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Geographic Variation in the Prescription of Schedule II Opioid Analgesics among Outpatients in the United States

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Objective. To measure geographic variation in opioid use in a large, commercially insured, outpatient population in the United States.

Data Sources. Outpatient prescription drug claims database of a national pharmaceutical benefit manager for 7,873,337 subjects with at least one prescription drug claim in 2000.

Study Design. We measured the period prevalence of claims for opioid analgesics and controlled-release oxycodone at the state level. We measured geographic variation using the weighted coefficient of variation and systematic component of variation. In county-level multivariable regression, we explored associations between potential explanatory variables and claims for opioid analgesics and controlled-release oxycodone.

Principal Findings. A total of 567,778 (64.2 per 1,000 total claims) were for oral opioid analgesics. Claim rates by state ranged from <20 to >100 claims per 1,000 total claims. States with long-standing prescription monitoring programs had among the lowest rates. In the county-level data, presence of a statewide prescription monitoring program and proportions of the population aged 15–24 and 65 years and older were independently and negatively associated with claim rates for all opioid analgesics. Surgeons per 1,000, proportion of the population reporting illicit drug use, and proportion who were female were independently and positively associated with claim rates for all opioid analgesics. Only the proportion of the population aged 25–34 and number of surgeons per 1,000 were independently and positively associated with claim rates for oxycodone.

Conclusions. Claim rates for opioid analgesics vary significantly by state. Presence of a statewide prescription monitoring program is associated with lower claim rates at the county level. Future research should use individual-level data to assess whether these findings reflect a reduction in abuse and diversion or suboptimal treatment of pain.

Key Words. Analgesics, opioid, health services accessibility, oxycodone

Effective management of pain often requires the use of opioid analgesics (American Pain Society 1999, 2002; World Health Organization 2000; American Pain Society 2004). Because of their potential for abuse, opioid analgesics are regulated under federal narcotics and controlled substances laws (Joranson et al. 2000). The Controlled Substances Act of 1970 authorizes the Drug Enforcement Administration to supervise the manufacturing and distribution of legal narcotics and places all substances regulated under existing federal law into one of five schedules. Schedule II is reserved for drugs or substances with (a) high potential for abuse, (b) currently accepted medical use in treatment in the United States, and (c) potential for severe psychological or physical dependence if abused. Currently, 11 oral opioid analgesics have a Schedule II assignment (*Drug Facts* 2002). In addition to federal regulations, many states have enacted programs to monitor the use of opioid analgesics. Although details vary by state, prescription monitoring programs typically collect prescribing and dispensing data from pharmacies, review and analyze the data, and disseminate information to appropriate law enforcement and regulatory authorities (Joranson et al. 2000).

Recent analyses suggest that the use of opioid analgesics has grown considerably over the last decade. From 1990 to 1996, there were steady increases in the use of morphine, fentanyl, oxycodone, and hydromorphone (Joranson et al. 2000). The same pattern persisted from 1997 to 2002, with marked increases in the use of fentanyl and oxycodone (Gilson et al. 2004). Considerable attention has been given to the use and abuse of controlled-release oxycodone hydrochloride (Clancy 2000; Gold 2000; Graettinger 2000; Ordway 2000; Tough 2001). Notably, abuse and diversion of controlled-release oxycodone has been concentrated in certain geographic areas, with abuse in rural Maine, Kentucky, Virginia, and West Virginia bringing national attention to the problem (Clines and Meier 2001; Rogers 2001; Rosenberg 2001; Drug Enforcement Administration 2002).

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Geographic variations in the use of other prescription medications have been previously examined. In particular, significant geographic variation has been documented in the use of stimulant medication in children (Zito et al. 1997; Wennberg and Wennberg 2000; Cox et al. 2003), antihypertensive medications in the Veterans Affairs health system (Lopez et al. 2004), and lipid lowering drugs, proton pump inhibitors, antianxiety drugs, and antihistamines among adults in Michigan (Wennberg and Wennberg 2000). By contrast, an analysis of medication use for five conditions (depression, asthma, congestive heart failure, rheumatoid/osteoarthritis, and upper respiratory infection) in 11 California regions found relatively little geographic variation (DuBois, Batchlor, and Wade 2002). To date, no study has explored geographic variation in the use of opioid analgesics.

