

# Prior Authorization for Antidepressants in Medicaid

## Effects Among Disabled Dual Enrollees

Alyce S. Adams, PhD; Fang Zhang, PhD; Robert F. LeCates, MA; Amy Johnson Graves, MPH; Dennis Ross-Degnan, ScD; Daniel Gilden, MS; Thomas J. McLaughlin, ScD; Christine Lu, PhD; Connie M. Trinacty, PhD; Stephen B. Soumerai, ScD

**Background:** Prior authorization is a popular, but understudied, strategy for reducing medication costs. We evaluated the impact of a controversial prior authorization policy in Michigan Medicaid on antidepressant use and health outcomes among dual Medicaid and Medicare enrollees with a Social Security Disability Insurance designation of permanent disability.

**Methods:** We linked Medicaid and Medicare (2000-2003) claims for dual enrollees in Michigan and a comparison state, Indiana. Using interrupted time-series and longitudinal data analysis, we estimated the impact of the policy on antidepressant medication use, treatment initiation, disruptions in therapy, and adverse health events among continuously enrolled (Michigan, n=28 798; Indiana, n=21 769) and newly treated (Michigan, n=3671; Indiana, n=2400) patients.

**Results:** In Michigan, the proportion of patients starting nonpreferred agents declined from 53% prepolicy to 20%

postpolicy. The prior authorization policy was associated with a small sustained decrease in therapy initiation overall (9 per 10 000 population;  $P = .007$ ). We also observed a short-term increase in switching among established users of nonpreferred agents overall (risk ratio, 2.88; 95% confidence interval, 1.87-4.42) and among those with depression (2.04; 1.22-3.42). However, we found no evidence of increased disruptions in treatment or adverse events (ie, hospitalization, emergency department use) among newly treated patients.

**Conclusions:** Prior authorization was associated with increased use of preferred agents with no evidence of disruptions in therapy or adverse health events among new users. However, unintended effects on treatment initiation and switching among patients already taking the drug were also observed, lending support to the state's previous decision to discontinue prior approval for antidepressants in 2003.

*Arch Intern Med.* 2009;169(8):750-756

**Author Affiliations:** Kaiser Permanente Division of Research, Oakland, California (Dr Adams); Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, Massachusetts (Drs Adams, Zhang, Ross-Degnan, Lu, Trinacty, and Soumerai, Mr LeCates, and Ms Graves); Jen Associates, Inc, Cambridge, Massachusetts (Mr Gilden); and Department of Pediatrics and Psychiatry, School of Medicine, University of Massachusetts, Worcester (Dr McLaughlin).

**P**SYCHOTROPIC MEDICATION spending among dual enrollees has contributed to the rising popularity of prior authorization (PA) among Medicaid and Medicare Part D plans.<sup>1,2</sup> Under PA, pre-approval is required for reimbursement of prescriptions for particular drugs or drug categories. Despite their widespread use, few studies have examined the impact of PA policies on rates of medication use and health outcomes among vulnerable Medicaid and Medicare enrollees.<sup>3-5</sup> In a recent study of Medicaid enrollees with schizophrenia, we observed increased gaps in treatment associated with PA requirements for atypical antipsychotic medications.<sup>5</sup> Nonelderly disabled dual enrollees may be especially vulnerable to PA-related disruptions in therapy due to a higher reliance on psychotropic medications, high prevalence of complex comorbidities, and lower socioeconomic status, which may inhibit their ability to navigate changes in coverage.<sup>2,4</sup> The heightened vulnerability of dual enrollees has sparked concerns about their

random assignment to Medicare Part D plans, many of which require PA for mental health drugs.<sup>6</sup>

*See also pages 737, 740, and 757*

The purpose of the present study was to evaluate the impact of the Michigan PA for nonpreferred antidepressants among nonelderly disabled dual enrollees. In March 2002, the Michigan Medicaid program began requiring PA for new prescriptions of nonpreferred antidepressants, including commonly used selective serotonin reuptake inhibitors (SSRIs) (citalopram hydrobromide [Celexa], fluvoxamine maleate [Luvox], brand fluoxetine hydrochloride [Prozac and Sarafem], and sertraline hydrochloride [Zoloft]) and a serotonin norepinephrine reuptake inhibitor (SNRI), venlafaxine hydrochloride. Preferred agents included generic fluoxetine hydrochloride (newly off patent) and paroxetine hydrochloride (Paxil and Paxil CR).<sup>7</sup>

Federal rules required the state to respond to physician requests for PA within 24 hours and to provide a 72-hour emergency drug supply while the request was being processed. In addition, Michigan Medicaid grandfathered or excluded from the policy patients already taking nonpreferred medications. Following policy implementation, patient advocacy groups reported barriers to medication access resulting from the Michigan antidepressant PA policy.<sup>7</sup> In late June 2003, after clinical review of the preferred drug list, the Medicaid director announced the removal of PA for antidepressants and other mental health medications, stating that, "Making more of these critical drugs available without the need for prior authorization helps to avoid possible setbacks in care due to changes in drug treatment therapy."<sup>8(p2)</sup> To date, an external evaluation of this policy has not been published.

Based on our previous study,<sup>5</sup> we hypothesized that the policy would reduce the use of nonpreferred SSRI/SNRI agents among dual enrollees. However, we also hypothesized that problems in the implementation of the PA policy may have resulted in short-term disruptions in treatment, including unintended switching of antidepressants among established users, and lower rates of initiation of antidepressant treatment.

