

Effects of a Medicaid Prior Authorization Policy for Pregabalin

Jay M. Margolis, PharmD; Stephen S. Johnston, MA; Bong-Chul Chu, PhD; Eberchukwu Onukwugha, PhD; Kyle Hvidsten, MPH; Jose Alvir, DrPH; Joseph G. Rossi, PharmD; and C. Daniel Mullins, PhD

State Medicaid agencies commonly seek to control drug expenditures by enacting prior authorization (PA) policies that restrict access to medications unless specific criteria have been met, such as particular diagnoses, experience with other medications, or the presence of other health conditions. While PA policies enable access to medications according to the predetermined criteria, they create a barrier for patients and providers that effectively reduces prescribing for the target medications.¹⁻⁵ Studies²⁻¹¹ on Medicaid prescription drug cost-containment strategies have shown mixed evidence on the overall effect of PA policies, with some documenting enhanced efficiency and others showing negative clinical and economic effects.

Few studies have examined the effect of PA policies on patients diagnosed as having illnesses or conditions in which pain is the cardinal feature. Pain management often involves several different classes of pharmacologic agents (analgesics, antidepressants, anxiolytics, and others), as well as supportive medical therapy,¹²⁻¹⁴ encompassing a heterogeneous approach to care that extends the physician's therapeutic options. Faced with the restrictions imposed by PA policies, physicians treating patients with these conditions may turn to other pharmacologic therapies and medical services to obtain the necessary degree of pain relief and to alleviate other effects of pain on patient well-being.⁸

Diabetic peripheral neuropathy (DPN), a complication of diabetes mellitus,^{15,16} and postherpetic neuralgia (PHN), a complication of herpes zoster infection,^{17,18} are 2 neuropathic pain conditions that share common pharmacologic treatments. These include opioids, antidepressants, and anticonvulsants¹⁸⁻²² such as the oral medication pregabalin (Lyrica [schedule V]), which is indicated for management of neuropathic pain associated with DPN and for management of PHN.²³ Although pregabalin is one of the medications recommended as first-line treatment in DPN or PHN,^{21,22,24-27} several states have restricted Medicaid beneficiaries' access to pregabalin by requiring a PA for reimbursement. The consequences of these restrictions remain unstudied. Potentially unintended clinical consequences may include the increased use of opioid analgesics and other medications (Table 1), as well as increases in the overall cost of care for these patients. This study

explored the effect of restricted access to pregabalin on prescription medications used in DPN or PHN, as well as healthcare resource utilization and expen-

In this article
Take-Away Points / e96
Published as a Web Exclusive
www.ajmc.com

Objective: To explore the effect of a prior authorization (PA) policy restricting access to pregabalin for the management of diabetic peripheral neuropathy (DPN) or postherpetic neuralgia (PHN) on the overall utilization of pharmacologic therapy and healthcare services among fee-for-service Medicaid plan beneficiaries.

Study Design: Retrospective claims data were obtained for 2005 and 2006 from 6 state Medicaid programs. Two states that had implemented pregabalin PAs beginning in 2006 were compared in terms of drug utilization and costs with 4 states having no such restrictions.

Methods: Patients at least 18 years old in a Medicaid fee-for-service program having a diagnosis of DPN or PHN and at least 1 claim for DPN- or PHN-specific pain medication were selected. Pharmacologic therapy, healthcare utilization, and expenditures were analyzed using bivariate statistics and generalized linear models in a difference-in-difference approach for comparing outcomes between cohorts year over year.

Results: The 2 cohorts included 424 patients in the restricted states and 5153 patients in the unrestricted states. Compared with the use in the unrestricted states, the probability of pregabalin use in the restricted states decreased by 4.0 percentage points ($P = .02$) from 2005 to 2006, while the probability of opioid use increased by 6.5 percentage points ($P < .01$). The DPN- or PHN-related total healthcare costs were \$418 higher for the restricted states versus the unrestricted states ($P < .001$).

Conclusion: Although the PA was shown to effectively control access to pregabalin, the overall effect was an increase in the use of opioids and alternative pain management therapies associated with increased disease-related healthcare costs.

(*Am J Manag Care.* 2009;15(9):e95-e102)

For author information and disclosures, see end of text.