Examining geographic variation in the use of opioid analgesics is particularly important given the presence of state policies that may limit the prescription of these drugs. That is, geographic variation may yield important insights about the effects of these state policies. Evidence from the 1989 National Ambulatory Medical Care Survey (NAMCS) suggests that physicians in states with multiple-copy prescription programs are significantly less likely to prescribe opioid analgesics during an office visit (Wastila and Bishop 1996). Although a nationally representative sample, the observed NAMCS sample visits that occurred in states with multiple-copy prescription programs were likely heavily weighted toward states with especially large populations. Consequently, the generalizability of the findings to other states is unclear.

Prior work has also identified other factors related to the medical and nonmedical use of abusable prescription drugs. A study using the 1987 National Medical Expenditure Survey found that female gender, age less than 35 years, socioeconomic status, and diagnosis were independently and positively associated with the probability of narcotic analgesic use (Simoni-Wastila 2000). Using the 1991 National Household Survey on Drug Abuse (NHSDA), Simoni-Wastila, Ritter, and Strickler (2004) identified female gender, age less than 35 years, annual income greater than $40,000, poor health status, and use of illicit drugs in the previous year as independent predictors of nonmedical use of prescription drugs. Simoni-Wastila and Strickler (2004) found that female gender and single marital status were positively and independently associated with problem use of narcotic analgesics, whereas age less than 25 years and illicit drug use in the previous year were negatively associated.

In the present study, we used a large, outpatient pharmaceutical claims database of commercially insured individuals to build upon prior work in two

ways. First, we examined state-level prevalence of and geographic variations in the use of Schedule II oral opioid analgesics. Second, we investigated the influence of prescription monitoring programs and a variety of other factors on county-level claim rates for all opioid analgesics and for controlled-release oxycodone alone. Based on prior work, we hypothesized that the presence of a prescription monitoring program would be negatively and independently associated with claim rates for opioid analgesics, whereas female gender, age less than 35 years, and prior use of illicit drugs would be positively and independently associated.

METHODS

We accessed the outpatient prescription claims database of AdvancePCS (now Caremark Rx, Inc., Nashville, TN), a large pharmaceutical benefit manager in the United States. Health insurance carriers contracted with AdvancePCS to manage their formularies and adjudicate their prescription drug claims. AdvancePCS maintained a computerized pharmacy system that recorded data on each prescription drug dispensed to its beneficiaries.

We limited the analysis to subjects whose health insurance plans or carriers required AdvancePCS to track claims at the individual level. Subjects with the same identifier for multiple family members were excluded. The analysis data set included all prescription drug claims adjudicated for 7,873,337 subjects who were enrolled continuously during calendar year 2000 and who filed at least one prescription drug claim for any drug during that period. All claims relating to the same person were linked using a unique beneficiary identifier (encrypted to ensure confidentiality for this study). Subject-level data were aggregated to the county and state levels using zip codes. Zip code data were unavailable for 224,582 subjects (2.9 percent), so we omitted those subjects from the county- and state-level analyses. A total of 1,171 health insurance carriers were represented in the data, covering all 50 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands.

The research team oversaw study design and data analysis. To ensure subject confidentiality, however, individual-level data were analyzed in the research division of AdvancePCS. Subject data aggregated at the state level and claims data aggregated at the county level were provided to the research team. The institutional review boards of Duke University Medical Center and Georgetown University Medical Center approved the data analysis protocol.

Analytic Approach

We evaluated claims for 11 Schedule II opioid analgesics—codeine phosphate, codeine sulfate, hydromorphone, levorphanol, meperidine, meperidine–promethazine combination, methadone, morphine, oxycodone–acetaminophen combination, oxycodone–aspirin combination, and controlled-release oxycodone. Because of growing concern about the use and abuse of controlled-release oxycodone, we also analyzed claims for that drug separately.

Using individual-level data, we calculated period prevalence as the proportion of subjects in the sample with at least one claim for an opioid analgesic. (Subjects with multiple claims were counted only once.) We also calculated the proportion of subjects with at least one claim for controlled-release oxycodone. A chronic disease score was calculated according to the method described by Von Korff, Wagner, and Saunders (1992) and later refined by Clark et al. (1995). This pharmacy-based risk-adjustment score increases with the number of chronic diseases and the complexity of the treatment regimen (Parker, McCombs, and Graddy 2003). Analgesics (including Schedule II opioids) are not included in the scoring algorithm. To test for differences between all beneficiaries in the study population and those with claims for any opioid analgesic or for controlled-release oxycodone, we used *t* tests for continuous variables and χ^2 tests or Fisher exact tests for categorical variables.

