from HEDIS 2014, Volume 2: Technical Specifications for Health Plans by the National Committee for Quality Assurance (NCQA). To purchase copies of this publication, contact NCQA Customer Support at 888-275-7585 or visit www.ncqa.org/publications.

HEDIS measures relating to schizophrenia are expected to improve monitoring, and consequently treatment, of diabetes and CVD in these patients, and also focus on improving treatment adherence.⁷⁴ As noted previously, CVD is the leading cause of death in schizophrenia, so improved identification and management of CVD and diabetes is expected to reduce mortality.^{6,7} In addition, antipsychotic treatment for schizophrenia has been linked to reduced mortality and resource utilization, so efforts to improve compliance should improve those outcomes.^{45,52} Identifying patients at risk for CVD, diabetes, and treatment nonadherence is a paramount first step in improving patient mortality outcomes in schizophrenia.

Once a patient is identified, an individualized treatment plan is required. Due to the pitfalls associated with switching medications and the nuances in efficacy, adverse effects, tolerability, and patient adherence among the various agents, it is likely that the metabolic and cardiovascular consequences associated with SGA therapies cannot be alleviated by simply discontinuing treatment.^{22,47,48,71} Fortunately, patients with schizophrenia can still be successfully managed with SGAs, as long as they are monitored for the metabolic and cardiovascular adverse effects of such treatment. A position statement from the European Psychiatric Association, supported by the European Association for the Study of Diabetes and the European Society of Cardiology, provides monitoring and treatment recommendations.⁷⁵ These guidelines provide recommendations for cardiovascular risk assess-

ment and management by requiring the following for all patients with severe mental illness first encountered by a clinician and all patients beginning or switching medication: A thorough history; examination of body weight, blood pressure, waist circumference, and body mass index; laboratory assessment of fasting glucose and lipids, total cholesterol, low-density lipoprotein cholesterol, HDL cholesterol, and triglycerides; and counseling on smoking cessation, food choices, and physical activity. Then, based on the risk assessment findings, the guideline provides recommendations for treatment, type, and timing of follow-up monitoring.⁷⁵

Medication adherence is also a critical component of care for patients with schizophrenia, and intensive counseling alone does not appear to improve outcomes.⁷⁶ Mitigating or eliminating high costs to the patient and selecting an antipsychotic agent that is efficacious and well tolerated are the best strategies to improve treatment adherence. The use of long-acting injectable formulations is one such method that may achieve a higher rate of compliance to therapies for schizophrenia, and may reduce disease relapse and hospital (re)admission in those who are nonadherent to oral therapies (even though studies have failed to show improvement in unselected populations, because they included all patients rather than only those who were nonadherent to therapy).⁷⁷⁻⁷⁹

Conclusion

The challenges outlined in this article underscore the

currently unmet need for managed care professionals to consider the whole picture when attempting to minimize the high costs associated with treating schizophrenia. While SGAs, the standard of care for schizophrenia, have certainly improved patient outcomes, disease relapse, and rates of hospital admissions, it is crucial to individualize the treatment of patients with the disease and to closely monitor the associated metabolic and cardiovascular consequences to prevent further poor clinical and economic outcomes downstream. The implementation of HEDIS and quality measures is expected to improve monitoring for adverse metabolic and CVD outcomes and improve medication adherence, resulting in improved overall care of patients with schizophrenia. Managed care professionals must translate the available evidence into comprehensive disease management plans that include stringent monitoring of disease progression and treatment adherence, and effectively balance the implementation of best clinical practices with cost-containment strategies.

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