Take-Away Points

This study compared the effect on healthcare utilization and expenditures between 2 groups of state Medicaid programs based on whether the states had implemented a prior authorization (PA) intervention policy for pregabalin. The states with PA policies had significantly lower proportions of patients with any pregabalin use compared with the states without restricted access.

- The PA was associated with increased opioid use and significantly greater disease-specific costs.
- Although the PA accomplished the objective of controlling pregabalin usage, the overall effect was no net savings from the PA policy, with increased use of opioid and other alternative pain management therapies.

long-term care, and prescription drug claims, were used for this study. The restricted states included 1 large industrial state and 1 smaller rural state. The unrestricted states included 2 large industrial states and 2 smaller rural states. None of the states included in the study had both restricted and unrestricted plans. The states' identities cannot be divulged because of contractual arrangements involved in acquiring their data.

ditures among the affected Medicaid populations of states with and without this PA policy.

The objective of this study was to evaluate the effect of a PA policy restricting access to pregabalin for the management of DPN or PHN in terms of the overall utilization of pharmacologic therapies, healthcare services, and direct medical costs for Medicaid beneficiaries with DPN or PHN in states with versus states without a PA policy.

Subject Selection

Patients were required to be at least 18 years old and enrolled in a Medicaid fee-for-service program for the entire duration of 2005 and 2006. They were required to have at least 1 claim with an *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis code for DPN (250.6x or 357.2x) or PHN (053.1x) at any point during 2005-2006 and at least 1 claim for a medication used in treating painful DPN or PHN (Table 1) or for a pain intervention procedure (Table 2) within 60 days after any diagnosis of DPN or PHN. Patients with DPN or PHN were analyzed as a single group because of the small PHN sample size (in both cohorts, 96.2% of patients had only DPN).

METHODS

Study Design

The evaluated intervention was the introduction of a PA for reimbursement of pregabalin for the treatment of painful DPN or PHN. Retrospective claims data were obtained from 6 state Medicaid programs (2 that had implemented pregabalin PAs beginning in 2006 and 4 with no known restriction on reimbursement for pregabalin during 2005 or 2006). For each state, calendar year 2005 was the baseline (preintervention) period, and calendar year 2006 was the follow-up (postintervention) period. The study sample was limited to patients having a diagnosis of DPN or PHN at any time during the 2005-2006 study period. Evidence of treatment for symptomatic relief of DPN or PHN was also required to indicate painful DPN (all PHN is acknowledged as painful).

The study tested the following 3 hypotheses: (1) States with restrictions on pregabalin use ("restricted" states) have lower utilization of pregabalin relative to states without restrictions ("unrestricted" states). (2) Restrictions on pregabalin use are associated with increased use of other medications utilized in the management of painful DPN or PHN, including increases in the use of opioid and nonopioid analgesics. (3) Restrictions on pregabalin use are associated with increases in DPN- or PHN-related direct medical costs.

Data Source

The 2005 and 2006 data of the Thomson Reuters MarketScan Medicaid Database, which includes complete longitudinal records of inpatient services, outpatient services,

Because most Medicaid dual-eligible beneficiaries started to receive their Medicare pharmacy benefits in 2006, we excluded Medicaid patients with Medicare coverage to represent the perspective of a contemporary Medicaid program. This study only included patients in fee-for-service plans because of Medicaid managed care plans' not having complete reporting of medical claims. Patients were also excluded if they had resided in a long-term care facility for 90 days or longer, had any claims with an *ICD-9-CM* diagnosis code for epilepsy (345.xx or 780.39), had 1 inpatient or 2 outpatient nondiagnostic claims for cancer (140.xx-172.xx, 174.xx-208.xx, and 235.xx-239.xx [except for basal cell and squamous cell skin cancers and benign neoplasms]), or had undergone transplant surgery (codes available on request) at any point during 2005-2006.

Table 3 gives the incremental attrition associated with each of these criteria. The resulting cohort sample sizes are given for the restricted states and the unrestricted states.