Measures of State-Level Variation

We measured state-level variation using the weighted coefficient of variation (COV) and the systematic component of variation (SCV). The weighted COV is the ratio of the standard deviation of the prevalence rates to the mean rate among the states, weighted by the AdvancePCS population in each state. The SCV estimates the variance across states that cannot be explained by the variation within the state (McPherson et al. 1981). We compared the calculated values for the COV and the SCV to the estimated 95th percentile tables generated by Diehr et al. (1990), who constructed the tables using an iterative resampling process for various sampling schemes and prevalence rates.

County-Level Analyses

To protect patient confidentiality, we were only allowed access to claims at the zip code level, not at the individual level. We calculated claims rates at the county level by dividing the number of claims for all opioid analgesics and for oxycodone by the total number of prescription drug claims for each zip code.

We mapped zip codes to Federal Information Processing Standards "county" codes using the algorithm provided by ZipInfo.com (2003), and we aggregated the claims to the county level. Counties with fewer than 100 total claims for prescription drugs were not included in the county-level analysis.

We conducted univariate and multivariable analyses of county-level use rates to explore the association of those rates with potential explanatory variables. One problem with applying multiple regression to geographic data is that geographic areas may vary considerably in population and in the number of events of interest. Areas with large populations provide the most reliable estimates and should, therefore, be weighted more heavily. In this analysis, we used a weighting procedure developed by Pocock, Cook, and Beresford (1981) that determines weights by using the relative contribution of sampling error to unexplained variation between counties. To account for the natural similarity or clustering of counties within states, we calculated robust estimates of variance using the method described by Huber (1967) and White (1980).

We drew potential explanatory variables from the 2002 Area Resource File (ARF) and the 2000 National Survey on Drug Use and Health (NSDUH). The ARF contains information on health facilities, health professions, measures of resource scarcity, economic activity, and sociodemographic characteristics for each county in the United States. From the ARF, we extracted female proportion of the population and proportion by age category. We also extracted proportion of the population with a high school diploma, surgical specialists per 1,000, and surgical procedures per 1,000 to control for geographic variability in the use of health services (Legler et al. 2002). For all ARF variables, we used estimates from the year 2000. From the 2000 NSDUH, we used state-level estimates of illicit drug use in the previous month (Wright 2002). The NSDUH is the primary source of statistical information on the use of illicit drugs by the U.S. civilian population aged 12 years and older. The survey collects data by administering questionnaires to a representative sample of the population through face-to-face interviews at their place of residence. Beginning in 1999, the NSDUH produced estimates at the state level for a selected set of variables, including past-month use of illicit drugs. Finally, we included a binary variable denoting the presence of a Schedule II prescription monitoring program at the state level in 2000 (Joranson et al. 2000; Pain and Policy Studies Group 2003).

We fit three multivariable regression models. The first and second models explored the association of the potential explanatory variables on all claims for opioid analgesics and claims for controlled-release oxycodone,

respectively. The third model refit the oxycodone model and included total claims for other opioid analgesics as explanatory variables. We examined correlations among predictor variables and examined the influence of outlier observations. AdvancePCS used *SAS* version 8.2 (SAS Institute, Inc, Cary, NC) to construct the analysis file and perform the analyses required for Table 1. We used *Stata* version 7.0 (Stata Corporation, College Station, TX) to conduct county-level analyses and adjust for clustering at the state level.

RESULTS

Characteristics of the study population are presented in Table 1. The mean age was 38.1 years (SD, 21.9), and 55.8 percent of the subjects were women. The population was geographically diverse, with representation from all 50 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands. Of the 7,873,337 subjects in the study population, 391,299 (5 percent) filled at least one prescription for an oral opioid analgesic. Less than 1 percent of the subjects filled a prescription for controlled-release oxycodone. Subjects with at

Table 1: Subject Characteristics*

Characteristic	*All Subjects*	*Subjects with ≥1 Claim for Any Oral Opioid Analgesic*†	*Subjects with ≥1 Claim for Controlled-Release Oxycodone*
N	7,873,337 (100.0)	391,299 (5.0)	47,432 (0.6)
Age, mean (SD), years	38.1 (21.9)	45.2 (16.3)	50.7 (15.8)
Age group (years)			
0–17	1,863,180 (23.7)	16,680 (4.3)	893 (1.9)
18–39	2,057,954 (26.1)	131,000 (33.5)	10,366 (21.9)
40–59	2,596,960 (33.0)	168,240 (43.0)	22,868 (48.2)
60–79	1,172,314 (14.9)	67,576 (17.3)	11,374 (24.0)
≥ 80	182,929 (2.3)	7,803 (2.0)	1,931 (4.1)
≥ 65	988,939 (12.6)	52,921 (13.5)	9,836 (20.7)
Female gender	4,392,358 (55.8)	224,668 (57.4)	26,791 (56.5)
Chronic disease score, mean (SD)	3.7 (2.5)	4.7 (3.0)	5.9 (3.4)

*Values are expressed as number (percentage) unless otherwise indicated.

