Do Strict Formularies Replicate Failure for Patients With Schizophrenia?

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Between 1995 and 2005, Medicaid spending on drugs increased an average of 13% per year—an increase due in part to physicians favoring newer, more expensive drugs.[1,2] To attempt to control costs, many state Medicaid programs responded by imposing policies that encourage the use of lower-cost drugs.[2,3] Prior authorization, for example, is designed to reduce pharmacy spending by requiring physicians to seek approval from the state's Medicaid program before prescribing certain high-cost drugs to patients. These controls are designed to reduce the demand for expensive drugs when lower-cost alternatives exist, which ultimately results in reduced Medicaid spending. But these policies may affect healthcare spending and utilization through other channels, especially if patients do not respond well to the preferred drugs. Physicians match patients to the drug and dosage that is optimal for each patient based on various practice guidelines, recommendations, and formulary practices.[4,5] On average, several treatments might be equally effective at the population level, but heterogeneous patients will respond differently to each. Removing a drug from coverage could adversely affect those who would have most benefited from it. If the use of these drugs leads to deteriorating health status, the result may be higher nonpharmaceutical medical spending.[6]

An important example of this trade-off is the second generation of drugs for the treatment of schizophrenia, called atypical antipsychotics, which account for almost 15% of Medicaid spending.[7] For this reason, they are increasingly popular targets of state Medicaid formulary restrictions.[8,9] Because a number of patients may respond only to 1 drug, formulary restrictions can place patients with idiosyncratic treatment responses at greater risk of uncontrolled symptoms.[10,11] Uncontrolled schizophrenia has dramatic costs for patients (about 10% of whom commit suicide), and for society in terms of increased social service use and crime.[12] Although lower-cost alternatives to atypicals do exist, they are problematic. The first generation of schizophrenia drugs resulted in improvement of symptoms but with potentially debilitating side effects.[10] Atypical antipsychotics were introduced in the 1990s and have largely replaced first-generation treatments because atypicals control schizophrenia better and have fewer negative side effects. For example, about 30% to 40% of patients relapse with first-generation drugs (relative to 80% without treatment), but with second-generation drugs, relapse rates fall to about 25%.[10]

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Objectives: We measure the impact of Medicaid formulary restrictions (FRs) on the rate at which patients who previously failed a drug therapy for schizophrenia are returned to that therapy.

Study Design: We collect drug-level information on FRs in state Medicaid programs and examine claims of noninstitutionalized Medicaid enrollees with schizophrenia.

Methods: A difference-in-differences technique is used to compute the change in the probability of adverse outcomes before and after a state adopts an FR. This change is compared with the change in failure probabilities in states with no FRs.

Results: Regardless of FRs, patients tend to resume the same drug after an adverse medical event. In 2005, 69% of inpatient mental health–related admissions resulted in patients resuming the same therapy within 6 months of the event, and 63% of patients resumed the same drug after a mental health–related emergency department admission. In states where FRs limit access to all atypicals, the likelihood of a patient resuming the same atypical after having ceased treatment for at least 30 days increases by 20.1% relative to patients in states without restrictions. Additionally, patients in states that impose FRs on all atypicals are 11.6% more likely to discontinue all treatments.

Conclusions: FR may increase the likelihood that patients will return to failed treatments or cease treatment altogether. Although formularies are designed to reduce drug spending, an unintended consequence may be an increase in the use of other services needed to treat patients with schizophrenia.

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Take-Away Points

We measure the impact of Medicaid formulary restrictions (FRs) on the rate at which patients who previously failed on a particular drug therapy for schizophrenia are returned to that same therapy. Our findings suggest that FRs increase the likelihood that patients will return to failed treatments, or totally cease treatment.

- In 2005, 69% of all schizophrenia patients' mental health–related admissions resulted in patients resuming the same schizophrenia treatment within 6 months
- Patients in states that impose FRs on all atypical antipsychotics are 20.1% more likely to resume use of the same atypical after having ceased treatment for at least 30 days and 11.6% more likely to discontinue all treatments relative to patients in states without restrictions.

Formulary restrictions appear to alter doctors' prescribing behavior. Previous studies have examined the impact of utilization management programs and found that formulary restrictions reduced the use of atypicals by about 5%.[9] After prior authorization of atypicals became a requirement in Maine, the risk of discontinuation rose by 29%.[2] Studies in Georgia and New Hampshire found that prior authorization reduced the use of targeted drugs and increased the use of other health services.[13,14] Previous studies of the impact of restrictions on treatment have focused on individual states. This study, to the best of our knowledge, is the first nationally representative study of formulary restrictions' impact on treatment. In this study, we examine how formulary restrictions of atypicals affect the likelihood that a patient who has been diagnosed with schizophrenia, and who has had some marker of an unsuccessful response to a particular drug therapy, is continued on that same drug therapy, changes the type of drug, or discontinues all treatment.

METHODS

Data Source

Policy information on the restrictions placed on atypical antipsychotics from 1999 to 2005 was collected from 24 state Medicaid programs via a mailed survey and personal communications with policy directors. States reported whether prior authorization, quantity limits, step therapy (fail-first), and other policies applied to a list of drugs identified by US brand name. To supplement this information, additional formulary information was collected using publicly available documents.

Regulation data were collected at the individual drug level. The survey included 10 atypicals. All major atypical antipsychotic agents are addressed in the survey, except for paliperidone (brand: Invega) and olanzapine/fluoxetine combined therapy (brand: Symbax), both of which were not yet commercially available during the study period. States reported if each drug was placed under prior authorization, quantity limits, step therapy, dose restriction, or duplicate therapy restrictions in each year.

Medicaid claims for 24 states (12 states that adopted formulary restrictions and 12 states that did not) for a 5-year period (2001-2005) were used to measure medical and pharmacy use at the individual level. We selected the states shown in **Table 1** based on the size of the Medicaid population; the fraction of enrollees in fee-for-service Medicaid (with complete claims); and whether the state Medicaid program had imposed restrictions on selected classes of medications over the study period. The years included in this study (2001-2005) captured the widespread introduction and use of prior authorization requirements in many state Medicaid programs, particularly for atypical antipsychotics.

The sample consisted of Medicaid enrollees 18 years and older who have schizophrenia in each of the study states. These patients were identified by (1) the presence of an *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)* code beginning with 295 in any diagnosis position for inpatient, outpatient, or long-term care claims, and (2) a confirmatory schizophrenia diagnosis at least 30 days after the initial diagnosis. Thus, we eliminated individuals who were diagnosed only once without a subsequent diagnosis. This eliminated individuals with a so-called "rule-out" diagnosis: a physician may make an initial diagnosis of suspected schizophrenia that is later ruled out. The requirement of a subsequent "confirmatory" diagnosis excluded "ruled out" cases from the sample. This criterion also imposed a 30-day minimum window of observation for inclusion in the study. In addition, to be included, a patient must have filled at least 1 prescription for one of the drugs included in our sample. In practice, this restriction eliminated very few patients because those with a subsequent confirmatory diagnosis are almost always given a prescription.

The **Figure** presents a consort diagram for the sample construction: 944,609 patients over the age of 18 years who have had at least 1 schizophrenia diagnosis. Of these, about 77% had a confirmatory diagnosis after 30 days. Of the remaining population, 63%, or 460,991 patients, were prescribed an atypical.

STUDY DESIGN

Estimation Approach

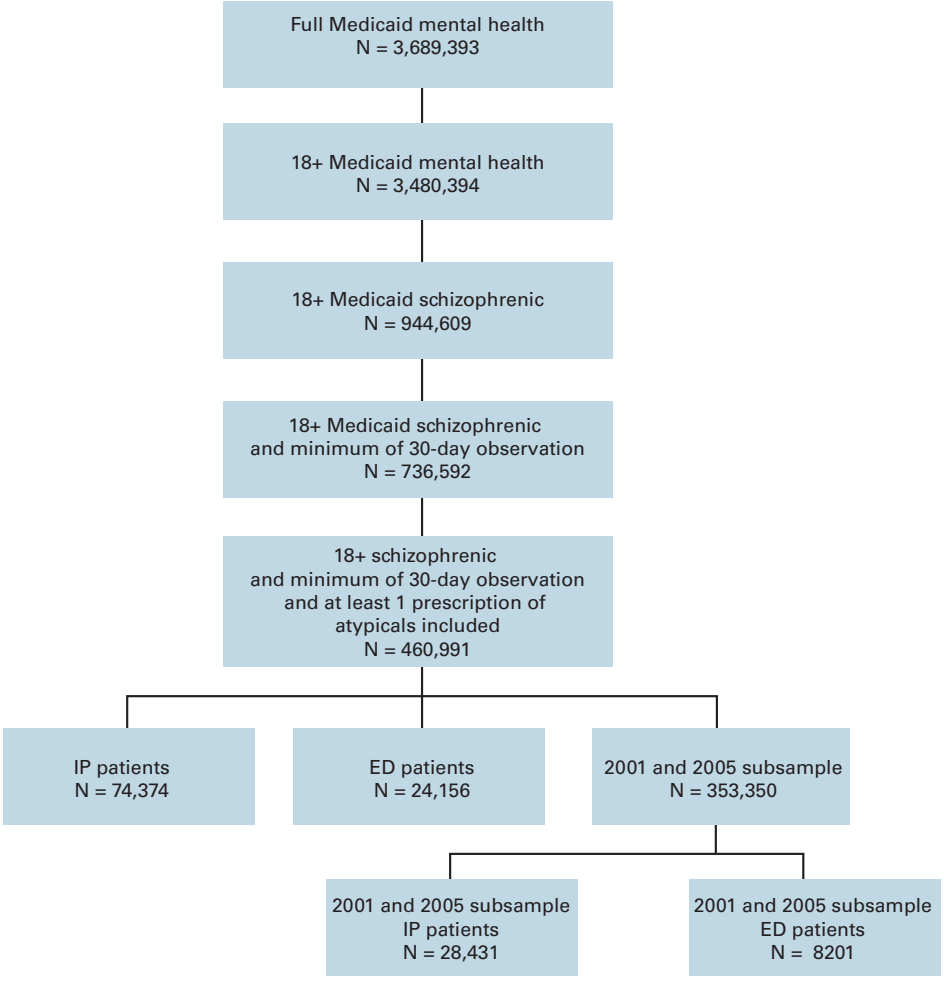
To estimate the impact of prior authorization on treatment failure and "replication of failure," a difference-in-differences

Table 1. Total 2005 Adult Medicaid Enrollment (in 1000s) by State, and Medicaid Formulary Restriction Status

Treatment States (atypicals faced formulary restrictions in 2005) (45.4% of total Medicaid population)			
Alabama	California	Florida	Illinois
228.1	3083.40	933.60	624.90
Kentucky	Massachusetts	Minnesota	New Mexico
330.6	567.9	250.3	106.5
New York	Pennsylvania	Texas	West Virginia
2514	885.2	401.8[a]	182.4[a]
Control States (atypicals did not face formulary restrictions in 2005) (37.5% of total Medicaid population)			
Arkansas	Idaho	Indiana	Louisiana
179.9[a]	60.3[a]	270.7	307.2
Maryland	Mississippi	New Jersey	North Carolina
189.1	237.7	337.9	426.5[a]
Ohio	South Carolina	Virginia	Wisconsin
593.3[a]	245.2[a]	235.5[a]	298.2

[a]Indicates that adult enrollment was not available, and is instead based on an estimate from the available state's total Medicaid enrollment. For states with restrictions: total enrollment 0.454. For states without restrictions: total enrollment 0.375.

Figure. Consort Diagram



For more details on the restricted sample by year, see Table 2.
Person counts shown here do not reflect observation counts in Tables 4-7 because individuals can have multiple observations in the data.

method (DD) was used. In the DD method, 2 groups—patients in states with restrictions and patients in states without restrictions—were observed in 2 different time periods: 2001 and 2005. Patients living in states that adopted formulary restrictions after 2001 were, in the terminology of DD models, exposed to "treatment" in 2005, while those in nonformulary states were not exposed in either period. This method first calculates the change in the average likelihood of the outcome variable in the treated group, and then calculates the corresponding change in the nontreated group. The excess change in the treated group, above and beyond the change in the nontreated group, represents the estimated DD effect. For example, in states with formulary restrictions, we calculated the change in the likelihood of a patient resuming the same medication after a 30-day gap before and after the implementation of the restriction. We then compared this with the corresponding difference in likelihood within states that never adopted restrictions. The approach removes the effects of trends due, for example, to general changes in atypical use between 2001 and 2005. Because formulary restrictions were measured at the state level, we clustered the standard errors at the state level. We utilized an alpha of 0.10, although the tables included alternative alpha values.

To examine the replication of failure, all patients currently with schizophrenia who are taking an atypical antipsychotic for their condition were identified. Then, patients were classified as failing on a particular therapy if they either were admitted to a hospital for their disease or had a medication gap greater than 30 days (in a baseline year). Patients who failed treatment were followed over time, and their claims were examined for resumption of treatment with the same drug after at least a 30-day gap. As a robustness check, we examined longer gaps, but faced serious sample size limitations due to the limited number of people observed restarting after longer gaps. Finally, we also examined whether individuals on an atypical discontinued drug therapy altogether, switched from an atypical to a typical (first generation) antipsychotic, or switced from one atypical to another.

We included an indicator variable equal to 1 in the year 2005 and an indicator for states that adopt formulary restrictions. The interaction between the 2 indicators, year 2005 and formulary restrictions, is the difference-in-differences estimate discussed above (labeled DD in the tables).

RESULTS

Descriptive Analyses

Table 2 shows summary statistics measuring atypical antipsychotic usage along with emergency department (ED) and inpatient admissions related to mental health causes, stratified by the number of atypicals under a formulary restriction in a given state-year. The observed population with schizophrenia increased slightly over time, from just fewer than 500,000 in 2001 to about 541,000 in 2005. The number of patients with schizophrenia receiving atypical antipsychotics increased from nearly 195,000 in 2001 to over 320,000 in 2004, and then fell to about 273,000 in 2005.

Each patient, on average, experienced 0.22 inpatient admissions related to mental health issues and 0.06 ED visits per year. Approximately 2.8% of the sample was admitted to the ED and 7.9% was admitted on an inpatient basis for issues related to mental health.

Table 3 summarizes the replication of failure by year, and the restrictiveness of Medicaid formulary in that year. The variable of interest is the number of times a patient goes off a particular medication for 30 days and then resumes that same medication. For example, a value of 1 indicates that the average patient had one 30-day gap in their medication. Patients in states with formulary restrictions tend to have slightly more replication of failure, measured as stoppages and restarts. For example, in 2005, individuals in states with all atypicals under restriction experienced an average of 1.04 stoppages and subsequent restarts of the same atypical in the same year, while those in states with no restrictions experienced an average of 0.99 stoppages and restarts per year.

Measuring replication of failure using inpatient or ED admission provides a more explicit measure of failure. Repeated failure here signifies that the patient was admitted for a mental health issue while on a particular drug, but then was put back on that atypical within 6 months of the admission. Approximately 65% of inpatient admissions result in the individual resuming the same atypical they were on before the admission, within 6 months. There is no significant difference over time. Among ED visits, 59% result in the same atypicals being resumed within 6 months in both restrictive and unrestrictive states.

Difference-in-Differences Estimates

Tables 4, 5, 6, and 7 (A and B) show the estimates from difference-in-differences regressions comparing outcomes from 2001 with those from 2005. The first outcome measured in Table 4 is for patients who resumed the same atypicals after experiencing at least a 30-day gap in stock of the drug. The sample is restricted to those patients who filled at least 1 atypical prescription in the given year. States that place some drugs on prior authorization are compared with states with no restrictions (Table 4A). The difference-in-differences coefficient is calculated to be 0.062 (standard error [SE] 0.009): formulary restrictions on some atypicals are associated with a 6.2% increase in the probability that an individual resumes the same atypical after a stoppage, relative to the control group. In the regressions that use the states that have placed all atypicals

Table 2. Sample Counts of Patients With Schizophrenia, Rate of Atypical Usage, Emergency Department Visits, and Inpatient Mental Health Visits, by Year

	Population With Schizophrenia	Patients Using Atypicals (%)	Mental Health Emergency Department (ED) Admissions (events per patient)	Mental Health Inpatient (IP) Admissions (events per patient)
2001	499,853	195,860 (39.2%)	27,592 (.055)	109,968 (.220)
2002	552,687	277,699 (50.2%)	33,952 (.061)	121,591 (.220)
2003	570,015	306,636 (53.8%)	37,241 (.065)	128,058 (.225)
2004	572,784	320,137 (55.9%)	34,442 (.060)	125,279 (.219)
2005	541,555	273,319 (50.5%)	32,251 (.060)	114,678 (.212)

Table 3. Summary Statistics Showing Replications of Failure by Year for Alternative Measurement Strategies

		Average Annual Number of Events per Person in Sample		
		Resume Same Drug After 30-Day Gap	Resume Same Drug Within 6 months of IP Admit	Resume Same Drug Within 6 Months of ED Admit
2001	No atypicals on FR	1.07	0.53	0.46
2002	No atypicals on FR	1.24	0.66	0.62
	At least 1 atypical on FR	1.27	0.57	0.53
	Total	1.25	0.64	0.56
2003	No atypicals on FR	1.29	0.75	0.70
	At least 1 atypical on FR	1.28	0.73	0.64
	Total	1.29	0.74	0.69
2004	No atypicals on FR	1.24	0.67	0.62
	At least 1 atypical on FR	1.25	0.68	0.56
	All atypicals on FR	1.33	0.62	0.59
	Total	1.26	0.67	0.61
2005	No atypicals on FR	0.99	0.72	0.63
	At least 1 atypical on FR	0.99	0.67	0.62
	All atypicals on FR	1.04	0.65	0.65
	Total	1.00	0.69	0.63

ED indicates emergency department; FR, formulary restriction, IP, inpatient.
All mean values conditional on either (1) taking an atypical in the given year, (2) taking an atypical and having an IP admit, or (3) taking an atypical and having an ED admit.

under a formulary restriction by 2005 as the treatment group (Table 4B), the difference-in-differences coefficient is found to be 0.201 (SE 0.011). This shows a substantial effect of placing all atypicals onto a formulary restriction, as the probability of resuming the same atypical after a stoppage of at least 30 days increased by 20.1% relative to the control group states.

The next outcomes measured were resumptions of the same atypical antipsychotic after an inpatient and ED admission with a mental health diagnosis. The sample was further restricted to patients meeting our inclusion criteria who were also admitted as an inpatient, or who visited the ED in the given year with a mental health condition. When states with no formulary restrictions are compared with those with only some atypicals restricted, the results suggest no statistical impact of these restrictions on resuming the same atypical after an admission. In states that restricted all atypicals, the policy was not shown to have any effect on resuming the same atypical after an ED visit.

Table 4A. Difference-in-Differences Regressions: Comparing Change in Replications of Failure per Patient Between 2001 and 2005, for States That Did and Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With a Single Atypical on Formulary Restriction			
	Alternative Measures of Replication of Failure		
	(1) Resume Same Drug After 30-Day Gap	(2) Resume Same Drug Within 6 Months of IP Admittance	(3) Resume Same Drug Within 6 Months of ED Admittance
Indicator variable for states with at least 1 atypical on FR	–0.015 [0.063]	–0.020 [0.038]	0.014 [0.038]
Indicator variable for year 2005	–0.144[a] [0.017]	0.196[a] [0.024]	0.189[a] [0.019]
Difference-in-differences estimate	0.062[b] [0.023]	–0.039 [0.036]	–0.006 [0.042]
Constant	1.074[a] [0.050]	0.544[a] [0.038]	0.451[a] [0.021]
Observations	373,649	23,787	5611
R^2	0.002	0.010	0.014

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
Replication of failure is defined here as resuming the same atypical after either (1) at least a 30-day gap in prescription coverage, (2) at least a 6-month gap in prescription coverage, (3) after a mental health–related inpatient admission, or (4) after a mental health–related ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

Table 4B. Difference-in-Differences Regressions: Comparing Change in Replications of Failure per Patient Between 2001 and 2005, for States That Did and Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With All Atypicals on Formulary Restriction			
	Alternative Measures of Replication of Failure		
	(4) Resume Same Drug After 30-Day Gap	(5) Resume Same Drug Within 6 Months of IP Admittance	(6) Resume Same Drug Within 6 Months of ED Admittance
Indicator variable for states with all atypicals on FR	0.010 [0.082]	–0.040 [0.043]	0.008 [0.042]
Indicator variable for year 2005	–0.144[a] [0.017]	0.196[a] [0.024]	0.189[a] [0.019]
Difference-in-differences estimate	0.201[b] [0.091]	–0.057 [0.033]	–0.031 [0.038]
Constant	1.074[a] [0.050]	0.544[a] [0.038]	0.451[a] [0.021]
Observations	223,161	13,249	5735
R^2	0.005	0.011	0.012

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
Replication of failure is defined here as resuming the same atypical after either (1) at least a 30-day gap in prescription coverage, (2) at least a 6-month gap in prescription coverage, (3) after a mental health–related inpatient admission, or (4) after a mental health–related ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

Table 5 (A and B) shows difference-in-differences results for the outcome of switching from one atypical to another. The control group includes patients in states with no formulary restrictions, while the 2 treatment groups consist of patients in (1) states that placed some atypicals on a formulary restriction, or (2) states that placed all atypicals on formulary restrictions. Individuals in restrictive states who were admitted as inpatients experienced a reduction of about 4.3% in the number of switches between atypicals relative to those in nonrestrictive states. In this case, a triggering event reduces the likelihood that a patient switches from one atypical to another. Similar effects are observed for ED admissions; the reduction in number of switches following an ED admission is 3.2%.

The results in Table 6 (A and B) examine the relationship between the introduction of formulary restrictions on atypicals and patients stopping the use of atypicals in favor of typical antipsychotics that are not on formulary restrictions. For states that placed all atypicals onto formulary restrictions, the number of patients stopping atypical usage in favor of typical antipsychotics is shown to have increased by less than 3.5%.

Table 5A. Difference-in-Differences Regressions: Comparing Changes in the Rate at Which Patients Switched From One Atypical to Another, Between 2001 and 2005 for States That Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With a Single Atypical on Formulary Restriction			
	Alternative Measures of Switching Between Atypicals		
	(1) Discontinue One Atypical and Switch to Another	(3) Switch Atypicals After IP Admittance	(5) Switch Atypicals After ED Admittance
Indicator variable for states with at least 1 atypical on FR	–0.015 [0.041]	–0.018 [0.029]	0.013 [0.011]
Indicator variable for year 2005	–0.101[a] [0.023]	0.090[a] [0.014]	0.066[a] [0.010]
Difference-in-differences estimate	0.035 [0.024]	–0.010 [0.023]	–0.008 [0.025]
Constant	0.223[a] [0.032]	0.128[a] [0.019]	0.072[a] [0.010]
Observations	373,649	23,787	5611
R^2	0.007	0.006	0.006

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
A switch from one atypical to another is defined here as (1) discontinuing usage of one atypical and starting another, (3) changing atypicals after a mental health–related inpatient admission, or (5) changing atypicals after a mental health–related ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

Table 5B. Difference-in-Differences Regressions: Comparing Changes in the Rate at Which Patients Switched From One Atypical to Another, Between 2001 and 2005 for States That Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With All Atypicals on Formulary Restrictions			
	Alternative Measures of Switching Between Different Atypicals		
	(2) Discontinue One Atypical and Switch to Another	(4) Switch Atypicals After IP Admittance	(6) Switch Atypicals After ED Admittance
Indicator variable for states with all atypicals on FR	0.025 [0.037]	–0.024 [0.020]	–0.001 [0.013]
Indicator variable for year 2005	0.101[a] [0.017]	0.090[a] [0.014]	0.066[a] [0.010]
Difference-in-differences estimate	0.093 [0.064]	–0.043[c] [0.024]	–0.032[c] [0.017]
Constant	0.223[a] [0.032]	0.128[a] [0.019]	0.072[a] [0.010]
Observations	223,161	13,249	5735
R^2	0.011	0.007	0.005

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
A switch from 1 atypical to another is defined here as (2) discontinuing usage of 1 atypical and starting another, (4) changing atypicals after a mental health–related inpatient admission, or (6) changing atypicals after a mental health–related ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

Finally, Table 7 shows estimates for when atypical users stopped the use of all mental health drugs. Among those in states that restrict all atypicals, the likelihood of discontinuation increased by 11.6%.

DISCUSSION

Although formulary restrictions hold the promise of reduced Medicaid outlays for pharmaceuticals, they may also have unintended effects that raise Medicaid costs in other areas. In this study, we examined the impact of formulary restrictions on the treatment of schizophrenia. Schizophrenia is very responsive to psychopharmacologic treatment, but the treatment response is highly heterogeneous across patients, and some patients respond only to a single medication. Moreover, the process of finding the appropriate medication is often one of trial and error. Because of this, treatment failures would be expected to cause a switch to a different medication.

We examined several different treatment failures, such as a patient going off medication, a patient being admitted to the

Table 6A. Difference-in-Differences Regressions: Comparing Changes in the Rate at Which Patients Switch From an Atypical Antipsychotic to a Typical Antipsychotic Between 2001 and 2005 for States That Did and Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With a Single Atypical on Formulary Restriction			
	Alternative Measures of Switching Between Atypicals and Typicals		
	(1) Discontinue One Atypical and Switch to Typical	(3) Switch From an Atypical to a Typical Within 6 Months of IP Admittance	(5) Switch From an Atypical to a Typical Within 6 Months of ED Admittance
Indicator variable for states with at least 1 atypical on FR	–0.036[a] [0.010]	0.009 [0.009]	–0.001 [0.010]
Indicator variable for year 2005	–0.012[c] [0.006]	0.019[b] [0.008]	0.011 [0.007]
Difference-in-differences estimate	0.006 [0.007]	–0.010 [0.008]	0.009 [0.015]
Constant	0.208[a] [0.007]	0.069[a] [0.004]	0.057[a] [0.006]
Observations	373,649	23,787	5611
R^2	0.001	0.000	0.001

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
A switch from an atypical to a typical is defined here as (1) discontinuing usage of one atypical and starting a typical, (3) changing from an atypical to a typical after a mental health–related inpatient admission, or (5) changing from an atypical to a typical after a mental health–related ED admission
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

Table 6B. Difference-in-Differences Regressions: Comparing Changes in the Rate at Which Patients Switch From an Atypical Antipsychotic to a Typical Antipsychotic Between 2001 and 2005 for States That Did and Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With All Atypicals on Formulary Restrictions			
	Alternative Measures of Switching Between Atypicals and Typicals		
	(2) Discontinue One Atypical and Switch to Typical	(4) Switch From an Atypical to a Typical Within 6 Months of IP Admittance	(6) Switch From an Atypical to a Typical Within 6 Months of ED Admittance
Indicator variable for states with all atypicals on FR	0.029 [0.027]	0.005 [0.009]	0.001 [0.012]
Indicator variable for year 2005	–0.012[c] [0.006]	0.019[b] [0.008]	0.011 [0.007]
Difference-in-differences estimate	0.035[c] [0.018]	–0.022[c] [0.011]	–0.006 [0.017]
Constant	0.208[a] [0.007]	0.069[a] [0.004]	0.057[a] [0.006]
Observations	223,161	13,249	5735
R^2	0.002	0.001	0.000

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
A switch from an atypical to a typical is defined here as (1) discontinuing usage of one atypical and starting a typical, (3) changing from an atypical to a typical after a mental health–related inpatient admission, or (5) changing from an atypical to a typical after a mental health–related ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

hospital or visiting the ED with a psychological episode, or a patient terminating drug treatment altogether. These rates of replication of failure are relatively large, with 65% of inpatient admissions and 59% of ED admissions resulting in a resumption of the same atypical, regardless of the formulary policies in place. Such rates suggest possible quality-of-care issues, but a deep examination of quality of care lies beyond the scope of this study.

We find that replication of failure increases when states adopt formulary restrictions. These findings are also suggestive of a causal effect. We found that formulary restrictions on atypical antipsychotics increase the likelihood that a patient

■ **Table 7A.** Difference-in-Differences Regressions: Comparing Changes in the Rate at Which Patients Discontinued Antipsychotic Treatment Between 2001 and 2005 for States That Did and Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With a Single Atypical on Formulary Restriction			
	Alternative Measures of Discontinuing Antipsychotic Therapy		
	(1) Discontinuation of Antipsychotic Prescription Medication	(3) Discontinuation of Antipsychotic Prescription Medication Within 6 Months of IP Admittance	(5) Discontinuation of Antipsychotic Prescription Medication Within 6 Months of ED Admittance
Indicator variable for states with at least 1 atypical on FR	0.035 [0.068]	0.028[c] [0.014]	0.021[b] [0.007]
Indicator variable for year 2005	–0.100[a] [0.021]	0.022[a] [0.005]	0.017[c] [0.008]
Difference-in-differences estimate	0.029 [0.025]	–0.018[a] [0.005]	–0.019 [0.015]
Constant	0.711[a] [0.045]	0.070[a] [0.007]	0.058[a] [0.005]
Observations	373,649	23,787	5611
R^2	0.002	0.001	0.001

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
A discontinuation of treatment is defined as (1) previously using an atypical and then ceasing treatment with all mental health drugs for the remainder of Medicaid enrollment, (3) ceasing the use of all mental health drugs for the remainder of enrollment after an IP admission, or (5) ceasing the use of all mental health drugs for the remainder of enrollment after an ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

■ **Table 7B.** Difference-in-Differences Regressions: Comparing Changes in the Rate at Which Patients Discontinued Antipsychotic Treatment Between 2001 and 2005 for States That Did and Did Not Adopt Formulary Restrictions by 2005

Comparing States With No Formulary Restrictions and States With All Atypicals on Formulary Restrictions			
	Alternative Measures of Discontinuing Antipsychotic Therapy		
	(2) Discontinuation of Antipsychotic Prescription Medication	(4) Discontinuation of Antipsychotic Prescription Medication Within 6 Months of IP Admittance	(6) Discontinuation of Antipsychotic Prescription Medication Within 6 Months of ED Admittance
Indicator variable for states with all atypicals on FR	–0.021 [0.066]	0.010 [0.009]	–0.001 [0.009]
Indicator variable for year 2005	–0.100[a] [0.021]	0.022[a] [0.005]	0.017[c] [0.008]
Difference-in-differences estimate	0.116[c] [0.065]	–0.032[a] [0.010]	–0.013 [0.019]
Constant	0.711[a] [0.045]	0.070[a] [0.007]	0.058[a] [0.005]
Observations	223,161	13,249	5735
R^2	0.002	0.001	0.001

ED indicates emergency department; FR, formulary restriction; IP, inpatient.
Robust standard errors in brackets.
A discontinuation of treatment is defined as (2) previously using an atypical and then ceasing treatment with all mental health drugs for the remainder of Medicaid enrollment, (4) ceasing the use of all mental health drugs for the remainder of enrollment after an IP admission, or (6) ceasing the use of all mental health drugs for the remainder of enrollment after an ED admission.
[a] $P < .01$.
[b] $P < .05$.
[c] $P < .1$.

who has stopped taking medication will end up back on the same drug—an indication that the drug failed, but was restarted. This likelihood increases by 6.2% if the patient resides in a state that has implemented formulary restrictions on some atypicals in its Medicaid program, and by 20.1% if the state of residence's formulary restrictions cover all atypicals. This suggests that formulary restrictions cause doctors to return patients to treatments for which there is evidence that the treatment is not effective.

Moreover, we found that the likelihood that a patient who was initially on an atypical switches to an older and less expensive medication (a typical/first generation) increases by 3.5% if the state's formulary restricts all atypicals, again relative to the control group of states without restrictions. This again suggests that state formulary restrictions are pushing doctors to alter their treatment choices in ways that they did not think benefited the patient before the formulary restriction. Finally, we found that when states impose formulary restrictions on atypicals, the likelihood that a patient on atypicals discontinues all treatment with either typicals or atypicals increases by 11.6% if the state restricts all atypicals under its formulary restrictions. These findings indicate that state formulary restrictions have an impact on the likelihood that doctors will try an alternative therapy when markers of failure present themselves, and that doctors are induced by formulary restrictions to switch to alternative therapies even when there are no indicators that the current treatment is ineffective.

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REFERENCES

1. Consumer Health Sourcebook. National health expenditures by type of service and source of funds: calendar years 1960 to 2009. http://www.chsourcebook.com/docs/nhe_aggregate_2009.pdf. Published 2009.

2. Soumerai SB, Zhang F, Ross-Degnan D, et al. Use of atypical antipsychotic drugs for schizophrenia in Maine Medicaid following a policy change. *Health Aff (Millwood).* 2008;27(3):w185-w195.

3. Mello MM, Studdert DM, Brennan TA. The pharmaceutical industry versus Medicaid: limits on state initiatives to control prescription-drug costs. *N Engl J Med.* 2004;350(6):608-613.

4. Nguyen NX, Derrick FW. Physician behavioral response to a Medicare price reduction. *Health Serv Res.* 1997;32(3):283-298.

5. Makoul G, Arntson P, Schofield T. Health promotion in primary care: physician-patient communication and decision making about prescription medications. *Soc Sci Med.* 1995;41(9):1241-1254.

6. Soumerai SB, McLaughlin TJ, Ross-Degnan D, Casteris CS, Bollini P. Effects of limiting Medicaid drug-reimbursement benefits on the use of psychotropic agents and acute mental health services by patients with schizophrenia. *N Engl J Med.* 1994;331(10):650-655.

7. Banthin JS, Miller GE. Trends in prescription drug expenditures by Medicaid enrollees. *Med Care.* 2006;44(5 suppl):I27-I35.

8. Polinski JM, Wang PS, Fischer MA. Medicaid's prior authorization program and access to atypical antipsychotic medications. *Health Aff (Millwood).* 2007;26(3):750-760.

9. Vogt WB, Joyce G, Xia J, Dirani R, Wan G, Goldman DP. Medicaid cost control measures aimed at second-generation antipsychotics led to less use of all antipsychotics. *Health Aff (Millwood).* 2011;30(12):2346-2354.

10. Freedman R. Schizophrenia. *N Engl J Med.* 2003;349(18):1738-1749.

11. Singh SP, Singh V, Kar N, Chan K. Efficacy of antidepressants in treating the negative symptoms of chronic schizophrenia: metaanalysis. *Br J Psychiatry.* 2010;197(3):174-179.

12. Amador XF, Friedman JH, Kasapis C, Yale SA, Flaum M, Gorman JM. Suicidal behavior in schizophrenia and its relationship to awareness of illness. *Am J Psychiatry.* 1996;153(9):1185-1188.

13. Farley JF, Cline RR, Schommer JC, Hadsall RS, Nyman JA. Retrospective assessment of Medicaid step-therapy prior authorization policy for atypical antipsychotic medications. *Clin Ther.* 2008;30(8):1524-1539; discussion 06-07.

14. Law MR, Ross-Degnan D, Soumerai SB. Effect of prior authorization of second-generation antipsychotic agents on pharmacy utilization and reimbursements. *Psychiatr Serv.* 2010;59(5):540-546. ■