Cost-Sharing Effects on Adherence and Persistence For Second-Generation Antipsychotics In Commercially Insured Patients

Teresa B. Gibson, PhD, Thompson Reuters (Healthcare) Inc.; Yonghua Jing, PhD, Bristol-Myers Squibb; Edward Kim, MD, MBA, Eisai Inc. (formerly Bristol-Myers Squibb); Erin Bagalman, MSW, Thomson Reuters (Healthcare) Inc.; Sara Wang, PhD, Thomson Reuters (Healthcare) Inc.; Richard Whitehead, (formerly of Otsuka America Pharmaceutical Inc.); Quynh-Van Tran, PharmD, Otsuka America Pharmaceutical Inc.; Jalpa A. Doshi, PhD, University of Pennsylvania School of Medicine

ABSTRACT

Purpose: To assess the relationship between patient cost-sharing (e.g., copayments or coinsurance) and adherence and persistence to second-generation (atypical) antipsychotic (SGA) medications.

Design and methodology: A retrospective, observational study of adults aged 18–64 years with schizophrenia or bipolar disorder (n=7,910) who initiated SGA medications with employer-sponsored insurance in the 2003–2006 MarketScan Commercial Claims and Encounters Database.

Adherence was defined as percent of days covered in each calendar quarter. Persistence was defined as days from initiation of SGA to the first 90-day gap in medication on-hand.

Generalized Estimating Equations were used to determine the effects of cost-sharing on adherence to SGA medications based on patient-quarter data.

A Cox proportional hazards model with patient cost-sharing as a time-varying covariate estimated the effects on persistence with SGA medication.

Principal findings: Higher cost-sharing was associated with a lower likelihood of adherence. When compared to plans with cost-sharing below $10, adherence rates were approximately 27% lower for patients in plans with SGA cost-sharing of $50 and above and about 10% lower for patients in plans with cost-sharing between $30 and $50. In both cases, the reduction in adherence was significant. Higher cost-sharing was also associated with a shorter time to discontinuation (HR: 1.028; 95% CI [1.006–1.051]).

Conclusion: High SGA cost-sharing appears to be a financial barrier to SGA medication compliance, especially when cost-sharing levels exceeded $30.

Our findings have implications for health plans, employers, and policymakers who have, or are, contemplating establishing cost-sharing tiers for SGA medications for commercially insured patients with serious mental illnesses.

Corresponding author
Teresa B. Gibson, PhD
Director, Health Outcomes
Healthcare & Science
Thomson Reuters
777 E. Eisenhower Parkway
Ann Arbor, MI 48108
D 734 913 3481
F 734 913 3850
M 734 223 5233
teresa.gibson@thomsonreuters.com

Disclosure of interests: Current or former employees, or consultants for Bristol-Myers Squibb: YJ, EK, TG, SW, EB, JAD; Current or former employees of Otsuka America Pharmaceutical Inc.: QVT, RW; Consultant for Eli Lily & Company: JAD
Acknowledgments: This study was funded by Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd. Authors would like to thank Tony Hebden, PhD, from Bristol-Myers Squibb for his helpful comments on the manuscript.

INTRODUCTION

Approximately 6% of adults in the United States suffer from serious mental illness (NIMHa 2009). Schizophrenia is characterized by disordered thinking, delusions, hallucinations, movement disorder, social withdrawal, and cognitive deficits; the annual prevalence is estimated at 1.1% of U.S. adults (NIMHb 2009). Bipolar disorder causes dramatic changes in mood, energy level, and daily functioning; the annual prevalence is estimated at 2.6 (NIMHa 2009) to 4.4% (Merikangas 2007) of U.S. adults. Both conditions present significant barriers to the health and wellbeing and require long-term pharmacological management. Antipsychotic medications, specifically second-generation antipsychotics, have become the cornerstone of management of both these conditions.

Compliance with these medications, however, is often poor among patients with schizophrenia or bipolar disorder. Using data from the Veterans Affairs (VA) National Psychosis Registry, a study of patients with bipolar disorder found that 51.9% were adherent to oral antipsychotic medications (Sajatovic 2006). A study of VA patients with schizophrenia found that 58.5% were adherent to SGA medications (Valenstein 2004). A study of Medicaid enrollees with schizophrenia reported that 60% of patients were adherent to antipsychotic medication or had excess prescription fills (Gilmer 2004).

Given the negative outcomes asso-

ciated with noncompliance to antipsychotic medications among patients with schizophrenia and bipolar disorder (Gianfrancesco 2008; Gilmer 2004; Hassan 2009), understanding the factors that contribute to noncompliance is important. Poor medication response and medication intolerability were the primary reasons for discontinuation among patients with schizophrenia in a pooled analysis of data from four clinical trials (Liu-Seifert 2005). To support long-term patient compliance, antipsychotic management has focused on minimizing side effects (Cutler 2008). However, side effects may not be the only factor contributing to noncompliance with SGA medications.

Extensive evidence demonstrates the negative effect of higher patient cost-sharing on medication compliance and the associated adverse impact on health care utilization and costs among patients with chronic conditions such as diabetes and cardiovascular disease (Gibson 2005; Goldman 2007). However, few studies have assessed the relationship between patient cost-sharing and antipsychotic medication adherence and health care utilization among patients with schizophrenia and bipolar disorder. A study of schizophrenia patients conducted in the early 1990s reported a reduction in the use of mental health drugs and increased nursing home admissions and use of acute mental health services in response to the imposition of a three-per-month limit on covered prescriptions in the New Hampshire Medicaid program (Soumerai 1991; Soumerai 1994). A recent study reported that an increase in VA copayments from $2 to $7 resulted in a sharp decrease in psychiatric prescription refills, coupled with an increased psychiatric admission risk in veterans with schizophrenia; however, the effect of the prescription copayment increase on antipsychotic medication refills was not separately assessed (Zeber 2007). Some evidence exists regarding the relationship between patient cost-sharing and compliance with schizophrenia-related medications. One study of the implementation of a copayment policy in a state Medicaid program noted a decline in the utilization of medications used to treat schizophrenia after the introduction of the policy (Hartung 2008). Another study of Medicare enrollees with supplemental drug coverage did not find lower rates of utilization of SGAs for patients with less generous coverage (Slade 2005). Furthermore, no similar studies have been conducted in commercially insured patients with schizophrenia or bipolar disorder.

The purpose of this retrospective analysis was to assess the relationship between patient cost-sharing for SGA medications and compliance with SGA medications, in terms of both persistence and adherence, among a population of commercially insured patients with schizophrenia or bipolar disorder.

METHODS

Data source

This analysis used data from the Medstat MarketScan Commercial Claims and Encounters Database, which contains the health care experience of tens of millions of individuals annually who have commercial health insurance provided primarily by large self-insured employers. The database includes detailed spending and utilization data for health care services provided in both inpatient and outpatient settings, covered by a variety of plan types, including preferred provider organizations, point-of-service plans, indemnity plans, and health maintenance organizations. Medical claims are linked to outpatient pharmacy claims and enrollment data using unique enrollee identifiers. No institutional review board (IRB) approval was required because the database meets criteria for a limited-use dataset in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Study population

Adult patients (aged 18–64 years) with at least one inpatient or two outpatient records carrying ICD-9-CM diagnosis codes for bipolar disorder (296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.8x) or schizophrenia (295.xx) were found in the MarketScan Database during the period of 2003–2006. At least one prescription fill for one of five SGA medications (aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone) was required for inclusion in the study. At present, all of these medications are approved by the FDA for these indications.

For each patient, the date of the first observed prescription fill for SGA medication was the index date. Patients were required to have 12 months of continuous enrollment with no prescription fill for an SGA medication prior to the index date, in order to ensure that the index prescription fill was the beginning of the episode of treatment. A minimum 24-month period of continuous enrollment following the index date was required. To assess adherence with and duration of SGA treatment, patients were followed through December 31, 2006 or through disenrollment, whichever was earlier. The maximum follow-up time was 48 months. Patients were excluded if they had any indication of pregnancy, institutionalization in a long-term care or assisted living facility, use of depot SGA medications, use of clozapine, prescriptions for multiple SGA medications on the index date, or a fixed-dose combination SGA/antidepressant at index. These criteria resulted in a sample of 7,946 patients. Another 36 (0.5%) patients were excluded if they had missing values for key variables in our analysis such as SGA cost-sharing. The final sample consisted of 7,910 patients.

Study design

We studied this cohort of patients over time in two ways to examine adherence and persistence as a function of cost-sharing. First, adherence to atypical antipsychotic medications (as measured by the percent of days covered [PDC] in each quarter) was assessed using a panel-data approach (repeated measures) with one observation per patient per calendar quarter through December 31, 2006 or disenrollment. The repeated measures approach captures variation over time and across patients. Within this context, adherence was measured in each quarter and modeled as a function of cost-sharing, along with the covariates: sociodemographic characteristics, income, plan type, health status, medication, and time.

Second, persistence with SGA medication was analyzed from the index date (defined as the date of the first SGA prescription) with a variable-length follow-up period through December 31, 2006, discontinuation or disenrollment using survival analysis techniques and the same set of covariates. Patients who disenrolled without discontinuing SGA treatment were flagged as censored.

OUTCOME MEASURES

Adherence

Adherence to SGA medication was defined as the percent of days covered in each quarter. The PDC is the ratio of the number of "usable" days supplied from all refills to the number of days in the quarter following (and including) SGA initiation. To calculate the PDC, each day was evaluated as "covered" or "not covered" by a refill. If all days were covered by an SGA refill, then the PDC was 100%.

The end date of each SGA prescription was calculated by the fill date plus the day's supply of the prescription. The days supplied on each prescription were retained and added to the fill date to determine the end date for the "usable" supply of prescription drugs. The end date for the usable supply of prescription drugs was extended as refills were made.

If a refill for the same prescription drug was made before the end date of the previous prescription, the days' supply for the new prescription was appended to the end date for the previous fill. If a refill was made after the end date of the previous prescription, the days between the two prescriptions were counted as "uncovered" (and the PDC was less than 100%).

If a prescription for another SGA was filled while the patient still had a usable supply of the first drug on-hand (prior to the end date of the previous drug), no double-counting of days occurred. The patient's end date of days on hand was extended only if the end date for the new prescription drug fell outside the end date of the previous prescription drug. Consistent with previous studies, patients were classified as adherent to SGA medications if the PDC was greater than or equal to 80% (Choudhry 2009; Lage 2009; Woltmann 2007).

Persistence

Persistence with SGA medication was the duration of time a patient remained on SGA medication, measured as days from initial prescription until a continuous gap in treatment of at least 90 days (equivalent to 3 times a 30-day supply), a conservative measure of persistence that has been used in previous studies (Dezii 2001).

EXPLANATORY VARIABLES

SGA copayment index

The main independent variable of interest was patient out-of-pocket cost-sharing for SGA medications. Cost-sharing for SGA medications was measured using a price index calculated for each employer/plan combination during each calendar quarter in the study period. For example, the SGA copayment index in a given quarter represents the SGA copayment or coinsurance amount that a patient faced (as opposed to paid) under their specific plan during that quarter. When measured in this way, a price was determined for each SGA in the patient's plan even if a patient did not fill a prescription for the drug. Within each employer/plan/quarter combination, the SGA copayment index was based on the plan level copayment amount for each SGA medication (standardized to a 30-day supply) and a weighted average of these amounts calculated based on the proportion of the fills for each SGA medication in that plan (Chernew 2008).

Other cost-sharing variables

Other variables included whether prescription drug cost sharing was in the form of coinsurance (as opposed to copayments) within each combination of employer and health plan offering for each calendar quarter in the study period.

As outpatient physician visit cost-sharing amounts have been associated with reductions in the use of prescription drugs (Joyce 2002), the patient copayment (or coinsurance) amount per office visit was calculated at the employer/plan level in each calendar quarter during the study period.

Control variables

Control variables included psychiatrist visits, socio-demographic characteristics, and clinical characteristics. Patients with any psychiatrist visit during the prior year were flagged. Socio-demographic characteristics included age in years, gender, employee status (versus spouse or dependent), and income. Median household income from the 2000 U.S. Census was merged onto the file by ZIP code of residence.

Patients identified with any diagnosis of schizophrenia (as opposed to bipolar disorder) were flagged. For each patient, the number of psychiatric diagnosis groups (PDGs) (Ashcraft 1989) was counted during the previous year. There are 12 possi-

ble PDGs, which are aggregated from ICD-9-CM diagnosis codes for mental health problems. Examples include alcohol use disorders, other substance use disorders, depression, bipolar disorder, post-traumatic stress disorders, and schizophrenia. The Charlson Comorbidity Index (CCI) (Romano 1993) is an aggregate measure of comorbidity created using select diagnoses associated with chronic disease. The CCI was defined in the previous year and was used to control for comorbid conditions in the study population.

Statistical analyses

Generalized Estimating Equation Models were employed to estimate the relationship between cost-sharing and SGA adherence (PDC ≥ 80%) with a binomial family and a logit link. Explanatory and control variables (sociodemographic characteristics, income, plan type, and time) were measured in each quarter and clinical characteristics were measured over the previous year. Standard errors were adjusted for clustering by patient over time.

A Cox proportional hazards model was used to estimate the relationship between cost-sharing and SGA medication persistence, defined as length of time from initiation of an SGA to discontinuation (or was right-censored, a statistical term meaning that discontinuation could fall outside the length of the measurement window), using the same explanatory variables (except time). Cost-sharing variables were time-varying covariates.

If higher cost-sharing is associated with lower compliance (i.e., persistence and/or adherence), a question arises: At what level(s) of cost-sharing does compliance drop off? In order to identify thresholds, SGA copayment was modeled as a continuous measure and in $10 increments.

RESULTS

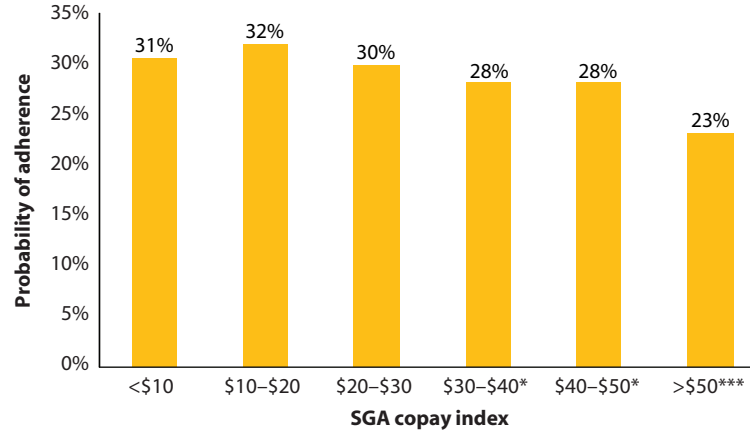
The study sample was made up of 7,910 patients, of whom 1,392 were identified with schizophrenia and 6,518 were identified with bipolar disorder. Table 1 displays the demographic and clinical characteristics of the sample. The mean age was 42.79 years (SD 11.86). The majority of patients were female (62%) and lived in urban areas (83%). Employees comprised 52% of the sample and spouses comprised 38% of the sample. Pluralities lived in the South (36%) and were enrolled in preferred provider organizations (44%).

Table 1 also presents the unadjusted outcome measures in our study sample. Less than a third (31.5%) of the patient-quarter measurements were classified as adherent at PDC≥80%. The mean time from index date to a 90-day gap in treatment was 285.38 days (SD 313.69). In the index quarter, the mean SGA copayment index was $22.89 (SD 13.17). The median SGA copayment index was $22.07, the 25th percentile was $11.74, and the 75th percentile was $29.62 in the index quarter. Approximately 76% of patients had a copayment index below $30, 21% had a copayment index between $30 and $50, and the remainder (about 3%) had a copayment index of $50 or more in the index quarter (not shown).

Table 2 displays the regression results from the adherence and persistence models with continuous measures of copayment index. In the adherence model, an odds ratio greater than 1 indicates a higher probability of adherence; in the persistence model, a hazard ratio less than 1 indicates a lower risk of a 90-day gap, meaning greater persistence. A higher SGA copayment was associated with lower odds of adherence (OR: 0.931; 95% CI [0.907–0.955]) and a shorter time to discontinuation, i.e., lower persistence (HR: 1.028; 95% CI [1.006–1.051]).

Figure 1 displays the results of the predicted probability of adherence estimated from adherence models in $10 increments of the SGA copayment index. Compared to SGA copayment index of less than $10, none of the increments below $30 ($10–$20, $20–$30) differed significantly at p<0.05; however, at values between $30 and $50, there was a 3 percentage point drop-off in the quarterly predicted probability of adherence from 31% to 28% (p<0.05)

FIGURE 1
Predicted probability of adherence



Note: <$10 is the reference category, * p<0.05, *** p<0.001
Adjusted results estimated using generalized estimating equations with binomial family and logit link.

TABLE 1
Demographic and clinical characteristics

	N = 7,910	
	n	%
Age (mean, SD)	42.79	11.86
Female	4,907	62.0%
U.S. census region		
Northeast	682	8.6%
North Central	2,611	33.0%
South	2,880	36.4%
West	1,707	21.6%
Unknown region	30	0.4%
Urban residence	6,557	82.9%
Median household income in 000s (mean, SD)	47.25	16.28
Relationship to employee		
Employee	4,077	51.5%
Spouse	2,986	37.8%
Dependent	847	10.7%
Insurance plan type		
Indemnity plan	1,462	18.5%
EPO/point of service (POS)	1,058	13.4%
Preferred provider organization	3,512	44.4%
Health maintenance organization	1,695	21.4%
Capitated POS	163	2.1%
Psychiatric visit (lagged)	5,192	65.6%
Charlson comorbidity index score (mean, SD) (lagged)	0.45	1.03
Psychiatric diagnosis groups (lagged)		
PDG1: Organic mental disorders	586	7.4%
PDG2: Alcohol use disorders	640	8.1%
PDG3: Opioid and other substance use	874	11.1%
PDG5: Other psychotic disorders	1,223	15.5%
PDG7: Major depressions	2,717	34.4%
PDG8: Other affective disorders	1,971	24.9%
PDG9: Post traumatic stress disorders	204	2.6%
PDG10: Anxiety disorders (NOS)	1,878	23.7%
PDG11: Personality disorders	249	3.2%
PDG12: Other mental disorders	2,578	32.6%
Qualifying diagnosis		
Schizophrenia	1,392	17.6%
Bipolar disorder	6,518	82.4%
Prescription drug use pre-index		
Conventional antipsychotic use	447	5.7%
Mood stabilizer use	6,399	80.9%
Year of index SGA prescription		
2003	2,257	28.5%
2004	2,818	35.6%
2005	2,835	35.8%
Cost-sharing at index quarter		
SGA copayment index (mean, SD)	22.89	13.17
SGA coinsurance flag	1,080	13.7%
Office visit copayment (mean, SD)	20.52	14.22
Outcomes		
Percent adherent (PDC≥80%) (all patient-quarters)	—	31.5%
Days from index date to 90-day gap (mean, SD)	285.38	313.69

and a larger, additional 5 percentage point drop-off to 23% at $50 or more ($p<0.01$). To further examine effects at $30, both adherence and persistence models were replicated with the SGA copayment index collapsed into a binary indicator (≥$30). SGA copayment index of $30 and above was associated with lower probability of adherence (OR: 0.879; 95% CI [0.827–0.934]) and shorter time to discontinuation (HR: 1.077; 95% CI [1.016–1.143]).

A Kaplan-Meier curve was also generated showing the risk of discontinuation over time for patients with index copayments at incremental costs. In Figure 2, the hazard curve for patients with copayments between $30 and $50 separated visibly from the curves for patients at lower copayments, while the separation for copayments at or above $50 was more obvious. These observations indicate a higher hazard of discontinuation at these levels of cost-sharing.

DISCUSSION

This study contributes new evidence to the literature regarding the impact of patient cost-sharing on medication compliance among patients with schizophrenia or bipolar disorder. Among a population of adults with schizophrenia or bipolar disorder who have employer-sponsored health insurance, higher cost-sharing for SGA medications was associated with lower adherence to and persistence with SGA medication.

The finding that higher cost-sharing is associated with lower adherence is consistent with prior studies in patients with other common chronic conditions (Gibson 2005; Goldman 2007). This study extends previous research on cost-sharing and medication adherence by identifying the largest effects at $50 and higher, and to a still significant but lesser extent $30 or higher, at which point both persistence and adherence on SGA medications are lower. While

TABLE 2

Adherence and persistence, continuous measure of SGA copayment index

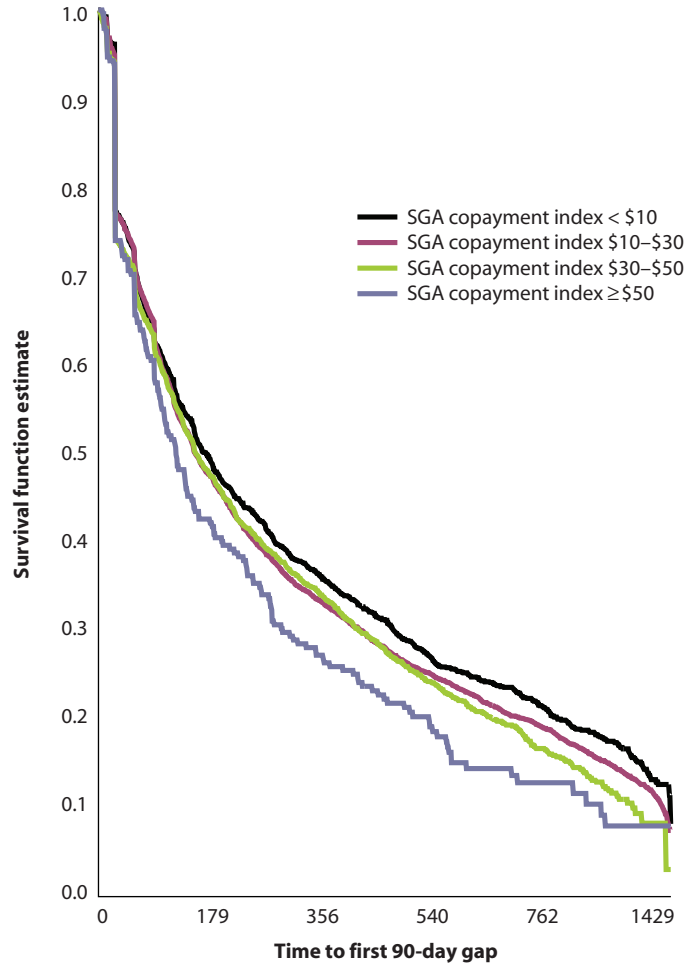
	Adherence model (% adherent)			Persistence model (Time to 90-day gap)		
	N = 67,124 patient-quarters among 7,910 patients			N = 7,910 patients		
	Percent adherent = 31.51%			Percent censored = 17.43%		
Variable	Odds ratio	95% odds ratio confidence limits		Hazard ratio	95% hazard ratio confidence limits	
SGA copayment index	0.931	0.907	0.955	1.028	1.006	1.051
Office visit copayment	0.968	0.943	0.995	1.014	0.992	1.037
Any coinsurance on SGA	1.001	0.921	1.089	0.984	0.904	1.072
Age	1.018	1.015	1.022	0.991	0.988	0.993
Female	1.066	0.992	1.145	0.993	0.941	1.047
U.S. census region						
Northeast	0.991	0.857	1.147	1.025	0.932	1.127
North Central	1.062	0.973	1.158	0.957	0.898	1.021
West	1.071	0.966	1.187	0.934	0.867	1.006
Urban residence	0.949	0.865	1.041	1.042	0.971	1.117
Median household income in 000s	1.002	1.000	1.004	1.000	0.998	1.001
Relationship to employee						
Spouse	1.159	1.077	1.247	0.944	0.894	0.997
Dependent	1.474	1.282	1.693	0.887	0.801	0.981
Insurance plan type						
Indemnity plan	1.008	0.913	1.112	0.994	0.917	1.078
EPO/point of service (POS)	0.953	0.865	1.049	1.013	0.938	1.093
Health maintenance organization	0.944	0.862	1.034	1.114	1.037	1.196
Capitated POS	1.111	0.893	1.382	0.957	0.803	1.141
Psychiatric visit	0.841	0.797	0.886	1.010	0.957	1.065
Charlson comorbidity index score	0.998	0.971	1.026	1.024	0.999	1.050
Psychiatric diagnosis groups						
PDG1: Organic mental disorders	0.930	0.836	1.035	0.933	0.845	1.030
PDG2: Alcohol use disorders	1.012	0.912	1.123	1.027	0.934	1.129
PDG3: Opioid and other SUD	0.902	0.822	0.989	1.113	1.027	1.207
PDG5: Other psychotic disorders	0.938	0.862	1.022	0.976	0.903	1.055
PDG7: Major depressions	0.946	0.885	1.012	0.976	0.924	1.030
PDG8: Other affective disorders	0.982	0.920	1.049	0.942	0.889	0.998
PDG9: Post traumatic stress	0.897	0.753	1.068	1.123	0.965	1.306
PDG10: Anxiety disorders (NOS)	0.941	0.883	1.003	1.006	0.947	1.068
PDG11: Personality disorders	0.996	0.857	1.156	1.007	0.874	1.159
PDG12: Other mental disorders	1.001	0.946	1.058	1.005	0.951	1.061
Schizophrenia	1.169	1.057	1.294	0.875	0.810	0.947
Conventional antipsychotic pre-index	0.952	0.844	1.074	0.770	0.682	0.870
Mood stabilizer use pre-index	0.599	0.565	0.636	0.970	0.906	1.038
Year of index (Reference = 2005)						
2003	1.021	1.010	1.031	0.943	0.884	1.005
2004	0.838	0.827	0.850	0.924	0.871	0.980

Note: Adherence (PDC≥ 80%) model estimated using generalized estimating equations with binomial and logit link, and persistence (time to 90-day gap) model estimated using a Cox proportional hazard model.

we found threshold effects, the models utilizing continuous measures of the copayment index show that lower copayments in general are associated with higher levels of adherence and persistence.

Among commercially insured populations, the price elasticity of demand for medications is largely inelastic (Gibson 2005). Our results translate to a price elasticity of –0.112 (calculated as the percent

FIGURE 2
SGA cost-sharing and time to discontinuation



change in adherence to SGAs associated with a percent increase in SGA cost-sharing), which is on the higher side of elasticity estimates from commercially insured patients with physical illnesses (Chernew 2008) — this indicates that SGA users are somewhat more responsive to changes in cost-sharing.

Our findings have important implications for health plans and employers responsible for policies establishing cost-sharing amounts for SGA medications for commercially insured patients with serious mental illnesses such as schizophrenia and bipolar disorder. While our study did not examine the impact of reduced adherence and persistence because of higher cost-sharing on health care utilization and costs, several studies in the literature have established a link between nonadherence to antipsychotics and increased risk of hospitalizations and outpatient visits (Gilmer 2004; Hassan 2009). For instance, in a study among commercially insured patients with bipolar disorder, decreased adherence to antipsychotics was associated with increased odds of all-cause and mental health-related rehospitalizations (Hassan 2009).

Some plans and payers are implementing approaches including Value-Based Insurance Design (VBID) where targeted incentives include copayment reductions for patients to use the right medications at a level of use that is appropriate to their health condition (Fendrick 2001). Alternatives, such as VBID where the level of cost-sharing is based upon the benefit to the patient may help improve adherence and persistence among these patient populations.

Implementation of other interventions targeted to improve SGA medication persistence and adherence should also be considered by insurers and employers, given that less than one third of the patients in our study sample were deemed adherent to their SGA medications, regardless of the cost-sharing amount. This overall rate of adherence in this sample (31.5%) was lower than that found in prior studies of adherence to antipsychotic medications (Sajatovic 2006) however, it is important to note that we followed patients in quarterly intervals for up to four years, regardless of treatment continuation. For example, one prior study found an adherence rate of 58.5% over one year among patients with schizophrenia taking one SGA medication (Valenstein 2004). Other than the time frame, methodological differences likely also explain why the adherence rate reported by this study is more than double the rate in our study. This prior study used a medication possession ratio (MPR, total days supplied/ambulatory days measured over a one-year period) of at least 80% to determine adherence and required a minimum of 90 days of medication use for sample inclusion, which establishes a minimum MPR of 90/365=25%. Some patients had medication possession ratios in excess of 110%, while our measure of adherence (PDC) could not exceed 100%. Also the study population comprised patients with schizophrenia receiving care through the Veterans Health Administration.

This study has several limitations. First, the study was based upon ad-

ministrative data; therefore, we were unable to determine each patient's actual SGA medication consumption patterns. Using administrative claims to measure persistence and adherence, we assume that prescription filling behavior is correlated with prescription drug consumption patterns. In addition, explanatory variables such as race were not available. Finally, the analysis was limited to patients with bipolar disorder or schizophrenia utilizing SGA medications. The results may be different in a different patient population.

Our study focused upon a well-insured population of patients with employer-sponsored health care benefits. In patient populations where the percentage of income spent on medical care and prescription drugs is higher, the effects of cost-sharing on adherence may be larger than the results reported here. Additional research is needed to evaluate whether the same $30 cost-sharing threshold is found in other patient populations.

CONCLUSION

In a commercially insured sample of patients with schizophrenia or bipolar disorder, cost-sharing for SGA medications is a financial barrier to adherence to and persistence with SGA medications. Therefore, any savings associated with implementation of or increases to cost-sharing may have adverse clinical and financial effects.

REFERENCE

Ashcraft ML, Fries BE, Nerenz DR, et al: A psychiatric patient classification system. An alternative to diagnosis-related groups. *Med Care.* 1989;27:543.

Chernew ME, Gibson TB, Yu-Isenberg K: Effects of increased patient cost sharing on socioeconomic disparities in health care. *J Gen Int Med.* 2008;23(8):1131–1136.

Chernew M, Gibson TB: Cost sharing and HEDIS performance. *Med Care Res Rev.* 2008;65:713–28.