†Opioid analgesics include codeine phosphate, codeine sulfate, hydromorphone, levorphanol, meperidine, meperidine and promethazine combination, methadone, morphine, oxycodone, oxycodone and acetaminophen combination, and oxycodone and aspirin combination.

Table 2: Claims for Opioid Analgesics by Location*

Location	*Subjects*	*Total Claims*	*Claims for All Oral Opioid Analgesics*[†‡]	*Claims for Controlled-Release Oxycodone*[†]
Overall	7,648,755	8,789,967	567,778 (64.6)	69,865 (7.9)
Alabama	57,139	66,416	5,381 (81.0)	697 (10.5)
Alaska	12,005	13,019	1,606 (123.4)	199 (15.3)
Arizona	111,239	146,101	14,787 (101.2)	1,787 (12.2)
Arkansas	37,561	34,291	2,879 (84.0)	235 (6.9)
California	362,296	414,517	7,010 (16.9)	1,527 (3.7)
Colorado	167,841	183,193	15,796 (86.2)	1,374 (7.5)
Connecticut	170,721	183,811	17,010 (92.5)	1,769 (9.6)
Delaware	46,496	58,208	6,078 (104.4)	522 (9.0)
District of Columbia	12,033	18,361	1,531 (83.4)	178 (9.7)
Florida	615,652	602,576	53,723 (89.2)	8,014 (13.3)
Georgia	179,321	203,499	19,600 (96.3)	2,107 (10.4)
Hawaii	1,202	3,299	244 (74.0)	37 (11.2)
Idaho	20,156	22,181	542 (24.4)	147 (6.6)
Illinois	613,439	734,358	6,608 (9.0)	2,020 (2.8)
Indiana	227,120	261,584	8,898 (34.0)	2,176 (8.3)
Iowa	74,598	79,342	2,556 (32.2)	295 (3.7)
Kansas	69,199	84,051	4,258 (50.7)	529 (6.3)
Kentucky	159,516	195,977	16,576 (84.6)	1,897 (9.7)
Louisiana	44,928	54,270	4,929 (90.8)	408 (7.5)
Maine	18,253	21,345	1,908 (89.4)	373 (17.5)
Maryland	232,075	253,337	28,953 (114.3)	3,169 (12.5)
Massachusetts	470,623	544,548	55,415 (101.8)	5,166 (9.5)
Michigan	163,493	187,931	2,893 (15.4)	1,168 (6.2)
Minnesota	149,926	193,256	8,733 (45.2)	1,079 (5.6)
Mississippi	155,627	181,832	13,950 (76.7)	1,056 (5.8)
Missouri	211,927	254,117	13,272 (52.2)	1,536 (6.0)
Montana	9,703	9,876	706 (71.5)	75 (7.6)
Nebraska	27,446	30,408	1,307 (43.0)	188 (6.2)
Nevada	22,150	26,669	1,962 (73.6)	289 (10.8)
New Hampshire	19,132	24,378	2,498 (102.5)	368 (15.1)
New Jersey	161,075	160,671	13,470 (83.8)	1,148 (7.1)
New Mexico	59,206	64,628	4,842 (74.9)	288 (4.5)
New York	298,827	282,339	4,730 (16.8)	821 (2.9)
North Carolina	162,754	165,533	15,324 (92.6)	1,697 (10.3)
North Dakota	4,423	4,488	214 (47.7)	20 (4.5)
Ohio	238,541	270,367	17,857 (66.0)	2,536 (9.4)
Oklahoma	56,281	64,759	5,448 (84.1)	471 (7.3)
Oregon	288,916	329,684	22,099 (67.0)	3,878 (11.8)
Pennsylvania	330,997	377,388	36,532 (96.8)	5,075 (13.4)
Puerto Rico	165,791	232,552	10,900 (46.9)	573 (2.5)
Rhode Island	5,457	6,580	431 (65.5)	75 (11.4)
South Carolina	60,998	68,976	7,006 (101.6)	981 (14.2)
South Dakota	11,968	11,411	428 (37.5)	68 (6.0)