Study Period

The study period spanned 2005 and 2006. At the time of the study, the most recent Medicaid data availability was through December 2006; therefore, with the PA policy intervention being initiated in January 2006 for the restricted

Medicaid Prior Authorization Policy for Pregabalin

Table 1. Medications Used for Managing Painful Diabetic Peripheral Neuropathy or Postherpetic Neuralgia

Drug Class	Generic Name
Nonopioid analgesics (prescription only)	Celecoxib, diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac tromethamine, mefenamic acid, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin sodium
Opioid analgesics	Buprenorphine, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol tartrate, meperidine, methadone, morphine sulfate, oxycodone, propoxyphene, tramadol, and combinations (with acetaminophen, aspirin, etc)
Anticonvulsants	Carbamazepine, gabapentin, lamotrigine, oxcarbazepine, phenytoin, pregabalin, topiramate, valproate sodium, valproic acid
Tricyclic antidepressants	Amitriptyline, desipramine, doxepin, imipramine, nortriptyline
Other antidepressants	Bupropion, citalopram, duloxetine, paroxetine, trazodone, venlafaxine
Anxiolytics	Alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, lorazepam, oxazepam
Other	Baclofen, clonidine, mexiletine, pamidronate, tizanidine, capsaicin cream, diclofenac cream, lidocaine patch, lidocaine or prilocaine cream

states, 2006 was the follow-up period, and 2005 was used as the baseline period. Pregabalin was approved for painful DPN and PHN in the United States in September 2005; however, the volume of claims for the few patients receiving pregabalin in 2005 was low (2.5% of patients [1.5 prescription claims per patient taking pregabalin]).

Outcome Measures

Diagnoses and pharmacologic therapy were derived from medical and pharmacy claims received according to service dates in 2005 and 2006. Medications for treating DPN or PHN were analyzed by drug class as summarized in Table 1 and for pregabalin individually. The DPN and PHN diagnoses and comorbidities were determined from nondiagnostic medical claims.

Healthcare utilization data included hospital admissions, length of stay, emergency department visits, physician office visits, other outpatient services, and numbers of outpatient prescriptions by drug class and for pregabalin individually. Healthcare expenditures were measured in 2006 Consumer

Price Index–adjusted US dollars using the financial fields on administrative claims in the Medicaid database. Healthcare expenditures were based on the gross covered payments for all healthcare services or products (ie, the amount eligible for payment after applying pricing guidelines such as fee schedules and discounts, including deductibles, copayments, and coordination of benefits). Utilization and expenditure were measured for all medical and pharmacy claims. Medical claims were designated as DPN or PHN specific based on a diagnosis or procedures for DPN or PHN. Any diagnosis code entered for the claim was used.

Statistical Analysis

Bivariate descriptive statistics were used to characterize the study population in terms of all key dependent, key independent, and control variables by year. All dependent and independent variables were compared in 2006 with the 2005 baseline within cohort, and then the year-over-year differences were contrasted between cohorts as follows: difference in difference (DID) = (restricted cohort 2006 – restricted

Table 2. Pain Management Procedures

Intervention	CPT Codes	ICD-9-CM Procedure Codes
Physical therapy	97001, 97002	—
Acupuncture	97801, 97811, 97813, 97814	99.92
Introduction of anesthetic agent, nerve block	64400-64530	04.8-04.89 or 05.31
Neurostimulators	63650, 63655, 63685, 64550-64595	03.93, 04.92, or 86.94-86.96
Nerve destruction by neurolytic agent	64600-64680	03.8x or 04.2x
Nerve decompression	64722-64727	04.4x

CPT indicates Current Procedural Terminology; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.

cohort 2005) – (unrestricted cohort 2006 – unrestricted cohort 2005). χ^2 Tests were used to evaluate differences for categorical variables and *t* tests for continuous variables. Tests for statistically significant differences between the restricted and unrestricted states’ differences in outcomes before and after the intervention (DID) were conducted. *P* < .05 represented statistical significance.

Multivariable analyses were used to explore the association between restricted access to pregabalin and the outcomes of interest. A series of generalized linear models (GLMs) was used to test the hypotheses based on state restrictions after controlling for the potential confounding effects of age, sex, race/ethnicity, other chronic pain conditions, and comorbidities. The following 5 dependent variables were included: (1) pregabalin use, (2) opioid use, (3) nonopioid analgesic use as summarized in Table 1, (4) other DPN or PHN medication use (Table 1), and (5) DPN- or PHN-related healthcare costs. A general form of the outcome function related to the study objectives is as follows: $Y_i = f(\text{Restrict}_i, \text{Post}_i, \text{Restrict}_i \times \text{Post}_i, \text{Age}_i, \text{Sex}_i, \text{Race/Ethnicity}_i, \text{Diagnostic_Flags}_i, e_i)$, where Y_i indicates an outcome variable for the individual “*i*”; e_i , a stochastic error term to capture nonsystematic variation; and f , the proper link function of the model such as log or probit. All multivariable models included an indicator for residence in a state with a PA policy (“Restrict”), a time indicator (“Post” for 2005 vs 2006), an interaction term (“Restrict- \times -Post” [except for the model comparing 2006 pregabalin use]), age, sex, race/ethnicity, and a set of diagnostic flags to control for the effect of comorbidities. In a linear regression model, the DID estimate is the coefficient associated with the interacted term, $\text{Restrict}_i \times \text{Post}_i$. Because this coefficient has no useful interpretation in nonlinear models, the marginal effects of the interaction terms were calculated to express these effects across the multivariable models using the same units of

measure as the original dependent variable (eg, percentage of patients, number of claims, and US dollars).^{28,29}

Probit models were used for modeling pregabalin and opioid use. Negative binomial models were used for count-level outcomes (ie, utilization of nonopioid and other DPN or PHN medications) because of overdispersion in the outcome variables (number of prescriptions) and a low proportion of zero values. A log-gamma regression model was used for DPN- or PHN-related costs, whose observed distribution was a reasonable fit to the empirical distribution. The family distributions for the GLM models were verified based on the results of the modified Park test on the raw scale residuals-given log link. Analyses were conducted using STATA release 9 (StataCorp LP, College Station, TX).

RESULTS

A total of 5577 patients met all subject selection criteria (Table 3), with 424 in the 2 restricted states and 5153 in the 4 unrestricted states. Compared with the unrestricted cohort, the restricted cohort was slightly older (mean [SD] age, 51.1 [10.9] vs 48.0 [9.8] years), had a higher percentage of non-white individuals (38.0% vs 29.9%), and had a higher mean comorbidity composite score (Deyo-Charlson Comorbidity Index, 3.5 [2.0] vs 3.1 [1.8]) (*P* < .01 for all). The cohorts had similar proportions of female subjects (73.6% in the restricted cohort and 71.1% in the unrestricted cohort, *P* = .28).

Pregabalin use increased from 1.9% in 2005 to 11.1% in 2006 among the restricted cohort and from 2.6% in 2005 to 16.2% in 2006 among the unrestricted cohort, representing increases of 9.2 and 13.6 percentage points, respectively, for a net unadjusted DID between the groups of -4.4 percentage points (*P* = .01). This indicated that the restricted states had a lower net increase of 4.4 percentage points in 2006 use

■ **Table 3. Sample Size Attrition**

Attrition Criterion ^a	Restricted States	Unrestricted States
DPN or PHN diagnosis	22,561	74,519
Exclusions for epilepsy, cancer, transplant surgery	20,752	70,677
Exclusion for >90 days in long-term care	18,218	64,427
Age \geq 18 y at the beginning of 2005	17,228	62,319
Not dual eligible for Medicare	8388	45,662
Only fee-for-service plans	4895	43,107
Continuous Medicaid plan eligibility	542	6223
Final cohort, DPN or PHN pain medication or procedure within 60 days after diagnosis	424	5153
No. of patients in final cohort receiving pregabalin in 2006	49	863

DPN indicates diabetic peripheral neuropathy; PHN, postherpetic neuralgia.
^aDuring 2005 to 2006 unless otherwise noted.

Medicaid Prior Authorization Policy for Pregabalin

Table 4. Unadjusted Prescription Utilization and Expenditures for Diabetic Peripheral Neuropathy (DPN) or Postherpetic Neuralgia (PHN)^a

Variable	2006 Minus 2005		Difference in Difference	
	Unrestricted States (n = 5153)	Restricted States (n = 424)	Restricted Minus Unrestricted	P
Outpatient DPN or PHN Prescription				
Pregabalin				
Patients with prescription claim, %	13.6	9.2	-4.4	.01
Expenditure, \$	77	50	-27	.01
Gabapentin				
Patients with prescription claim, %	-1.6	1.7	3.2	.18
Expenditure, \$	-94	-109	-16	.41
Other anticonvulsants				
Patients with prescription claim, %	-2.5	-0.9	1.6	.26
Expenditure, \$	-22	20	42	<.01
Opioid analgesics				
Patients with prescription claim, %	-0.9	4.7	5.6	.02
Claims for patients with prescription	-0.2	0.8	1.0	<.01
Expenditure, \$	6	90	84	.09
Nonopioid analgesics				
Patients with prescription claim, %	-10.3	-3.8	6.6	.02
Expenditure, \$	-34	-13	21	<.01
Tricyclic antidepressants				
Patients with prescription claim, %	-3.1	-3.3	-0.2	.93
Expenditure, \$	-3	-1	2	.40
Other antidepressants				
Patients with prescription claim, %	-6.0	1.4	7.5	<.01
Claims for patients with prescription	-0.2	0.3	0.5	<.01
Expenditure, \$	-72	28	100	<.01
Anxiolytics				
Patients with prescription claim, %	-21.8	1.7	23.5	<.01
Claims for patients with prescription	-0.6	0.3	0.9	<.01
Expenditure, \$	-31	4	36	<.01
Total Expenditures, \$				
DPN or PHN prescription claims	-184	90	274	<.01
DPN or PHN related	-143	127	270	<.01

^aExpenditures are the mean per member per year.

(Table 4). The estimate of the marginal effect in the restricted states is a 4.0-percentage-point decrease in the probability of any pregabalin use in 2006 relative to the unrestricted states ($P = .02$) (Table 5).

Opioid analgesics were the most commonly used medications. The percentage of patients with opioid claims increased from 63.9% to 68.6% in the restricted states but dropped

slightly from 74.1% to 73.2% in the unrestricted states, netting a 5.6-percentage-point unadjusted DID increase among patients taking opioids in the restricted states year over year (Table 4). The marginal effect (Table 5) indicates that the PA, represented by the DID interaction term, was associated with a 6.5-percentage-point increase in the probability of any opioid use ($P < .01$).

■ **Table 5.** Marginal Effects of Utilization Variables

Variable	Marginal Effect (SE) ^a	z Score	P > z	95% Lower Confidence Limit	95% Upper Confidence Limit
Pregabalin use probability	-0.040 (0.017)	-2.36	.02	-0.072	-0.007
Opioid use probability	0.065 (0.025)	2.59	<.01	0.004	0.086
Nonopioid analgesics claims	0.36 (0.14)	2.60	<.01	0.09	0.63
Other antidepressants claims	1.01 (0.21)	4.73	<.01	0.59	1.42
Anxiolytics claims	1.91 (0.14)	13.36	<.01	1.63	2.19
DPN- or PHN-related total costs, \$	418.05 (107.21)	3.90	<.01	207.92	628.17

DPN indicates diabetic peripheral neuropathy; PHN, postherpetic neuralgia.

^aMarginal effects are the adjusted annual effects for the 2006 follow-up year. Standard errors of the marginal effects were computed using the delta method.

Unadjusted DID metrics for gabapentin and other anticonvulsants, tricyclic antidepressants, and miscellaneous DPN- or PHN-related medications were not significantly different between the restricted and unrestricted cohorts year over year (Table 4). However, nonopioid analgesics, other antidepressants, and anxiolytics were shown to have higher utilization year over year in the restricted versus unrestricted states. Unadjusted percentages of patients using nonopioid analgesics decreased from 2005 to 2006 by 3.8 percentage points in the restricted states and by 10.3 percentage points in the unrestricted states, for a net 6.6-percentage-point smaller decrease in the restricted states year over year ($P = .02$). From 2005 to 2006, utilization of other antidepressants (nontricyclic) increased by 1.4 percentage points in the restricted states and decreased by 6.0 percentage points in the unrestricted states, for a net 7.5-percentage-point increase in the restricted states year over year ($P < .01$). Last, anxiolytic medication utilization increased from 2005 to 2006 by 1.7 percentage points in the restricted states and decreased by 21.8 percentage points in the unrestricted states, for a net 23.5-percentage-point increase in the restricted states for these agents year over year ($P < .01$).

Multivariable analyses were used to determine whether the number of prescription claims for these agents was affected by the presence of the PA after adjusting for covariates. The coefficient on the DID estimator was positive and statistically significant for nonopioid analgesics ($P = .01$), nontricyclic antidepressants ($P < .01$), and anxiolytics ($P < .01$), indicating that the PA restriction was associated with increased use of these agents after controlling for baseline characteristics. The marginal effect for these drug classes (Table 5) shows that the PA was associated with annual increases of 0.36 prescription claims for nonopioid analgesics, 1.01 prescription claims for other antidepressants, and 1.91 prescription claims for anxiolytic drugs.

Per patient from 2005 to 2006, the mean unadjusted DPN- or PHN-specific healthcare total expenditures increased by \$127 ($P = .05$) for the restricted states and decreased by \$143 ($P < .01$) for the unrestricted states, for a net higher cost to the restricted states of \$270 ($P < .01$) per patient (Table 4). The marginal effect of the DID estimator (Table 5) shows that, after controlling for baseline patient characteristics, the PA restriction was associated with a relative increase of \$418 in annual DPN- or PHN-specific expenditures.

DISCUSSION

This study compared 2 cohorts of Medicaid patients diagnosed as having DPN or PHN, consisting of patients in 2 states with a PA for pregabalin in 2006 versus patients in 4 states without pregabalin restricted use policies. The 2 cohorts were different at baseline in terms of age, race/ethnicity, and relative comorbidity and may have differed in unobserved characteristics as well. There were numerous changes affecting healthcare services within each state over the 2005-2006 study period, including the inception of Medicare Part D in 2006. To provide the most even playing field for comparing the states over time and to account for a known contemporaneous change (Medicare Part D), we excluded dual-eligible patients. While the DID design is a powerful method for adjusting baseline differences between the restricted states and the unrestricted states, we acknowledge that it cannot account for unobserved contemporaneous changes that were not parallel across states. The DID analysis approach allowed comparison of the relative differences seen year over year for each cohort, while isolating the effect of the PA policy.

According to the descriptive results and the adjusted multivariable analysis, the PA resulted in lower relative use of pregabalin for the restricted states (4.0-percentage-point

lower probability in 2006 for the restricted states, $P = .02$) and was effective in controlling the use of this agent in the context of DPN or PHN. Compared with the unrestricted states, there was also a statistically significant increase of 6.5 percentage points in the probability of patients in the restricted states using opioids in 2006. Furthermore, there were statistically significant increases in the number of claims by patients with DPN or PHN in the restricted states for non-opioid analgesics, nontricyclic antidepressants, and anxiolytics. These results support the hypothesis that physicians who are treating patients with DPN or PHN and are unable to obtain reimbursement for pregabalin may have an increased likelihood to prescribe alternative therapies (such as opioids, nonopioid analgesics, antidepressants, and anxiolytics) that are associated with DPN or PHN pain management. Some of these agents, particularly antidepressants and anxiolytics, may also be used to relieve depression or anxiety associated with chronic pain.

The DPN- or PHN-related total direct costs were statistically significantly higher in the restricted states year over year in the unadjusted descriptive statistics (net difference, \$270) and in the regression model, which showed a marginal effect for the PA restriction associated with \$418 higher costs incurred in the restricted states, despite the lower incidence of pregabalin use. While the descriptive statistics showed a year-over-year savings for the restricted states in pregabalin prescription costs of \$27 ($P = .01$), there was a net year-over-year increase for the restricted states in all DPN- or PHN-specific medication prescription costs of \$274 ($P < .001$), which seems to be the largest contributor to the total cost differences compared with the unrestricted states. These results support the hypothesis that restrictions on pregabalin use are associated with increases in DPN- or PHN-related direct medical costs or with no net cost savings.

This study is limited by the inclusion of only 6 states; nonetheless, the states were grouped into those with and without a PA policy so that associations between PA policies and drug utilization could be compared across states. In the absence of randomization, it is impossible to establish the causal effect of the PA on the DPN or PHN treatment practices observed in this study. Claims analysis is limited in its ability to account for all possible differences among patients and providers residing in different states. In addition, misclassification error is possible when relying on diagnosis coding from administrative claims data and where the extent of undercoding of DPN or PHN is unknown. The sample was limited to non-dual-eligible Medicaid patients because of a lack of Medicare Part D prescription claims data availability in dual-eligible patients. The sample was also limited to patients who were continuously eligible for Medicaid benefits during all of 2005

and 2006; if these patients were systematically different from patients who move in and out of the Medicaid system, the study results may not be generalizable to the entire Medicaid population. This analysis focused on pregabalin use for painful DPN or PHN, and the results should not be interpreted outside of these labeled indications. In the absence of a specific diagnosis code for painful DPN or PHN, this study relied on pharmaceutical claims for pain treatment after DPN or PHN diagnosis to identify patients with a painful manifestation of their condition. In the absence of diagnosis coding on pharmacy claims, it was assumed that the drugs shown to be used for treating painful DPN or PHN (Table 1) were actually used as such. Comparison of pregabalin utilization and costs was limited by the small sample size of pregabalin users in the restricted states, possibly as a result of the hypothesized effect of the PA on pregabalin use. Last, the administrative costs of the PA program, which may vary among states, were not considered in this analysis.

CONCLUSIONS

This study explored the effect of Medicaid policies instituting a PA for pregabalin use in DPN and PHN in 2 states with PA policies compared with 4 states without such policies. The states with PA policies restricting access were found to have a significantly lower proportion of patients with any pregabalin use compared with the states without restricted access. Using a DID modeling approach with calculation of marginal effects, the PA was shown to be associated with significantly increased probability of the use of opioids, nonopioid analgesics, certain nontricyclic antidepressants, and anxiolytics, as well as with significantly greater disease-specific costs. This study of PA policy was applied to a patient population with chronic conditions involving moderate-to-severe pain and high incentive to seek alternative pain management treatments that provide therapeutic relief. Although the PA policy accomplished the objective of controlling access to pregabalin, the overall effect was an increase in the use of opioid medications and alternative therapies associated with increased disease-related healthcare costs.

Acknowledgment

We acknowledge the key contributions of Robert Fowler, MS, whose tireless work in extracting, assembling, and analyzing the data made this study possible.

Author Affiliations: Thomson Reuters Healthcare (JM, SSJ, B-CC), Washington, DC; School of Pharmacy (EO, CDM), University of Maryland, Baltimore; and Pfizer Inc (KH, JA, JGR), New York, NY.

Funding Source: This study was sponsored by Pfizer Inc.

Author Disclosures: Dr Margolis, Mr Johnston, and Dr Chu are employees of Thomson Reuters Healthcare, who was paid by Pfizer Inc in connection with the development of the manuscript. Mr Hvidsten, Dr Alvir, and Dr Rossi are employees of Pfizer Inc, the manufacturer of pregabalin, and report

owning stock in the company. Dr Mullins and Dr Onukwugha report serving as a paid consultant and receiving grants from Pfizer Inc, as well as receiving payment for their involvement in the preparation of the manuscript.

Authorship Information: Concept and design (JMM, SSJ, B-CC, EO, KH, JA, JGR, CDM); acquisition of data (JMM, JGR); analysis and interpretation of data (JMM, SSJ, B-CC, EO, KH, JA, JGR, CDM); drafting of the manuscript (JMM, SSJ, B-CC, KH, JA, JGR); critical revision of the manuscript for important intellectual content (JMM, SSJ, B-CC, EO, KH, JA, JGR, CDM); statistical analysis (JMM, SSJ, B-CC, KH); obtaining funding (JMM, KH, JGR); administrative, technical, or logistic support (JMM, SSJ, KH); and supervision (JMM, KH, JA).

Address correspondence to: Jay Margolis, PharmD, Thomson Reuters Healthcare, 332 Bryn Mawr Ave, Bala Cynwyd, PA 19004. E-mail: jay.margolis@thomsonreuters.com.

REFERENCES

1. **MacKinnon NJ, Kumar R.** Prior authorization programs: a critical review of the literature. *J Manag Care Pharm.* 2001;7(4):297-302.
2. **Moore WJ, Newman RJ.** Drug formulary restrictions as a cost-containment policy in Medicaid programs. *J Law Econ.* 1993;36(1):71-97.
3. **Smalley WE, Griffin MR, Fought RL, Sullivan L, Ray WA.** Effect of a prior-authorization requirement on the use of nonsteroidal antiinflammatory drugs by Medicaid patients. *N Engl J Med.* 1995;332(24):1612-1617.
4. **Kotzan JA, McMillan JA, Jankel CA, Foster AL.** Initial impact of a Medicaid prior authorization program for NSAID prescriptions. *J Res Pharm Econ.* 1993;5(1):25-41.
5. **Phillips CR, Larson LN.** Evaluating the operational performance and financial effects of a drug prior authorization program. *J Manag Care Pharm.* 1997;3(6):699-706.
6. **Fischer MA, Schneeweiss S, Avorn J, Solomon DH.** Medicaid prior authorization programs and the use of cyclooxygenase-2 inhibitors. *N Engl J Med.* 2004;351(21):2187-2194.
7. **Delate T, Mager DE, Sheth J, Motheral BR.** Clinical and financial outcomes associated with a proton pump inhibitor prior-authorization program in a Medicaid population. *Am J Manag Care.* 2005;11(1):29-36.
8. **Soumerai SB.** Benefits and risks of increasing restrictions on access to costly drugs in Medicaid. *Health Aff (Millwood).* 2004;23(1):135-146.
9. **Balkrishnan R, Joish VN, Bhosle MJ, Rasu RS, Nahata MC.** Prior authorization of newer insomnia medications in managed care: is it cost saving? *J Clin Sleep Med.* 2007;3(4):393-398.
10. **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.
11. **Olson BM.** Approaches to pharmacy benefit management and the impact of consumer cost sharing. *Clin Ther.* 2003;25(1):250-272.
12. **National Pain Foundation.** Diabetic Neuropathy. <http://www.nationalpainfoundation.org/articles/369/medications>. Accessed September 29, 2009.
13. **National Pain Foundation.** Neuropathic Pain. <http://www.nationalpainfoundation.org/articles/357/medications>. Accessed September 29, 2009.
14. **National Pain Foundation.** Postherpetic Neuralgia. <http://www.nationalpainfoundation.org/articles/521/medications>. Accessed September 29, 2009.
15. **Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA.** The health care costs of diabetic peripheral neuropathy in the US. *Diabetes Care.* 2003;26(6):1790-1795.
16. **Vinik A.** Clinical review: use of antiepileptic drugs in the treatment of chronic painful diabetic neuropathy. *J Clin Endocrinol Metab.* 2005;90(8):4936-4945.
17. **Cunningham AL, Dworkin RH.** The management of post-herpetic neuralgia. *BMJ.* 2000;321(7264):778-779.
18. **Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H; Quality Standards Subcommittee of the American Academy of Neurology.** Practice parameter: treatment of postherpetic neuralgia: an evidence-based report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2004;63(6):959-965.
19. **Gore M, Sadosky A, Tai KS, Stacey B.** A retrospective evaluation of the use of gabapentin and pregabalin in patients with postherpetic neuralgia in usual-care setting. *Clin Ther.* 2007;29(8):1655-1670.
20. **Adriaensen H, Plaghki L, Mathieu C, Joffroy A, Vissers K.** Critical review of oral drug treatments for diabetic neuropathic pain: clinical outcomes based on efficacy and safety data from placebo-controlled and direct comparative studies. *Diabetes Metab Res Rev.* 2005;21(3):231-240.
21. **Attal N, Cruccu G, Haanpää M, et al; EFNS Task Force.** EFNS guidelines on pharmacological treatment of neuropathic pain. *Eur J Neurol.* 2006;13(11):1153-1169.
22. **Argoff CE, Cole BE, Fishbain DA, Irving GA.** Diabetic peripheral neuropathic pain: clinical and quality-of-life issues. *Mayo Clin Proc.* 2006;81(4, suppl):S3-S11.
23. **Lyrica (Pregabalin) Full Prescribing Information.** New York, NY: Pfizer Inc; June 2007.
24. **Dworkin RH, Backonja M, Rowbotham MC, et al.** Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. *Arch Neurol.* 2003;60(11):1524-1534.
25. **Dworkin RH, O'Connor AB, Backonja M, et al.** Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain.* 2007;132(3):237-251.
26. **Boulton AJ.** Management of diabetic peripheral neuropathy. *Clin Diabetes.* 2005;23(1):9-15.
27. **King SA.** Diabetic peripheral neuropathic pain: effective management. *Consultant Live.* 2008;48(11). <http://www.consultantlive.com/display/article/10162/1337377>. Accessed December 2, 2008.
28. **Ai CR, Norton EC.** Interaction terms in logit and probit models. *Econ Lett.* 2003;80(1):123-129.
29. **Norton EC, Wang H, Ai C.** Computing interaction effects and standard errors in logit and probit models. *Stata J.* 2004;4(2):154-167. ■