Among newly treated dual enrollees, the population targeted by the policy, we investigated the impact of the policy on patterns of medication use (ie, switching/augmentation, discontinuation, persistence) and use of nondrug health services (ie, hospitalization, emergency department admission). We hypothesized that the policy may result in treatment disruptions that may reflect differences in treatment effectiveness, confusion about the policy, and other factors. Finally, we hypothesized that undesired changes in medication use (ie, early discontinuation) may have resulted in adverse health events (eg, hospitalization, emergency department use) within this vulnerable subset of Medicaid patients.

## METHODS

### DATA SOURCES AND STUDY POPULATION

We linked Medicaid and Medicare enrollment and claims data from January 1, 2000, through December 31, 2003, to identify 2 distinct cohorts in Michigan and Indiana. First, we identified patients who were continuously enrolled in Michigan or Indiana Medicaid and concurrently enrolled in Medicare for all 4 years. We included only patients who were between the ages of 18 and 64 and who had a Social Security Disability Insurance designation of permanent disability. We excluded patients with any Medicare or Medicaid managed care enrollment. Within the continuously enrolled cohort, we identified analytic subgroups of potential initiators and established users of antidepressant treatment (see the "Outcome Measures" subsection of the "Methods" section).

We defined a second cohort of nonelderly fee-for-service enrollees between November 1, 2000, and December 31, 2002, who filled an outpatient prescription for an SSRI/SNRI with no evidence of a dispensing of any antidepressant agent during the previous 6 months.<sup>9</sup> Within this cohort of newly treated patients, we identified 2 subcohorts: the prepolicy cohort, who began SSRI/SNRI therapy between November 2000 and August 2001; and the postpolicy cohort, who began therapy between March 2002 and December 2002. This allowed 10 months

for accrual and a minimum of 6 months of medication follow-up with no overlap between the 6-month follow-up period for the prepolicy cohort and the accrual period for the postpolicy cohort. Newly treated patients were required to be continuously dually enrolled in Michigan or Indiana Medicaid and Medicare for 10 months before and 1 year after the initiation of SSRI/SNRI therapy. We further required that newly treated patients spent fewer than 45 days in an institution (eg, hospital) during the 90 days before initiation of treatment.

While we did not require a depression diagnosis for inclusion in the continuously enrolled or newly treated cohorts, we conducted subgroup analyses for patients with evidence of depression, indicated by at least 1 inpatient or 2 outpatient diagnoses of depression (*International Classification of Diseases, Ninth Revision* codes 296.2, 296.3, 298.0, 300.4, 309.1, and 311).<sup>10</sup> We also examined high-risk subgroups of patients with diagnoses of schizophrenia or schizoaffective disorder (295) and bipolar disorder (296.0, 296.1, 296.4-296.7, 296.89, and 301.11).<sup>10</sup>

## OUTCOME MEASURES

### Rates of Medication Use

To examine overall trends in medication use within the continuously enrolled population, we used an interrupted time-series analysis with comparison-series design to examine changes in trends in the proportion of patients using any, SSRI/SNRIs (preferred and nonpreferred), and other antidepressants. Preferred and nonpreferred categories were determined by the state PA rules except for fluoxetine. Because of the introduction of generic fluoxetine to the market before policy implementation, we included both generic and brand fluoxetine in the preferred medication category. This allowed us to separate shifts in market share due to generic entry from the effect of the policy. For each generic entity, we then used information from pharmacy claims on the amount dispensed to create daily patient-level measures of medication use among defined subpopulations (ie, potential initiators, established users, newly treated patients).

### Rates of Therapy Initiation

From the continuously enrolled cohort, we identified a rolling subcohort of potential antidepressant initiators, defined as having no antidepressant use in the previous 6 months and fewer than 45 days in an institution during the previous 3 months. This denominator was then used to calculate the proportion of patients in each month who initiated any, SSRI/SNRI, or other antidepressant treatments. This proportion was the primary outcome measure in a time-series model predicting changes in the level and trend in rates of initiation.

### Rates of Switching Among Established Users

Similarly, we identified a rolling cohort of established SSRI/SNRI users, defined as having had at least 2 dispensings of a single SSRI or SNRI therapy during the previous 6 months. We calculated the monthly proportion of these individuals who received a second antidepressant agent and no subsequent dispensing of the first agent in the following 6-month period. This indicator was the primary outcome of interest in a patient-level analysis examining changes in the likelihood of unintended switching among those previously taking antidepressant drugs. Given the rolling cohort design used for this outcome, we used a different definition of the prepolicy and postpolicy period to allow for an examination of switching during the period of policy implementation (prepolicy, March 2001–January 2002; policy implementation, February–April 2002; postpolicy, May 2002–April 2003).

## Patterns of Antidepressant Use Among Newly Treated Patients

Among newly treated patients, we also examined 3 patient-level medication use outcomes: switching/augmentation, discontinuation, and persistence with therapy. We defined switching/augmentation as dispensing of a second antidepressant agent during the 6 months following initiation of treatment. This definition was broader than that used for the cohort of current users as it allowed for augmentation (ie, addition of a second agent without discontinuation of the first agent). We treat switching/augmentation as an indicator of lack of response to the initial therapeutic regimen. Discontinuation was defined as a gap in available therapy of at least 30 days during the first 6 months following initiation of treatment. Time until switching/augmentation and discontinuation were the primary outcomes for patient-level survival analysis.

We defined persistence as having medication available for at least 4 of 6 months following initiation of treatment.<sup>11</sup> This measure was included as a dichotomous outcome for patient-level analyses exploring the impact of the policy on continuity of treatment. We censored patients with no evidence of use for 30 days or longer.

## Hospitalization and Emergency Department Use Among Newly Treated Patients

We assessed potential adverse clinical effects of the policy by examining changes in the risk of hospitalization and emergency department use, comparing patients who initiated therapy before or after the policy implementation in the study state and the comparison state. Hospital events were counted if they included at least 1 overnight stay. Emergency department visit counts excluded those that resulted in a hospital episode. We examined all hospital and emergency department events.

## COVARIATES

From the Medicaid and Medicare enrollment files, we identified patient age ( $\leq 34$ , 35-54, and  $\geq 55$  years old), race/ethnicity (black, white, and other), and sex, which may have influenced the timing and use of antidepressant therapy.<sup>12,13</sup> We approximated level of comorbidity using a count of the total number of nonantidepressant medications used by each patient at baseline.<sup>14</sup>

## STATISTICAL ANALYSIS

We estimated population-level changes in our medication utilization measures in Michigan and Indiana (ie, level, trend) using interrupted time-series models,<sup>15,16</sup> including the proportion of enrollees using antidepressant medications per month and the proportion of patients initiating treatment in each month. Model fit was assessed using a Durbin-Watson statistic, and we tested for autocorrelation and nonlinearity of the outcomes of interest. For parsimony, nonsignificant terms ( $P > .05$ ) were excluded from the final time-series models.<sup>17</sup>

Patient-level effects of the policy were assessed using generalized estimating equations<sup>18</sup> and survival analysis.<sup>19</sup> First, we used a segmented generalized estimating equation to estimate the likelihood of switching from current SSRI or SNRI monotherapy overall, and then we stratified by preferred and nonpreferred drug status. The model included 3 periods: 1 year prepolicy (March 2001-January 2002), a 3-month policy implementation period (February 2002-April 2002), and 1 year postpolicy (May 2002-April 2003). An interaction term between state (Michigan = 1; In-

diana = 0) and the postpolicy time segments provided an indicator of short- and long-term policy impact.

These models also included age, race/ethnicity, sex, level of comorbidity, and the number of dispensings of antidepressant drugs in the previous 6 months to control for frequency of use. The robust sandwich estimator was used for the modeling of the correlated error structure.<sup>17</sup> We also conducted a subgroup analysis for patients with evidence of depression.

Among the newly treated cohort, we used Cox proportional hazards models to estimate the hazard of switching/augmentation and discontinuation for patients who initiated treatment before (November 2000–August 2001) and after (March 2002–December 2002) the policy in each state. The models included age, sex, race/ethnicity, and level of comorbidity. We also conducted analyses for patients with depression. We tested the proportional hazards assumption using the supremum test.<sup>18</sup> The models controlled for age, race/ethnicity, sex, and comorbidity as described earlier.

To estimate the impact of the policy on persistence of treatment, we used generalized linear models to assess the impact of the policy on the likelihood of having medication available for use during at least 4 of the 6 months following initiation of treatment.<sup>11</sup> An interaction between the policy period and state represented the total policy effect. Other covariates included in the model were age, sex, race/ethnicity, and level of comorbidity. Model fit was assessed using likelihood statistics.<sup>18</sup>

Survival models similar to those described earlier were used to assess changes in the hazard of hospitalization or emergency department use during the 12 months following initiation of antidepressant treatment among patients starting in the prepolicy and postpolicy period in each state. We ran these models for all newly treated patients and for the subset of patients who had evidence of depression or severe mental illness (ie, schizophrenia, bipolar diagnosis) at baseline. Furthermore, we examined the subset of hospitalizations and emergency department visits with a psychiatric diagnosis (depression, bipolar disorder, schizophrenia, or schizoaffective disorder) or that occurred in a psychiatric inpatient facility. Model fit was assessed using the supremum test.<sup>19</sup>

We engaged an expert panel of clinical psychiatrists to provide an internal review of our study methods and our interpretation of the key findings. In addition, a draft of this report was provided to the director's office at the Michigan Department of Community Health Medicaid Program before submission for publication. This study was approved by the institutional review board at Harvard Pilgrim Health Care.

## RESULTS

### COHORT CHARACTERISTICS

**Table 1** shows the similarities in baseline demographic and other characteristics of the continuously enrolled cohort of dual enrollees in the study and comparison state. Overall, dual enrollees in the continuously enrolled and newly treated cohorts were similar across states.

### INTENDED EFFECTS

#### Rates of Antidepressant Use by Preferred Status

Among continuously enrolled dual enrollees in Michigan, there was a 1 percentage point absolute decrease in the use of nonpreferred SSRI/SNRI agents attributed to

**Table 1. Baseline<sup>a</sup> Characteristics of the Study and Comparison Cohorts**

| Characteristic                     | Continuously Enrolled Patients    |                                       | Newly Treated Patients          |                                     |
|------------------------------------|-----------------------------------|---------------------------------------|---------------------------------|-------------------------------------|
|                                    | Study Cohort, Michigan (n=28 798) | Comparison Cohort, Indiana (n=21 769) | Study Cohort, Michigan (n=3671) | Comparison Cohort, Indiana (n=2400) |
| Female sex, %                      | 48.1                              | 52.2 <sup>b</sup>                     | 57.0                            | 60.8                                |
| Age group, y, %                    |                                   |                                       |                                 |                                     |
| ≤34                                | 12.8                              | 13.6                                  | 17.8                            | 17.1                                |
| 35-54                              | 65.9                              | 61.9                                  | 61.2                            | 57.4                                |
| 55-64                              | 21.3                              | 24.5 <sup>b</sup>                     | 21.0                            | 25.5 <sup>b</sup>                   |
| Race/ethnicity, %                  |                                   |                                       |                                 |                                     |
| White                              | 78.3                              | 85.2                                  | 74.2                            | 86.9                                |
| Black                              | 19.1                              | 13.2                                  | 22.9                            | 11.4                                |
| Other                              | 2.4                               | 1.4                                   | 2.9                             | 1.5                                 |
| Unknown                            | 0.2                               | 0.2 <sup>b</sup>                      | 0.03                            | 0.2 <sup>b</sup>                    |
| Antianxiety use, %                 | 25.4                              | 27.5 <sup>b</sup>                     | 31.0                            | 35.0                                |
| Antipsychotic use, %               |                                   |                                       |                                 |                                     |
| Typical                            | 12.3                              | 11.2 <sup>b</sup>                     | 11.8                            | 9.4                                 |
| Atypical                           | 22.1                              | 23.6 <sup>b</sup>                     | 21.6                            | 21.0                                |
| Antimanic use, %                   | 3.7                               | 3.4                                   | 3.3                             | 3.0                                 |
| Antidepressant use, %              | 35.7                              | 39.7 <sup>b</sup>                     | NA                              | NA                                  |
| SSRI/SNRI only <sup>c</sup>        | 48.8                              | 43.7                                  | ...                             | ...                                 |
| SSRI/SNRI + TCA/other <sup>c</sup> | 23.0                              | 28.8                                  | ...                             | ...                                 |
| Tricyclics only <sup>c</sup>       | 12.2                              | 10.4                                  | ...                             | ...                                 |
| Other only                         | 14.1                              | 14.8                                  | ...                             | ...                                 |
| Any other combination              | 1.9                               | 2.3 <sup>b</sup>                      | ...                             | ...                                 |
| % With hospital admission          | 18.7                              | 22.6 <sup>b</sup>                     | 28.5                            | 30.3                                |

Abbreviations: SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants.  
<sup>a</sup>Baseline period is 2001 for continuously enrolled cohort and 10 months before antidepressant therapy initiation for the newly treated cohort.

<sup>b</sup> $P < .001$  between 2 states.

<sup>c</sup>Calculated for continuously enrolled patients who had at least 1 antidepressant prescription filled during the baseline period.

the policy ( $P < .001$ ), which was accompanied by a declining trend postpolicy ( $b = -0.001$ ;  $P < .001$ ). These declines were largely offset by an increase in the use of preferred SSRI agents. In Indiana, there was a 2% ( $P < .01$ ) absolute increase in the use of nonpreferred agents during the same period, accompanied by a slight decline in trend ( $b = -0.001$ ;  $P < .01$ ) (Figure 1). Changes in Michigan were driven by a dramatic shift away from nonpreferred agents among newly treated patients. While more than 50% of newly treated patients initiated on these agents prepolicy, fewer than 20% did so postpolicy (data not shown).

## UNINTENDED EFFECTS

### Rates of Therapy Initiation

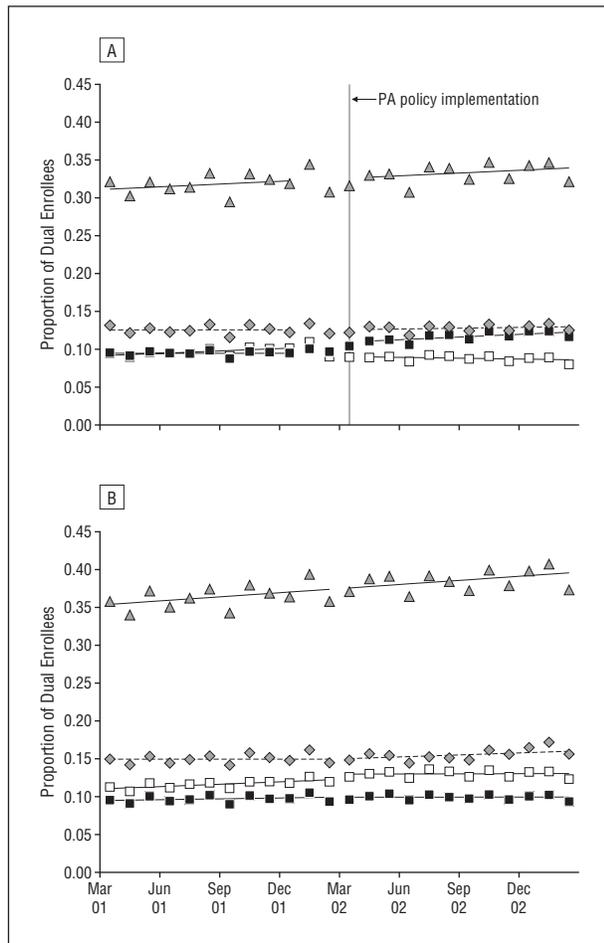
In Michigan, there was a slight decrease in the number of dual enrollees starting any antidepressant therapy (eg, SSRI/SNRI, tricyclics, bupropion) (9 per 10 000 population;  $P = .02$ ) immediately following the implementation of the PA policy that was largely driven by declines in SSRI/SNRI initiations (Figure 2, A). There was no change in the level or rate of antidepressant therapy initiation among dual enrollees in Indiana during this time. For the subgroup of dual enrollees with depression, we observed a slight declining trend in rates of antidepressant initiation in Michigan postpolicy (5 per 10 000;  $P = .005$ ) (data not shown). Trends in initiation of antidepressant therapy for this subgroup in Indiana were stable over time.

### Switching From Current Therapy

Among the rolling cohort of established SSRI/SNRI users (Figure 2, B), there was a visible increase in rates of switching therapy during policy implementation (the month before, during, and immediately after). We modeled these trends using generalized estimating equation models and found a 2-fold higher risk of switching during implementation among dual enrollees in Michigan relative to Indiana overall (risk ratio [RR], 2.07; 95% confidence interval [CI], 1.48-2.88) and among those with depression (1.53; 1.01-2.32) (Table 2, column 6). Dual enrollees taking nonpreferred agents (approximately 49% of established users) had the highest odds of switching therapy (overall, 2.88; 1.87-4.42; depression, 2.04; 1.22-3.42) (Table 2, column 6). There was no evidence of increased risk during the remainder of the follow-up period (Table 2, column 7).

### Discontinuities in Therapy Among Newly Treated Patients

Comparing rates of switching/augmentation and discontinuation among newly treated dual enrollees in Michigan prepolicy and postpolicy to those in Indiana (Table 3, column 4), we found no evidence of greater risk of treatment disruptions in the study state overall (switching/augmentation, RR, 1.02; 95% CI, 0.78-1.35; discontinuation, 1.02; 0.90-1.17) (Table 3) or among those with a depression diagnosis (switching/augmentation, 1.30; 0.85-

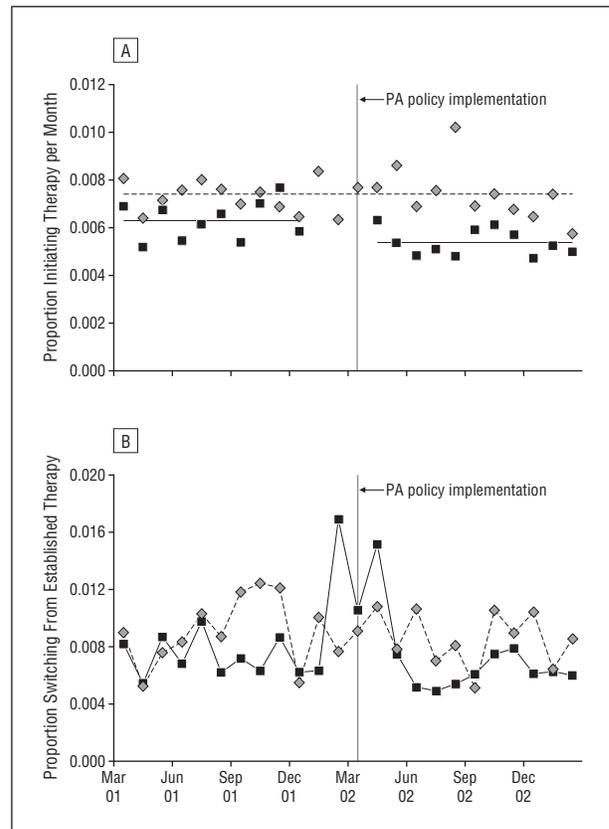


**Figure 1.** Prevalence of use by type of antidepressant (Michigan, n=28 798 [A]; Indiana, n=21 769 [B]). PA indicates prior authorization; gray triangles, all antidepressants; gray diamonds, other antidepressants; open boxes, nonpreferred selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors (SSRIs/SNRIs); solid boxes, preferred SSRIs/SNRIs.

1.97; discontinuation, 0.95; 0.75-1.21) (data not shown). Persistence with therapy was slightly higher in Michigan postpolicy but was not statistically significant (1.37; 0.86-2.18) (data not shown).

### Hospitalization and Emergency Visits Among Newly Treated Patients

Table 3 shows results from the survival models assessing time until emergency department visit and hospitalization in the 12 months following initiation of antidepressant therapy in the postpolicy vs prepolicy period among dual enrollees in each state and comparing these ratios across states. No statistically significant differences in the risk of an event were identified in the overall cohort (emergency department: RR, 0.95; 95% CI, 0.83-1.09; hospitalization, 1.11; 0.92-1.33) (Table 3, column 4). We found similar results for dual enrollees who had a diagnosis of depression (emergency department, 0.94; 0.75-1.18; hospitalization, 1.09; 0.83-1.43) or a diagnosis of severe mental illness (emergency department, 0.96; 0.73-1.25; hospitalization, 1.08; 0.78-1.48) at baseline. Last, we observed no statistically significant changes in



**Figure 2.** Rates of antidepressant therapy initiation (Michigan, n=28 798, solid boxes; Indiana, n=21 769, gray diamonds) (A) and switching among established selective serotonin reuptake inhibitor/serotonin norepinephrine reuptake inhibitor users (Michigan, n=14 638; Indiana, n=10 398) (B). PA indicates prior authorization.

rates of psychiatric hospitalizations or emergency department visits (data not shown).

### COMMENT

The PA policy for new users of SSRI/SNRI therapy in Michigan Medicaid was associated with a small shift in use toward preferred agents among dual enrollees. We found no evidence of discontinuities in medication use or greater risk of emergency department use or hospitalization among newly treated dual enrollees. However, the policy was associated with a small, but immediate, decrease in the number of dual enrollees starting any antidepressant therapy and a decreasing trend in new starts among dual enrollees with a diagnosis of depression. Furthermore, despite the intent of the policy to affect only new users, we also observed a short-term increase in switching among dual enrollees already taking non-preferred SSRI/SNRI agents.

The decrease in the initial rates of therapy may indicate that the policy created a barrier to initial treatment. This is consistent with the Kaiser Family Foundation case study of the Michigan policy, which indicated that some Medicaid patients may have been turned away at the pharmacy after being prescribed a nonpreferred agent without prior approval.<sup>7</sup> In addition, our results are consistent with those of McCombs and colleagues,<sup>20</sup> who found

**Table 2. Likelihood of Switching Among Established Users of SSRI/SNRI Monotherapy<sup>a</sup>**

|   | Adjusted Odds Ratio (95% CI)                                     |  |   |  | Risk Ratio (95% CI)<br>(Michigan vs Indiana) |                            |
|---|--|--|---|--|--|----------------------------|
|   | Michigan   |  | Indiana   |  | Implementation<br>vs Prepolicy               | Postpolicy<br>vs Prepolicy |
|   | Implementation<br>(n=4284) vs<br>Prepolicy (n=5093) <sup>b</sup> | Postpolicy<br>(n=5261) vs<br>Prepolicy | Implementation<br>(n=2930) vs<br>Prepolicy (n=3633) | Postpolicy<br>(n=3835) vs<br>Prepolicy |  |                            |
| All established users                                   | 2.43 (1.99-2.97) <sup>c</sup>                                    | 0.97 (0.81-1.16)                       | 1.18 (0.90-1.54)                                    | 1.00 (0.82-1.22)                       | 2.07 (1.48-2.88) <sup>c</sup>                | 0.97 (0.74-1.26)           |
| Using nonpreferred<br>agents before switch <sup>d</sup> | 3.52 (2.74-4.51) <sup>c</sup>                                    | 0.87 (0.67-1.14)                       | 1.22 (0.86-1.74)                                    | 1.00 (0.77-1.30)                       | 2.88 (1.87-4.42) <sup>c</sup>                | 0.87 (0.60-1.26)           |
|   | Implementation<br>(n=1859) vs<br>Prepolicy (n=2291)              | Postpolicy<br>(n=2366) vs<br>Prepolicy | Implementation<br>(n=1461) vs<br>Prepolicy (n=1890) | Postpolicy<br>(n=1986)<br>vs Prepolicy | Implementation<br>vs Prepolicy               | Postpolicy vs<br>Prepolicy |
| Established users with<br>depression                    | 2.05 (1.57-2.67) <sup>c</sup>                                    | 0.93 (0.73-1.17)                       | 1.34 (0.97-1.84)                                    | 1.05 (0.83-1.33)                       | 1.53 (1.01-2.32) <sup>c</sup>                | 0.88 (0.63-1.23)           |
| Using nonpreferred<br>agents before switch <sup>d</sup> | 2.98 (2.16-4.12) <sup>c</sup>                                    | 0.84 (0.60-1.17)                       | 1.46 (0.98-2.18)                                    | 1.05 (0.77-1.43)                       | 2.04 (1.22-3.42) <sup>c</sup>                | 0.80 (0.51-1.27)           |

Abbreviations: CI, confidence interval; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor.

<sup>a</sup>Models control for age, sex, race/ethnicity, comorbidity, and frequency of antidepressant use during the past 6 months.

<sup>b</sup>Prepolicy: March 2002–January 2002; implementation period: February 2002–April 2002; post policy: May 2002–April 2003.

<sup>c</sup>P < .05.

<sup>d</sup>Sample size of all established users using nonpreferred agents before switch in Michigan (prepolicy, 2490; implementation, 2090; postpolicy, 2236) and Indiana (prepolicy, 1857; implementation, 1516; postpolicy, 2038); established users with depression using nonpreferred agents before switching medications in Michigan (prepolicy, 1131; implementation, 912; postpolicy, 1038) and Indiana (prepolicy, 993; implementation, 774; postpolicy, 1076).

**Table 3. Results of Survival Models for Patients Newly Treated With Antidepressants<sup>a,b</sup>**

|   | Adjusted Hazard Ratio, Postpolicy<br>vs Prepolicy Hazard (95% CI) <sup>c</sup> |                  | Change in Michigan<br>vs Indiana Risk Ratios<br>(95% CI) |
|---|--|------------------|--|
|   | Michigan (n=3671)  | Indiana (n=2400) |  |
| <b>Therapy Disruption 6 Months Following Initiation</b> |  |                  |  |
| All newly treated patients                              |  |                  |  |
| Switching/augmentation to another SSRI/SNRI             | 0.75 (0.57-0.98) <sup>d</sup>  | 0.77 (0.56-1.05) | 0.97 (0.64-1.47)   |
| Switching/augmentation to any antidepressant            | 0.94 (0.78-1.13)   | 0.92 (0.75-1.12) | 1.02 (0.78-1.35)   |
| Discontinuation of SSRI/SNRI therapy                    | 1.10 (1.01-1.19) <sup>c</sup>  | 1.07 (0.97-1.18) | 1.03 (0.91-1.17)   |
| Discontinuation of all antidepressants                  | 1.10 (1.01-1.20) <sup>c</sup>  | 1.08 (0.97-1.19) | 1.02 (0.90-1.17)   |
| <b>Adverse Events 12 Months Following Initiation</b>    |  |                  |  |
| All events  |  |                  |  |
| Emergency department                                    | 1.04 (0.95-1.14)   | 1.09 (0.98-1.21) | 0.95 (0.83-1.09)   |
| Hospitalization   | 1.00 (0.88-1.13)   | 0.90 (0.79-1.04) | 1.11 (0.92-1.33)   |

Abbreviations: CI, confidence interval; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

<sup>a</sup>The SSRIs and SNRIs only.

<sup>b</sup>Models controlled for age, sex, race/ethnicity, and comorbidity.

<sup>c</sup>Prepolicy: November 2000–August 2001; postpolicy: March 2002 and December 2002.

<sup>d</sup>P < .05.

that removal of a PA policy for antidepressants resulted in an increase in new treatment episodes.

Increased rates of switching among established users may be explained by physician avoidance of the PA process. Previous studies have identified administrative burden (eg, time spent understanding PA requirements) associated with PA programs.<sup>21</sup> The short-lived nature of this effect may be indicative of physician learning and/or improved administrative processes within the state Medicaid program.

In contrast with our previous studies of PA policies for atypical antipsychotic and anticonvulsant therapy, we did not observe an increased risk of therapy disruptions among newly treated dual enrollees in Michigan.<sup>5</sup> This difference may reflect greater similarities in efficacy and

effectiveness among newer antidepressants relative to antipsychotic and anticonvulsant therapies.<sup>22-25</sup>

This study has several limitations that merit discussion. Because of incomplete ascertainment of diagnoses of depression in claims data,<sup>26</sup> we did not require that patients in this study have a depression diagnosis. However, our findings of lower rates of initial treatment and increased rates of short-term switching in the overall population were mirrored in the subset of patients with a depression diagnosis, indicating potential effects on access to quality care.

Our requirement of continuous enrollment may have reduced the generalizability of the study findings. We did not have explicit justification for our definition of new users. However, adjustments to definition (ie, 4 months

without any use vs 6 months) did not change study results. Also, our measure of discontinuation may have been imprecise. However, sensitivity analyses around our definition of discontinuation of therapy (ie, 30 vs 45 vs 60 days) did not affect study results.

In summary, PA policies among newly treated dual enrollees receiving SSRI/SNRI therapy may be effective in shifting market share without adverse consequences for treatment continuity. However, challenges in implementation may lead to unintended reductions in rates of initial treatment and short-term disruptions in treatment for established users, even among those with a clinical diagnosis of depression. To the extent that PA policies create a barrier to initial treatment, particularly among dual enrollees with a depression diagnosis, they may reduce access to care as recommended in standard treatment guidelines. These findings indicate a need for frequent and systematic monitoring of PA policies, like that used in Michigan, to identify and mitigate potential unintended consequences for vulnerable dual enrollees.

Accepted for Publication: October 20, 2008.

Correspondence: Alyce S. Adams, PhD, Division of Research, Kaiser Northern California, 2000 Broadway, Oakland, CA 94612 (Alyce.S.Adams@kp.org).

Author Contributions: Drs Adams, Ross-Degnan, McLaughlin, and Soumerai had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Adams, Ross-Degnan, McLaughlin, and Soumerai. *Acquisition of data:* Adams, Gilden, and McLaughlin. *Analysis and interpretation of data:* Adams, Zhang, LeCates, Graves, Gilden, McLaughlin, Lu, Trinacty, and Soumerai. *Drafting of the manuscript:* Adams, LeCates, Ross-Degnan, McLaughlin, and Soumerai. *Critical revision of the manuscript for important intellectual content:* Adams, Zhang, Graves, Ross-Degnan, McLaughlin, Lu, Trinacty, and Soumerai. *Statistical analysis:* Zhang, Ross-Degnan, and McLaughlin. *Obtained funding:* Adams and Soumerai. *Administrative, technical, and material support:* LeCates, Graves, Gilden, McLaughlin, and Trinacty. *Study supervision:* Adams, Ross-Degnan, and Soumerai.

Financial Disclosure: None reported.

Funding/Support: This study was supported by grant 5R01MH069776-03 from the National Institute for Mental Health (NIMH) and was conducted at the Department of Ambulatory Care and Prevention at Harvard Medical School and Harvard Pilgrim Health Care. Dr Lu was supported by the Fellowship Program in Pharmaceutical Policy Research at Harvard Medical School. Dr Trinacty was supported by the Department of Ambulatory Care and Prevention.

Disclaimer: The NIMH had no role in the design or conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

Additional Contributions: We gratefully acknowledge Carl Salzman, MD, Anthony Rothschild, MD, Daryl Tanski, MD, and Alisa Busch, MD, for their clinical expertise and guidance; Jen Associates, Inc for data processing; and Mai Manchanda, AB, for assisting with data acquisition and quality assurance.

## REFERENCES

1. Koyanagi C, Forquer S, Alfano E. Medicaid policies to contain psychiatric drug costs. *Health Aff.* 2005;24(2):536-544.
2. Huskamp HA, Stevenson DG, Donohue JM, Newhouse JP, Keating NL. Coverage and prior authorization of psychotropic drugs under Medicare Part D. *Psychiatr Serv.* 2007;58(3):308-310.
3. Lexchin J. Effects of restrictive formularies in the ambulatory care setting. *Am J Manag Care.* 2002;8(1):69-76.
4. Donohue JM, Frank RG. Estimating Medicare Part D's impact on medication access among dually eligible beneficiaries with mental disorders. *Psychiatr Serv.* 2007;58(10):1285-1291.
5. Soumerai SB, Zhang F, Ross-Degnan D, et al. Use of atypical antipsychotic drugs for schizophrenia in Maine Medicaid following a policy change [published online April 1, 2008]. *Health Aff (Millwood).* 2008;27(3):w185-w195.
6. Elliott RA, Majumdar SR, Gillick MR, Soumerai SB. Benefits and consequences of the new Medicare drug benefit for the poor and the disabled. *N Engl J Med.* 2005;353(26):2739-2741.
7. Kaiser Commission on Medicaid and the Uninsured. Case study: Michigan's Medicaid prescription drug benefit, January 2003. <http://www.kff.org/medicaid/loader.cfm?url=/commonspot/security/getfile.cfm&PageID=14316>. Accessed January 15, 2009.
8. Michigan Department of Community Health. Michigan Department of Community Health Releases update to preferred drug list. July 27, 2003 <http://www.kff.org/medicaid/loader.cfm?url=/commonspot/security/getfile.cfm&PageID=14316>. Accessed January 15, 2009.
9. Croghan TW, Melfi CA, Crown WE, Chawla A. Cost-effectiveness of antidepressant medications. *J Ment Health Policy Econ.* 1998;1(3):109-117.
10. American Medical Association Hospital International Classification of Diseases, 9th Revision, Clinical Modification 2005. Chicago, IL: American Medical Association; 2005.
11. Croghan TW, Melfi CA, Dobrez DG, Kniesner TJ. Effect of mental health specialty care on antidepressant length of therapy. *Med Care.* 1999;37(4)(suppl Lilly):AS20-AS23.
12. Melfi CA, Chawla AJ, Croghan TW, Hanna MP, Kennedy S, Sredli K. The effects of adherence to antidepressant treatment guidelines on relapse and recurrence of depression. *Arch Gen Psychiatry.* 1998;55(12):1128-1132.
13. Hylan TR, Crown WH, Meneades L, et al. SSRI antidepressant drug use patterns in the naturalistic setting: a multivariate analysis. *Med Care.* 1999;37(4)(suppl Lilly):AS36-AS44.
14. Schneeweiss S, Seeger JD, Maclure M, Wang PS, Avorn J, Glynn RJ. Performance of comorbidity scores to control for confounding in epidemiologic studies using claims data. *Am J Epidemiol.* 2001;154(9):854-864.
15. Soumerai SB, Avorn J, Ross-Degnan D, Gortmaker S. Payment restrictions for prescription drugs under Medicaid: effects on therapy, cost, and equity. *N Engl J Med.* 1987;317(9):550-556.
16. Gillings D, Makuc D, Siegel E. Analysis of interrupted time series mortality trends: an example to evaluate regionalized perinatal care. *Am J Public Health.* 1981;71(1):38-46.
17. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther.* 2002;27(4):299-309.
18. Diggle PJ, Heagerty P, Liang KY, Zeger SL. *Analysis of Longitudinal Data.* Oxford, England: Oxford University Press; 2002.
19. Allison PD. *Survival Analysis Using SAS: A Practical Guide.* Cary, NC: SAS Institute Inc; 1995.
20. McCombs JS, Stimmel GL, Croghan TW. A retrospective analysis for the revocation of prior authorization restrictions and the use of antidepressant medications for treating major depressive disorder. *Clin Ther.* 2002;24(11):1939-1959.
21. Wilk JE, West JC, Rae DS, Rubio-Stipec M, Chen JJ, Regier DA. Medicare Part D prescription drug benefits and administrative burden in the care of dually eligible psychiatric patients. *Psychiatr Serv.* 2008;59(1):34-39.
22. Hansen RA, Gartlehner G, Lohr KN, Gaynes BN, Cacy TS. Efficacy and safety of second-generation antidepressants in the treatment of major depressive disorder. *Ann Intern Med.* 2005;143(6):415-426.
23. Katzman BA, Tucco AC, McIntosh D, et al. Paroxetine versus placebo and other agents for depressive disorder: a systematic review and meta-analysis. *J Clin Psychiatry.* 2007;68(12):1845-1859.
24. Manschreck TC, Boshes RA. The CATIE schizophrenia trial: results, impact, controversy. *Harv Rev Psychiatry.* 2007;15(5):245-258.
25. Johannessen Landmark C. Antiepileptic drugs in non-epilepsy disorders: relations between mechanisms of action and clinical efficacy. *CNS Drugs.* 2008;22(1):27-47.
26. Hermann RC. Risk adjustment for mental health care. In: Iezzoni I, ed. *Risk Adjustment for Measuring Health Care Outcomes.* 3rd ed. Chicago, IL: Health Administration Press; 2003:349-362.