Continued

Table 2: *Continued*

Location	*Subjects*	*Total Claims*	*Claims for All Oral Opioid Analgesics*[†‡]	*Claims for Controlled-Release Oxycodone*[†]
Tennessee	454,005	568,110	59,194 (104.2)	4,475 (7.9)
Texas	498,039	594,619	8,640 (14.5)	2,379 (4.0)
Utah	46,780	54,502	5,234 (96.0)	846 (15.5)
U.S. Virgin Islands	15,219	17,808	509 (28.6)	24 (1.3)
Vermont	3,695	4,222	396 (93.8)	40 (9.5)
Virginia	96,212	163,879	15,374 (93.8)	1,366 (8.3)
Washington	74,260	85,052	7,605 (89.4)	1,151 (13.5)
West Virginia	29,885	33,447	2,718 (81.3)	553 (16.5)
Wisconsin	104,788	122,552	5,537 (45.2)	914 (7.5)
Wyoming	17,821	19,649	1,681 (85.6)	101 (5.1)

*Does not include data for 224,582 subjects who could not be matched to states due to missing zip code data.

[†]Values are expressed as number (claims per 1,000 total claims).

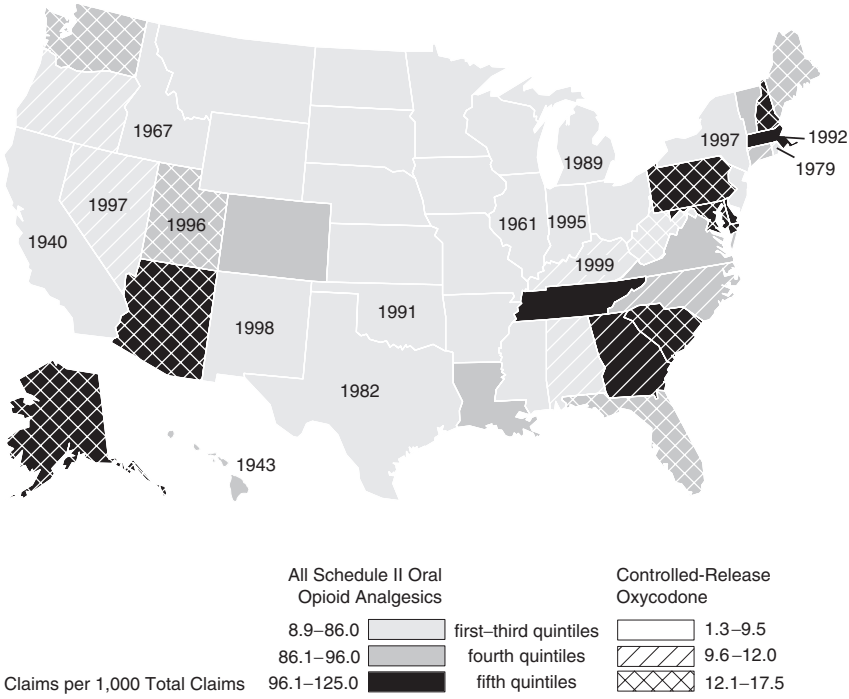
[‡]Opioid analgesics include codeine phosphate, codeine sulfate, hydromorphone, levorphanol, meperidine, meperidine and promethazine combination, methadone, morphine, oxycodone, oxycodone and acetaminophen combination, and oxycodone and aspirin combination.

least one claim for any opioid analgesic or for controlled-release oxycodone were older, were slightly more likely to be female, and had higher mean chronic disease scores than the overall study population.

Claims for all opioid analgesics and for controlled-release oxycodone are shown in Table 2. Of nearly 9 million prescription drug claims in 2000, 567,778 (64.2 per 1,000 total claims) were for an oral opioid analgesic. Claim rates varied considerably by state, with the highest rates exceeding 100 claims per 1,000 total prescription claims (Alaska, Arizona, Delaware, Maryland, Massachusetts, New Hampshire, South Carolina, and Tennessee) and the lowest rates falling below 20 claims per 1,000 (California, Illinois, Michigan, New York, and Texas). The two measures of variation reflect the dispersion of values. The weighted COV was 0.45 for all opioid analgesics and 0.48 for controlled-release oxycodone. The SCV was 156.8 for all opioid analgesics and 81 for controlled-release oxycodone. All values are outside of the 95th percentile values estimated by Diehr et al. (1990).

Figure 1 shows claim rates for all opioid analgesics and for controlled-release oxycodone. In most states, relatively high claim rates for opioid analgesics were accompanied by relatively high claim rates for controlled-release oxycodone. West Virginia departed from that pattern; it had a slightly higher than average claim rate for opioid analgesics (81.3 per 1,000 total claims) but

Figure 1: Claim Rates by State for All Opioid Analgesics and Controlled-Release Oxycodone The figure also displays the year in which state-based Schedule II prescription monitoring programs were first enacted in the states that have such a program.



the second highest claim rate for controlled-release oxycodone (16.5 per 1,000 total claims). Figure 1 also displays the year in which state-based Schedule II prescription monitoring programs were first enacted in the states that have such a program. With few exceptions, states with long-standing prescription monitoring programs had among the lowest claim rates for both opioid analgesics and controlled-release oxycodone. Of states with programs enacted before 1995, Rhode Island, Oklahoma, and Massachusetts were the only states with higher than average claim rates for opioid analgesics (but not for controlled-release oxycodone).

Of the 3,141 counties in the United States, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands, 3,059 (97.4 percent) were represented in the AdvancePCS database. Of those, 2392 (80.7 percent) had at

Table 3: Multivariable Regression Models for County-Level Opioid Analgesic Prescription Claim Rates per 1,000 Total Prescription Claims*

	Parameter Estimate (Robust SE)		
	Model 1[†]	*Model 2*[‡]	*Model 3*[§]
Intercept	60.9 (42.0)	− 10.2 (5.7)	− 14.1 (5.4)
Schedule II prescription monitoring program	− 36.5 (7.6)[‖]	− 2.0 (0.7)[‖]	0.0 (0.6)
Proportion of population female	1.9 (0.6)[‖]	− 0.2 (0.1)[¶]	0.1 (0.1)
Proportion of population aged 15–24 years[#]	− 1.5 (0.4)[‖]	− 0.1 (0.0)[‖]	− 0.1 (0.0)
Proportion of population aged 25–34 years[#]	0.2 (0.7)	0.3 (0.1)[‖]	0.3 (0.1)[‖]
Proportion of population aged 65 years and older[#]	− 2.3 (0.7)[‖]	0.0 (0.1)	0.1 (0.1)
Proportion reporting past month use of any illicit drug	6.2 (2.7)[‖]	0.7 (0.3)[‖]	0.4 (0.2)
Proportion of population with high school diploma	− 0.8 (0.3)[‖]	0.0 (0.0)	0.0 (0.0)
Surgical specialists per 1,000	12.9 (3.2)[‖]	1.8 (0.5)[‖]	1.2 (0.4)[‖]
Claims for opioid analgesics (excluding oxycodone) per 1,000 prescription claims	—	—	0.1 (0.0)[‖]

*Based on 2,392 counties.

[†]Explored associations between the potential explanatory variables and claims for all opioid analgesics; R^2, 0.41.

[‡]Explored associations between the potential explanatory variables and claims for controlled-release oxycodone; R^2, 0.11.

[§]Model 2 with total claims for other opioid analgesics included as a potential explanatory variable; R^2, 0.18.

[¶]$p < .05$.

[‖]$p < .01$.

[#]Proportion aged 35–64 years is the reference category.

least 100 total prescription claims and were included in the county-level multivariable analysis. The mean number of claims for all oral opioid analgesics was 58.9 per 1,000 total claims (SD, 34.6), and the median was 57.3 per 1,000 (interquartile range, 29.9–85.8). Claim rates ranged from 0 to 220 per 1,000.

Table 3 displays the results of the county-level multivariable regression models. The presence of a prescription monitoring program and the proportion of the county population aged 15–24 years and 65 years and older (compared to the proportion aged 35–64 years) were negatively and independently associated with claim rates for all opioid analgesics, whereas the proportion of the county population that was female, surgical specialists, and proportion reporting illicit drug use at the state level were positively and independently

associated with claim rates (Model 1). Controlling for sociodemographic characteristics, surgical specialists, and reported illicit drug use, the presence of a prescription monitoring program reduced the expected claims for opioid analgesics by nearly 40 claims per 1,000 total claims. Correlations among variables were modest (all <0.3), and the results did not change measurably with the exclusion of outliers (i.e., the five smallest counties and the five counties with the highest claim rates), so the final model includes those counties. The results were not qualitatively different when we refit the model substituting surgical procedures per 1,000 for surgical specialists per 1,000 (data not shown).

Models 2 and 3 display results for the analysis of claims for controlled-release oxycodone at the county level. The presence of a prescription monitoring program, proportion of population female, and proportion of population aged less than 25 years were independently and negatively associated with claim rates for controlled-release oxycodone. The proportion of the population aged 24–35 years, the proportion reporting use of illicit drugs, and surgical specialists per 1,000 were independently and positively associated with claim rates for controlled-release oxycodone. When total claims for other opioid analgesics were included in the model, only the proportion aged 15–24 years and the number of surgeons per 1,000 remained statistically significant. Again, the results did not change measurably with the exclusion of outliers, so the final model includes those counties. Again, the results were largely unchanged when surgical procedures per 1,000 were included instead of surgical specialists per 1,000 (data not shown).

DISCUSSION

This population-based study revealed 12-fold variation in claims for Schedule II oral opioid analgesics at the state level (114.3 claims per 1,000 total prescription claims in Maryland versus 9 claims per 1,000 in Illinois). State-level variation of a similar magnitude exists in claims for controlled-release oxycodone. Analysis of claim rates at the county level suggests that the presence of a statewide prescription monitoring program and the proportions of the population aged 15–24 years and 65 years and older were independently and negatively associated with claims for oral opioid analgesics, whereas the number of surgeons per 1,000, the proportion of the population reporting illicit drug use, and the proportion of the population female were independently and positively associated with claim rates for all opioid analgesics. Only

the proportion of the population aged 25–34 years and the number of surgeons per 1,000 were independently and positively associated with claim rates for controlled-release oxycodone.

Our findings are noteworthy for several reasons. First, the study adds to existing evidence that geographic variations permeate the health care delivery system (Welch et al. 1993; Wennberg 1996; O'Connor et al. 1999), from the use of surgical procedures (Wennberg and Gittelsohn 1973) and rates of hospitalization for chronic conditions (Gornick 1982) to the use of stimulant medication in children (Cox et al. 2003). The pattern of claims for controlled-release oxycodone is remarkably similar to the pattern for all opioid analgesics, though claims for controlled-release oxycodone represent only slightly more than 10 percent of total claims for opioid analgesics. With few exceptions, claim rates for controlled-release oxycodone mirror total claim rates for all oral opioid analgesics. West Virginia, Oregon, and Nevada are notable exceptions, with moderate claim rates for opioid analgesics and relatively high claim rates for controlled-release oxycodone. Previous studies have documented geographic variations in the use of other prescription medications (Wennberg and Wennberg 2000; Cox et al. 2003). To our knowledge, however, geographic variation in claims for opioid analgesics has not been described previously.

Second, consistent with the findings of Wastila and Bishop (1996), the presence of a statewide prescription monitoring program is associated with significantly lower claim rates for Schedule II opioid analgesics. A Department of Justice report (2000) suggests that prescription monitoring programs have diminished the use of controlled substances and may have reduced the illicit use and abuse of controlled substances. Other studies have reached similar conclusions, although often based on a single state's experience (Sigler et al. 1984; Weintraub et al. 1991). State prescription monitoring programs may also have unintended consequences. Recent studies examining the effect of such programs on prescriptions for benzodiazepines suggest that both problematic and nonproblematic benzodiazepine use may be reduced following the initiation of such programs. Of note, the use of benzodiazepines decreased markedly in patients for whom the treatment was both effective and appropriate (Wagner et al. 2003; Simoni-Wastila et al. 2004). In 2000, 16 states had active programs designed to monitor the prescribing and dispensing of certain controlled substances (Joranson et al. 2000; Pain and Policy Studies Group 2003). Of states with long-standing (prior to 1995) prescription monitoring programs, only Massachusetts, Oklahoma, and Rhode Island had high claim rates for opioid analgesics.

Third, patterns of outpatient claims from a large, commercially insured population are consistent with national estimates presented in a Drug Enforcement Administration brief (2002), which identified 13 states that have high rates of dispensing controlled-release oxycodone per capita (Alabama, Alaska, Connecticut, Delaware, Florida, Maine, Massachusetts, New Hampshire, Ohio, Pennsylvania, Rhode Island, South Carolina, and West Virginia). With the exception of Massachusetts and New Hampshire, our data suggest high claim rates in these states, as well. However, an additional five states in our study have relatively high claim rates for controlled-release oxycodone—Arizona, Nevada, Oregon, Utah, and Washington.

Other factors emerged as significant independent predictors of claim rates for opioid analgesics. Consistent with previous work (Simoni-Wastila, Ritter, and Strickler 2004), the proportion of female subjects in the population and the proportion reporting illicit drug use in the previous month were significant independent predictors of state-level opioid analgesic claims. Density of surgical specialists was also a significant predictor of opioid analgesic claims, likely reflecting the use of the drugs in the management of postoperative pain. The proportion of the population aged 25–34 years was a significant predictor of county-level claim rates for controlled-release oxycodone, but not for county-level claim rates for all opioid analgesics. In addition, the supply of surgical specialists at the county level and claim rates for other Schedule II opioid analgesics were significant predictors of claim rates for controlled-release oxycodone. This finding contrasts somewhat with the picture of controlled-release oxycodone use that has emerged in the news media. News reports cite considerable geographic variation in the use and abuse of controlled-release oxycodone (Clancy 2000; Gold 2000; Graettinger 2000; Ordway 2000; Tough 2001) but are silent about geographic variations in the use and abuse of other Schedule II opioid analgesics. Our findings suggest that although there are important geographic variations in claim rates for controlled-release oxycodone, those variations are consistent with geographic variations in the use of other Schedule II opioid analgesics.

As with any study of geographic variation, our analysis provides no information regarding overuse or underuse. Although prescription monitoring programs have been shown to reduce the use of Schedule II opioid analgesics, some believe that physicians may under-prescribe these drugs in states with monitoring programs. On the other hand, monitoring programs may have a Hawthorne effect, whereby physicians prescribe scheduled drugs more appropriately because their behavior is being observed. Finally, we cannot say how much of the variation arises because patients "shop" for

physicians who are willing to prescribe the drugs. Highlighting variations is a first step. Understanding the variations will require detailed analyses of the costs, risks, and benefits of the therapies and of the circumstances in which they are used.

Our analysis has some limitations. The explanatory models rely on data aggregated at the area level and not on individual-level data. Although analysis of aggregate data may provide clues about individual behavior, relationships observed in the aggregate may not hold at the individual level. It will be important to validate these findings using individual-level data. Also, the explanatory models account for only modest degrees of variation in claims patterns. This fact suggests that other, unobserved factors may drive the geographic variations. Of particular importance may be the omission of promotional spending and sales force detailing by manufacturers of opioid analgesics. Because patient-level data were unavailable, we were unable to control for geographic variations in underlying medical conditions and assess the analytical impact of multiple claims from a given subject. In addition, we were unable to account for variations in insurance coverage for narcotics, other medications, and behavioral health programs that may have included treatment for narcotic addiction. Notably, the lack of patient-level data represents an important loss of information that may make the regression more vulnerable to the presence of confounders.

Although subjects' zip codes were available in over 80 percent of cases, we used the dispensing pharmacy's zip code as a proxy when the subject's zip code was missing. To the extent that those substitutions mapped to different counties with different characteristics, the misclassification could be problematic. Also, we did not account for spatial correlations in medical service areas that cross state boundaries. Moreover, although prescription claims databases are considered reliable and valid sources of data (West and Strom 2000; Strom 2001), they record only whether a claim was filed, not whether the drug was taken. In addition, if patients pay out of pocket or have alternative sources of prescription drug coverage, the data would tend to underestimate use of the drugs. Finally, it is possible that clients of pharmaceutical benefit managers (e.g, employers providing prescription drug coverage) restricted access to controlled substances for individual patients through prescription monitoring programs or dispensing rules implemented at the level of the pharmaceutical benefit manager.

Our study reveals a 12-fold variation in claims for all Schedule II oral opioid analgesics and for controlled-release oxycodone at the state level. Analysis of claim rates at the county level suggests that the presence of a

statewide prescription monitoring program is independently associated with lower claim rates for oral opioid analgesics. The specific mechanism through which these programs work is unclear and requires additional study. In light of recent studies showing the potential for unintended, negative consequences of these programs on prescribing, future work must use subject-level data to assess whether these findings reflect a reduction in abuse and diversion or suboptimal pain treatment.

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REFERENCES

American Pain Society. 1999. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th Edition. Glenview, IL: American Pain Society.

———. 2002. *Guideline for the Management of Pain in Osteoarthritis, Rheumatoid Arthritis, and Juvenile Chronic Arthritis. Clinical Practice Guideline Number 2.* