Formulary Restrictions on Atypical Antipsychotics: Impact on Costs for Patients With Schizophrenia and Bipolar Disorder in Medicaid

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Objectives: To measure the impact of state Medicaid formulary policies on costs for patients with schizophrenia and bipolar disorder.

Study Design: Retrospective analysis of medical and pharmacy claims for patients diagnosed with schizophrenia or bipolar disorder in 24 state Medicaid programs.

Methods: We combined information on formulary restrictions in Medicaid with the medical and pharmacy claims of 117,908 patients with schizophrenia and 170,596 patients with bipolar disorder in Medicaid who were single-eligible, and newly prescribed a second-generation antipsychotic from 2001 to 2008. We tested the impact of formulary restrictions on the medical costs and utilization of patients in the 12 months after the index prescription. To capture social costs in addition to medical expenditures in Medicaid, we estimated the incremental costs of incarcerating patients with schizophrenia and bipolar disorder associated with formulary restrictions.

Results: Patients with schizophrenia subject to formulary restrictions were more likely to be hospitalized (odds ratio 1.13, $P<.001$), had 23% higher inpatient costs ($P<.001$), and 16% higher total costs ($P<.001$). Similar effects were observed for patients with bipolar disorder. Our estimates suggest restrictive formulary policies in Medicaid increased the number of prisoners by 9920 and incarceration costs by $362 million nationwide in 2008.

Conclusions: Applying formulary restrictions to atypical antipsychotics is associated with higher total medical expenditures for patients with schizophrenia and bipolar disorder in Medicaid. Combined with the other social costs such as an increase in incarceration rates, these formulary restrictions could increase state costs by $1 billion annually, enough to offset any savings in pharmacy costs.

Am J Manag Care. 2014;20(2):e52-e60

For author information and disclosures, see end of text.

In an effort to contain rising expenditures on prescription drugs, state Medicaid programs around the United States have increasingly adopted formulary restrictions designed to restrict access to specified high-cost medications.[1-5] Second-generation antipsychotics (SGAs), or "atypical" antipsychotics, have been among the most frequently targeted class of drugs.[6] Since the first atypical antipsychotics were introduced in the 1990s, they have increasingly replaced first-generation or "typical" antipsychotics and in 2005 accounted for over 15% of all Medicaid spending on pharmaceuticals.[7] Their high cost and rapid growth within Medicaid made them natural targets for cost containment. More than one-third of state Medicaid programs and Medicare Part D (MPD) prescription drug plans now require prior authorization or some other restriction for at least 1 atypical antipsychotic.[1,2,8]

Formulary restrictions on atypical antipsychotics are controversial because they affect patients with severe chronic mental illness, including schizophrenia and bipolar disorder. While these conditions are relatively uncommon in the general population—schizophrenia affects about 1.1% of people in the United States[9] while bipolar disorder affects about 2.6%[10]—they are more common in the Medicaid population. Estimates suggest that the prevalence of diagnosed schizophrenia in the Medicaid population is approximately 1.7%, and it is estimated that over 30% of individuals with schizophrenia are Medicaid beneficiaries.[11] Formulary restrictions influence clinical decisions about the type of atypical antipsychotic that a patient receives, but it is known that the efficacy and tolerability of these agents varies substantially from one patient to another.[8] This heterogeneity across different treatments means that providers and patients sometimes need to try different treatment regimens to attain desired clinical outcomes, and restricting access to some medications can lead to possible noncompliance with therapy or treatment non-response.

Given the vulnerable nature of these patients, there is concern that such disruption could have adverse consequences. For example, one study of medication nonadherence for individuals with schizophrenia found a 50% increase in the risk of a mental health hospitalization in the first 10 days following a missed prescription refill.[12] Other studies have found that adherence to

atypical antipsychotics fell[3] or that healthcare costs rose.[13,14] There is some evidence of a small decrease in pharmacy expenditures associated with formulary restrictions for patients with bipolar disorder, but this was also associated with an increase in treatment discontinuation.[5,15]

While informative, these studies are limited in that each focuses on only small groups of states (usually 1). More work on a larger number of states with a more diverse set of policy changes is needed to understand the impact of formulary restrictions on health outcomes and medical costs for patients with severe mental illness.[6,16] Moreover, while Medicaid expenditures are an important metric of social costs, there are others. Disruptions in antipsychotic therapy could lead to more acute psychotic episodes by affected patients. This can lead to public unrest or even violence, which can be reflected as an uptick in incarceration rates among the mentally ill, driving up the burden of mental illness on society.[17]

This study examines the relationship between formulary restrictions and healthcare utilization and expenditures for patients with schizophrenia and bipolar disorder from 24 state Medicaid programs. We combined information on formulary restrictions for atypical antipsychotics in these states with data on all of the medical and pharmacy claims in Medicaid for patients with schizophrenia and bipolar disorder from 2001 to 2008. We combined our estimates of formulary restriction effects on healthcare costs with evidence of their effect on incarceration costs. This provides a more complete accounting of the potential unintended consequences of trying to contain costs by restricting access to the full range of therapies for mental illness.

Take-Away Points

Applying formulary restrictions to atypical antipsychotics is associated with higher total medical expenditures for patients with schizophrenia and bipolar disorder in Medicaid.

- Adherence to medication declined due to formulary restrictions.
- Because a longer half-life means an active drug remains in the circulation longer after the last dose, oral antipsychotics with longer half-lives might be less impacted by partial nonadherence than those with shorter half-lives.
- Because the prescriber can individualize a patient's treatment, our results suggest autonomous prescribers constitute an asset to payers, since these prescribers achieve lower hospitalization rates than prescribers who operate within a restricted payer environment.

METHODS

Data

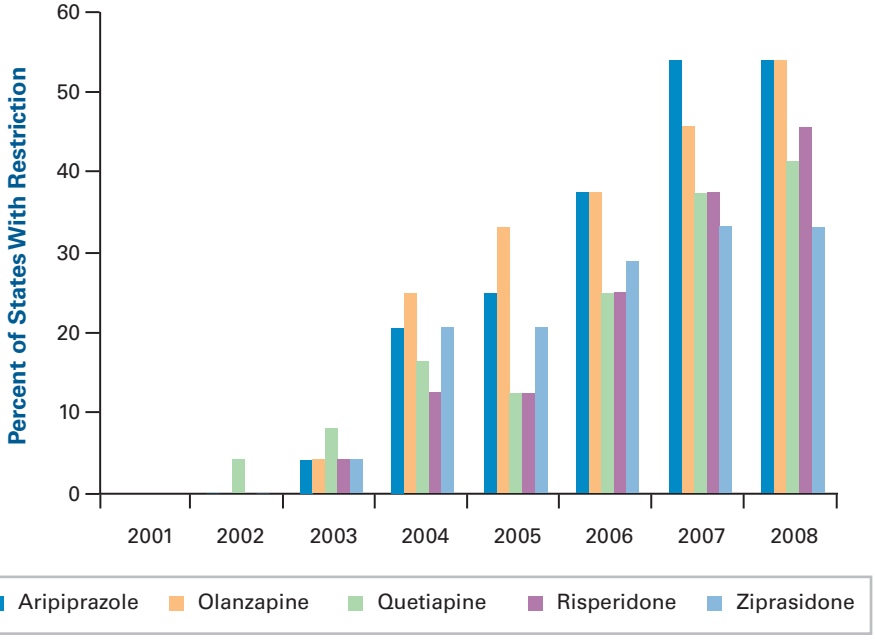
We used claim-level data on inpatient, outpatient, long-term care, and pharmacy claims from the Medicaid Analytic eXtract (MAX) files. Our data included all patients diagnosed with schizophrenia or bipolar disorder from 24 states from 2001 to 2008. (The states are: Alabama, Arkansas, California, Florida, Idaho, Illinois, Indiana, Kentucky, Louisiana, Massachusetts, Maryland, Minnesota, Mississippi, North Carolina, New Jersey, New Mexico, New York, Ohio, Pennsylvania, South Carolina, Texas, Virginia, Wisconsin, and West Virginia. We did not receive 2008 data for Pennsylvania or Wisconsin because they were unavailable at the time of data extraction.) We selected these because other states often deliver services to Medicaid beneficiaries through the use of managed care, and there are issues related to the availability and reliability of claims data for enrollees in Medicaid-funded managed care plans.

Study Sample

The study sample includes all working-age adult enrollees (aged 18-64 years) diagnosed with schizophrenia or bipolar disorder who were first prescribed an atypical antipsychotic (olanzapine, risperidone, quetiapine, aripiprazole, or ziprasidone) during the study period (N = 375,934). We restricted the study sample to patients newly prescribed an atypical antipsychotic, because these patients were more likely to be newly treated for their condition, and thus were most likely to be affected by formulary restrictions. An index date was identified using the start date of the first filled prescription for the first atypical prescribed. We tracked all medical and pharmacy claims 6 months before and 12 months after the index date.

Patients with schizophrenia were identified based on medical claims with primary or secondary *International Classification of Diseases, Ninth Edition (ICD-9)* diagnosis codes of *ICD-9-CM* 295.x during the study period (2001-2008). Patients with bipolar disorder were identified based on *ICD-9-CM* codes of 296.0x, 296.1x, and 296.4x-296.8x. We excluded patients with both schizophrenia *and* bipolar diagnoses (N = 106,314, 28%), because these patients likely had more uncertainty over their disease status, which could have affected treatment patterns (including use of atypical antipsychotics). We also excluded enrollees who were dually eligible for Medicare because of changes in prescription drug coverage that occurred with the introduction of MPD in 2006, which could have affected atypical antipsychotic use. We also excluded patients with prior first-generation antipsychotic use or a prescription for clozapine prior to the index date, because it is unclear how these patients would be affected by the restrictions (eg, clozapine is only approved for treatment-resistant schizophrenia, so there are already significant restrictions on its use). Finally,

Figure 1. Percent of States With Formulary Restrictions by Drug and Year



we excluded any patients who died in the 12-month follow-up period. Our final study samples included 117,908 patients with schizophrenia and 170,596 patients with bipolar disorder.

Formulary Restrictions

Data on formulary restrictions were obtained from a 2009 survey of state Medicaid programs that asked about their formulary policies affecting atypical antipsychotics and other drugs treating mental illness. The survey, used in prior work,[6] covered 30 states (including the 24 states in our study sample) from 1999 to 2008 and asked whether specified restrictions applied to a list of drugs identified by US brand name, including the atypical antipsychotics examined in our study. Programs were asked to identify whether a given type of restriction applied to each drug in the list and over which years it applied. Survey responses were supplemented using the Medicaid pharmacy program websites for relevant documents (eg, preferred drug lists) and with direct contact with Medicaid program personnel.

The survey collected information about the most commonly used restrictions to contain Medicaid pharmacy costs. *Prior authorization* requires providers to obtain prior permission to prescribe a specified medication, or the Medicaid program will not guarantee reimbursement. *Quantity limits* are direct restrictions to how many units of a drug may be dispensed in a fixed time period, usually a month or day (this includes daily quantity limits—sometimes referred to as *dose optimizations*—that operate in the same way as monthly limits). *Step therapy* requires that medication be prescribed only after a provider tries other selected medications, usually cheaper alternatives. Under these policies, providers must document that the patient has had unsatisfactory responses, and needs the nonpreferred medication. Other, less common policies were also surveyed, including *age edits*, which restrict use by patients in certain age groups.

Following prior work, we implemented our measure of these policies using binary indicators when any of the policies affected patients using a drug in a state in a year.[6] Figure 1 summarizes the share of states that had a restriction by drug and year in our sample. The figure shows that the use of formulary restrictions grew rapidly over the study sample. The most commonly restricted drug in the sample was olanzapine, particularly early on, followed closely by aripiprazole. By 2008, both olanzapine and aripiprazole were targeted in more than half of the states in our sample.

As a sensitivity analysis, we examined how the effects differed based on the type(s) of atypical antipsychotics targeted. Specifically, in our empirical analysis, we created binary categories to allow us to test for the effects of:

- Any of the policy types against any of the 5 molecules
- Any of the policy types targeting olanzapine only
- Any of the policy types targeting olanzapine and any of the other 4 molecules, or
- Any of the policy types targeting any of the 4 molecules but not olanzapine.

We used these specific categories rather than breaking down the analysis to separately consider policies targeting all

5 drugs because there were an insufficient number of drug-policy combinations.

Main Outcome Measures

We measured healthcare utilization and spending over a range of potential outcomes. This includes: whether we observe any hospitalization episode for the patient in the follow-up period, the total Medicaid dollars spent on inpatient spending, total medical spending (defined as the sum of inpatient and outpatient spending), total prescription drug spending (including spending on atypical antipsychotics), and total Medicaid spending from all sources. Dollar values were normalized to 2008 using the medical care component of the Consumer Price Index. Finally, we tested the impact of formulary restrictions on adherence to the index atypical antipsychotic, defined as the proportion of days covered (PDC) over the 365 day period after the index date.

Statistical Analysis

To identify the effects of formulary restrictions on outcome, we employed a difference-in-difference study design using multivariate regression techniques.[18] Specifically, we examined the difference in outcomes for patients prescribed an atypical antipsychotic in states with and without formulary restrictions before and after those restrictions were adopted. This method allowed us to estimate the impact of state policies while controlling for other state and time heterogeneity that could confound the results.

If individual patient characteristics systematically differed in states with and without restrictive formulary policies, this could confound our analysis. In addition to state and year fixed effects, which would capture fixed state differences or general trends, we also used patient demographics and claims-based measures of patient health at baseline to control for potentially confounding variation. The MAX files provided basic demographics including age, gender, and race. The zip code of residence for each enrollee was used to measure median household income in their area to provide information on socioeconomic status of patients and their families. Zip code was also used to categorize the primary residence of the enrollee into a rural/urban location.

To control for patient health at baseline, we used medical claims from the 6-month period prior to the index date to construct a claims-based index of individual health using the Charlson-Deyo method.[19] We also included an indicator for whether the patient experienced an all-cause hospitalization prior to baseline. Because atypical antipsychotics are associated with elevated metabolic risk, we included controls for the presence of metabolic syndrome (*ICD-9*-CM code of 277.7), dyslipidemia (272.xx), diabetes mellitus (250.xx), or overweight and obesity (278.xx) prior to baseline. We also controlled for other, nonmetabolic, comorbid chronic health conditions, including: stroke, vascular disease, chronic obstructive pulmonary disease, asthma, malignant cancer, gastric acid disorder, anemia, arthritis, allergic rhinitis, and epilepsy. Finally, we used the claims data to control for the severity of mental illness, based on whether or not the individual saw a psychiatrist in the pre-index period. For patients with bipolar disorder, we also control for the use of mood stabilizers in the pre-index period.

We use logistic regression to estimate the effect of formulary policies on hospitalization rates and ordinary least squares to estimate the effect on expenditures and adherence to therapy. We logged the expenditures to correct for the skewness in medical expenditures,[20] and added $1 to expenditures to avoid dropping zero values. To describe the magnitude of the expenditure differences associated with formulary restrictions, we predicted values of different expenditure categories with and without formulary restrictions based on our regression models holding other covariates at mean values. We used mixed effects models—specifically, models that included both fixed and random effects at the state level—to reflect the fact that our key policy variables were at the state level, which can cause correlation in the error terms (or "clustering") within groups.[21,22] A smearing estimate was used to eliminate retransformation bias when calculating predicted values.[23]

Measuring Societal Costs of Formulary Restrictions

To study incarceration costs, we relied on past work that used logistic regression to estimate the association between formulary restrictions in Medicaid and the share of the prison population with mental illness in a national survey.[24,25] This work found that formulary restrictions increase the share of the prison population afflicted with mental illness by up to 17%. Approximately 12% of the prison population is affected by schizophrenia or bipolar disorder, implying a 2 percentage point increase in the overall prison population. We combined these estimates with data from the Bureau of Justice Statistics Expenditure and Employment Extracts on prison costs by state and year. With these data, we estimate the incremental costs that arose as a result of states that had restrictive formulary policies.

RESULTS

Summary Statistics

Table 1 summarizes outcomes and covariates for the schizophrenia and bipolar patient samples. Average medical expenditures in the follow-up period for both sets of patients were high for both schizophrenia ($18,896) and bipolar ($18,770) patients. Pharmacy costs were also high, at $5597 (schizo-

Table 1. Summary Statistics of Other Covariates

	Patients with Schizophrenia (N = 117,908)	Patients with Bipolar Disorder (N = 170,596)
Outcomes		
Hospitalization, %	23	29
Inpatient expenditures, $, mean (SD)	3739 (14,622)	4769 (17,196)
Total medical expenditures, $, mean (SD)	13,298 (22,232)	13,734 (23,768)
Prescription drug expenditures, $, mean (SD)	5597 (5858)	5036 (6482)
Total expenditures, $, mean (SD)	18,896 (23,945)	18,770 (25,794)
Proportion of days covered, mean (SD)	0.76 (0.33)	0.72 (0.36)
Demographic Characteristics		
Aged 30 to 39 years, %	20	26
Aged 40 to 49 years, %	30	26
Aged 50 to 64 years, %	28	16
Non-white, %	66	43
Male, %	53	33
Lives in urban area, %	8	11
Health Indicators Prior to Baseline		
Any hospitalization, %	21	26
Psychiatrist visit, %	70	66
Charlson Comorbidity Index score, mean (SD)	.67 (3.69)	.60 (3.44)
Had metabolic comorbidity, %	16	12
Used mood stabilizer, %		5
Stroke, %	1	1
Vascular disease, %	1	1
COPD, %	2	2
Asthma, %	6	9
Malignant disease, %	1	1
Gastric acid disorder, %	7	8
Anemia, %	6	5
Arthritis, %	3	4
Allergic rhinitis, %	3	4
Epilepsy, %	1	1
Type of Index Atypical Antipsychotic Used		
Aripiprazole, %	12	11
Olanzapine, %	16	10
Quetiapine, %	24	40
Risperidone, %	40	30
Ziprasidone, %	9	8

COPD indicates chronic obstructive pulmonary disease; SD, standard deviation.
Notes: Data include patients with schizophrenia and patients with bipolar disorder from 24 state Medicaid programs initiating new therapy for an atypical antipsychotic from 2001-2008. All dollar values normalized to 2009.

phrenia) and $5036 (bipolar). Other characteristics were similar, although schizophrenia patients were more likely to be non-white and more likely to be male (P <.001 for both).

Regression Estimates

Table 2 reports estimated effects from the regression models. Patients with schizophrenia subject to formulary restrictions were more likely to experience a hospitalization (odds ratio 1.13, P <.001), had 23% higher inpatient costs (P <.001), and had 16% higher total costs (P <.001). For patients with bipolar disorder, those subject to formulary restrictions were also more likely to experience a hospitalization (odds ratio 1.07, P = .016), had 20% higher inpatient costs (P <.001), and had 10% higher total costs (P <.001). Formulary restrictions were not associated with statistically significantly lower pharmacy expenditures for either patient sample. Patients with schizo-

Table 2. Estimated Effect of Formulary Restrictions on Different Health Expenditure and Utilization Measures

Dependent variable	(1) Any Hospitalization	(2) Hospital Expenditures	(3) Total Medical Expenditures	(4) Prescription Drug Expenditures	(5) Total Expenditures	(6) PDC, Index Atypical Antipsychotic
Patients With Schizophrenia						
Overall effects						
Any formulary restriction	1.134[a] (0.041)	0.226[a] (0.049)	0.203[a] (0.020)	–0.036[c] (0.021)	0.156[a] (0.013)	–0.018[a] (0.004)
Effects of formulary restrictions targeting specific atypical antipsychotics						
Formulary restriction for olanzapine	1.079 (0.062)	0.101 (0.079)	–0.025 (0.032)	0.041[c] (0.033)	0.007 (0.022)	0.009 (0.007)
Formulary restriction for olanzapine and other atypical antipsychotics	1.082 (0.052)	0.211[a] (0.063)	0.232[a] (0.025)	–0.202[a] (0.026)	0.152[a] (0.017)	–0.024[a] (0.005)
Formulary restriction for drugs other than olanzapine	1.366[a] (0.080)	0.561[a] (0.084)	0.646[a] (0.034)	0.271[a] (0.035)	0.512[a] (0.023)	–0.062[a] (0.007)
Patients With Bipolar Disorder						
Overall effects						
Any formulary restriction	1.073[b] (0.031)	0.197[a] (0.022)	0.107[a] (0.045)	0.029 (0.016)	0.102[a] (0.019)	–0.005 (0.012)
Effects of formulary restrictions targeting specific atypical antipsychotics						
Formulary restriction for olanzapine	0.970 (0.043)	–0.049 (0.072)	–0.077[a] (0.025)	0.069[b] (0.031)	–0.021 (0.019)	0.010[c] (0.006)
Formulary restriction for olanzapine and other atypical antipsychotics	1.090[b] (0.042)	0.274[a] (0.057)	0.176[a] (0.020)	–0.050[b] (0.025)	0.140[a] (0.015)	–0.012[b] (0.005)
Formulary restriction for drugs other than olanzapine	1.451[a] (0.081)	0.793[a] (0.092)	0.480[a] (0.033)	0.330[a] (0.040)	0.398[a] (0.024)	–0.029[a] (0.008)

Table reports the results of multivariate regression estimates of the effect of different formulary restrictions for second-generation antipsychotics on different health expenditure and utilization measures. Sample includes all patients from 24 state Medicaid plans with a schizophrenia (N = 117,908) or bipolar disorder (N = 170,596) diagnosis who initiated a second-generation antipsychotic from 2001 to 2007.
Standard errors in parentheses.
[a] $P < .01$; [b] $P < .05$; [c] $P < .1$.

phrenia subject to formulary restrictions had worse adherence (–0.02 lower PDC, $P < .001$). For patients with bipolar disorder, formulary restrictions had no significant effect on adherence.

In the subanalysis by drug categories, restrictions that target olanzapine alone had no consistently positive or significant effect on medical costs in either patient sample. Policies targeting other molecules, with or without olanzapine, were associated with significantly higher hospitalization rates and medical expenditures and lower adherence in both patient samples.

Predicted inpatient expenditures for patients with schizophrenia increased from $2983 to $3740 with a formulary restriction in place (Figure 2). Predicted medical expenditures increased from $10,852 to $13,299 and predicted total expenditures increased from $16,171 to $18,897. The savings in medication costs were small: predicted pharmacy spending declined from $5806 to $5598. The effects on patients with bipolar disorder were similar but smaller overall (Figure 3). Predicted inpatient expenditures for patients with bipolar disorder increased from $3918 to $4770 and total expenditures increased from $16,958 to $18,771. The predicted expenditures on prescription drugs rose slightly with formulary restrictions in place.

Social Costs

In the 24 states in our data, approximately 62% of prisoners were in states with restrictive formulary policies. Using data on state prison costs, combined with prior estimates that formulary policies increased the overall prison population by 2 percentage points due to more mentally ill patients being arrested,[24] we estimate that restrictive formulary policies in Medicaid increased the number of prisoners by 9920 and incarceration costs by $362 million nationwide in 2008.

Figure 2. Predicted Expenditures With and Without Formulary Restrictions: Patients With Schizophrenia

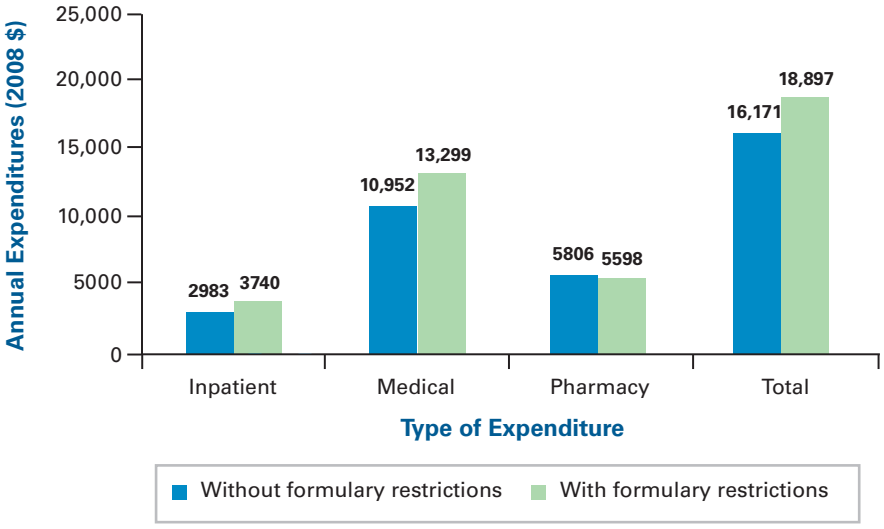


Figure reports predicted values based on ordinary least squares regressions with and without formulary restrictions, with all other covariates held constant at mean values. Medical expenditures include the sum of both inpatient and outpatient expenditures. Smearing estimates are used to eliminate retransformation bias.

DISCUSSION

This study examined the relationship between formulary restrictions on atypical antipsychotics and healthcare spending and utilization among schizophrenia and bipolar patients in Medicaid. We found that patients prescribed atypical antipsychotic medications had significantly worse outcomes when a formulary restriction was present. This included increased risk of hospitalization, higher medical costs, and higher total costs.

These results fit with a growing body of evidence questioning the benefits of formulary restrictions on atypical antipsychotics in Medicaid. Prior studies have found that formulary restrictions decrease adherence. For instance, patients with schizophrenia and bipolar disorder in Maine were significantly more likely to discontinue therapy after prior authorization was introduced.[3,5] We also found that adherence to medication declined due to formulary restrictions.

Our analysis demonstrated, at best, modest evidence of savings on medication costs in our sample. This is also consistent with past studies, which have found that formulary restrictions had no effect on pharmacy spending,[13] or lowered it slightly.[3,5] Any cost savings from pharmaceuticals among atypical antipsychotic users appears to be more than offset by the higher medical costs associated with worse adherence and poorer health outcomes. The financial burden to the states may be even higher if states forgo additional rebates from manufacturers for branded medications due to restrictive formulary policies, or if the policies generate significant administrative costs. However, the recent availability of generic atypical antipsychotics and the implications for the impact of restrictions on pharmacy costs needs to be reevaluated in future research.

Our results consistently displayed worse outcomes for patients when they faced restrictions targeting molecules other than olanzapine, consistent with the finding that these policies had more impact on adherence. One explanation for this result is that olanzapine is associated with a worsening metabolic profile that could result in adverse health outcomes. For instance, olanzapine is associated with worse metabolic side effects compared with aripiprazole and ziprasidone.[26,27] Restrictions on molecules with better metabolic profiles could result in more disruptions from therapy and worse outcomes for patients, such as higher rates of cardiovascular disease. Our estimates also indicated that the effects of restrictions were more pronounced for patients with schizophrenia than patients with bipolar disorder. Although atypical antipsychotics act as an important component of the treatment of both diseases, the smaller effects of atypical antipsychotic restriction within the bipolar disorder population may stem from polypharmacy with mood stabilizers that patients with bipolar disorder commonly receive.

We also estimated the other costs that could potentially be associated with formulary restrictions to atypical antipsychotics based on a predicted increase in the size of the prison population. Recent work shows that disruptions to therapy using atypical antipsychotics are associated with an increase in incarcerations by the mentally ill, imposing large costs on society.[24] Our estimates suggest that restrictive formulary policies in Medicaid led to over $350 million in prison costs per year. If we were to extrapolate the average increase in Medicaid ex-

Figure 3. Predicted Expenditures With and Without Formulary Restrictions: Patients With Bipolar Disorder

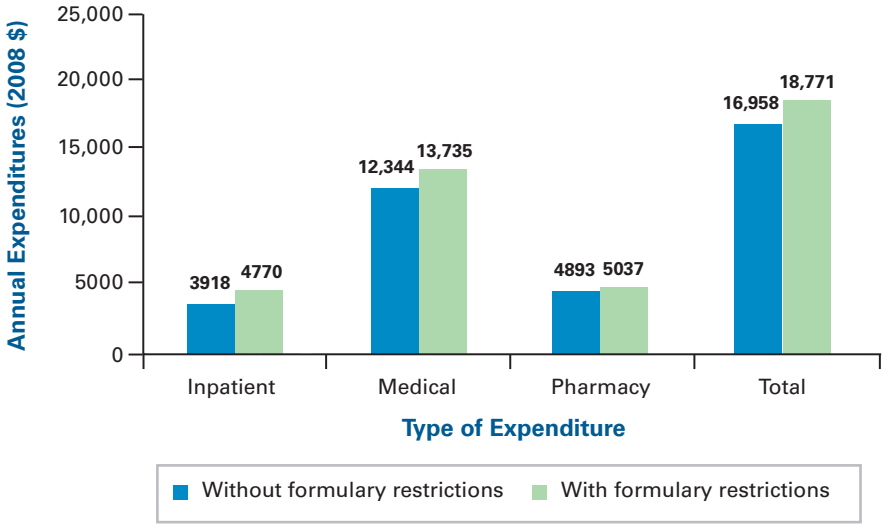


Figure reports predicted values based on ordinary least squares regressions with and without formulary restrictions, with all other covariates held constant at mean values. Medical expenditures include the sum of both inpatient and outpatient expenditures. Smearing estimates are used to eliminate retransformation bias.

penditures for patients with schizophrenia and patients with bipolar disorder, and then combine these costs with excess prison costs, the estimated total social costs of formulary restrictions for atypical antipsychotics would exceed $1 billion per year.

Several factors could drive the relationship between worse patient outcome and increasing access restrictions among patients with serious mental illness. First, atypical antipsychotics constitute a well-differentiated class of medications. The drugs work with different mechanisms of action, including dopamine antagonism and dopamine partial agonism, and vary widely in their affinity for other receptors.[28] The drugs vary widely in the specific side effects that occur most frequently with a particular agent.[29-31] A review of the package inserts for atypical antipsychotics clearly demonstrates a wide variation in the pharmacokinetic profile of these agents, with half-lives ranging from 6 to 75 hours. Because a longer half-life means active drug remains in the circulation longer after the last dose, oral antipsychotics with longer half-lives might be less impacted by partial nonadherence than those with shorter half-lives. The drop in antipsychotic blood levels caused by missed doses might be bridged more effectively by longer half-life antipsychotics. A recent database analysis of Medicaid patients confirmed this hypothesis, showing that patients using antipsychotics with a longer half-life experienced a lower rate of hospital admissions/emergency department visits than patients treated with short half-life antipsychotic agents.[32]

The APA Practice Guidelines for Schizophrenia recommend clinicians consider 7 factors when selecting pharmacotherapy: past response to treatment, a medication's side effect profile, patient preference, patient's side effect history, intended route of administration, comorbid medical conditions, and potential drug interactions. Because the prescriber can individualize a patient's treatment, our results suggest that autonomous prescribers constitute an asset to payers, since these prescribers achieve lower hospitalization rates than prescribers who operate within a restricted payer environment.

Our study had limitations. While our data included information from a large number of states, it was not fully nationally representative and it is possible that outcomes could differ in the states that were not in our sample. We also had a number of exclusion restrictions (eg, dual eligibility with Medicare). While justifiable, these restrictions could further limit the generalizability of our findings. Finally, we only consider the impact of formulary restrictions on atypical antipsychotic users. If formulary restrictions generate significant savings by limiting adoption of atypical antipsychotics in favor of alternatives, these savings would have to be considered against the costs that we observe among atypical users. However, it is possible that policy restrictions can cause disruptions in diagnosis and treatment and thus deprive patients of any atypical antipsychotic (an important treatment option for these patients) and thus lead to worse outcomes and increased medical costs. As we excluded such patients from our analysis, we could have potentially underestimated the negative consequences of formulary restrictions. Finally, the atypical antipsychotic landscape is changing rapidly, given that many of the major molecules either are or will soon become generic. This does not affect the negative implications of disruptions in therapy for patient health, but it does suggest that some of the financial burden for some of those therapies will be mitigated.

CONCLUSIONS

Despite these limitations, our study provides strong evidence that the disruption to therapy that formulary restrictions cause offsets much, if not all, of the possible savings to Medicaid, at least among atypical antipsychotic users with schizophrenia or bipolar disorder. Policy makers should consider whether these restrictions actually succeed in lowering costs in the long run. At the very least, more should be done to consider how to ensure that patients with schizophrenia or bipolar disorder receive the therapy that is most appropriate to them while still maintaining acceptable levels of costs.

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Funding Source: Bristol-Myers Squibb funded this research.

Authorship Information: Concept and design (DNL, IK, DPG, JJS, SAS); acquisition of data (DNL, DPG); analysis and interpretation of data (KL, DNL, IK, DPG, JJS, SAS); drafting of the manuscript (KL, IK, JJS, SAS); critical revision of the manuscript for important intellectual content (KL, DNL, IK, DPG, JJS, SAS); statistical analysis (SAS); obtaining funding (DNL, IK, DPG); supervision (DNL, IK, DPG).

Author Disclosures: Dr Seabury reports receiving payment for work as a subcontractor from Precision Health Economics. Drs Goldman and Lakdawalla report holding the position of "partner" at Precision Health Economics, which has a research contract with Bristol-Myers Squibb. Dr Laubmeier reports employment with Otsuka America Pharmaceutical, which manufactures an atypical antipsychotic drug. Drs Sheehan and Kalsekar report employment with Bristol-Myers Squibb, which funded this research and also manufactures and markets an atypical antipsychotic drug. Dr Kalsekar reports ownership of Bristol-Myers Squibb stock.

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