Choudhry NK, Shrank WH, Levin RL, et al: Measuring concurrent adherence to multiple related medications. *Am J Man Care.* 2009;15:457–464.

Cutler A, Ball S, Stahl S: Dosing atypical antipsychotics. CNS Spectrums: *Intern J of Neuropsych Med.* 2008;13(5 Suppl 9):1–16 .

Dezii CM: Persistence with drug therapy: A practical approach using administrative claims data. *Man Care.* 2001;10:42–45.

Fendrick AM, Smith DG, Chernew ME, et al: A benefit-based copay for prescription drugs: Patient contribution based on total benefits, not drug acquisition cost. *Am J Man Care.* 2001;7(9):861–867.

Gianfrancesco FD, Sajatovic M, Rajagopalan K, et al: Antipsychotic treatment adherence and associated mental health care use among individuals with bipolar disorder. *ClinTher.* 2008;30:1358–1374.

Gibson TB, Ozminkowski RJ, Goetzel RZ: The effects of prescripion drug cost sharing: A review of the evidence. *Am J Man Care.* 2005;11: 730–740.

Gilmer TP, Dolder CR, Lacro JP, et al: Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psych.* 2004;161:692–699.

Goldman DP, Joyce GF, Zheng Y: Prescription drug cost sharing. Associations with medication and medical utilization and spending and health. *JAMA.* 2007;298:61–69.

Hartung DM, Carlson MJ, Kraemer DF, et al. Impact of a Medicaid copayment policy on prescription drug and health services utilization in a fee-for-service Medicaid population. *Med Care.* 2008;469(6):565–572.

Hassan M and Lage M: Risk of rehospitalization among bipolar disorder patients who are nonadherent to antipsychotic therapy after hospital discharge. *Am J Health-Sys Pharm* 2009;66:358–365.

Joyce GF, Escarce JJ, Solomon MD, et al: Employer drug benefit plans and spending on prescription drugs. *JAMA.* 2002;288:1733–1739.

Lage MJ and Hassan MK. The relationship between antipsychotic medication adherence and patient outcomes among individuals diagnosed with bipolar disorder: a retrospective study. *Ann Gen Psych.* 2009;8:7.

Liu-Seifert H, Adams, DH, Kinon, BJ: Discontinuation of treatment of schizophrenic patients is driven by poor symptom response: A pooled post-hoc analysis of four atypical antipsychotic drugs. *BMC Med.* 2005;3:21.

Merikangas KR, Akiskal HS, Angst J, et al: Lifetime and 12-Month prevalence of bipolar spectrum disorder in the National Comorbidity Survey Replication. *Arch Gen Psych.* 2007;64: 543–552.

National Institute of Mental Health: The Numbers Count: Mental Disorders in America. 2008. Retrieved July 19, 2010 from: http://www.nimh.nih.gov/health/publications/the-numbers-count-mental-disorders-in-america/index.shtml.

National Institute of Mental Health: Schizophrenia. 2009. Retrieved July 19, 2010 from: http://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml.

Romano PS, Roos LL, Jollis JG: Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *J Clin Epid.* 1993;46:1075–1079.

Sajatovic M, Valenstein M, Blow FC, et al: Treatment adherence with antipsychotic medications in bipolar disorder. *Bipolar Dis.* 2006;8: 232–241.

Slade EP, Salkever DS, Rosenheck R, et al: Cost-sharing requirements and access to mental health care among Medicare enrollees with schizophrenia. *Psych Serv.* 2005;56(8):960–966.

Soumerai SB, McLaughlin TJ, Ross-Degnan D, et al: Effects of limiting Medicaid drug-reimbursement benefits on the use of psychotropic agents and acute mental health services by patients with schizophrenia. *N Eng J of Med.* 1994; 331: 650–655.

Soumerai SB, Ross-Degnan D, Avorn J, et al: Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Eng J Med.* 1991;325:1072–1077.

Valenstein M, Blow FC, Copeland LA et al: Poor antipsychotic adherence among patients with schizophrenia: Medication and patient factors. *Schiz Bull.* 2004;30:255–264.

Woltmann EM, Valenstein M, Welsh DE, et al: Using pharmacy data on partial adherence to inform clinical care of patients with serious mental illness. *Psych Serv.* 2007;58:864–867.

Zeber JE, Grazier KL, Valenstein M, et al: Effect of a medication copayment increase in veterans with schizophrenia. *Am J Man Care.* 2007;13(6 Pt 2):335–346.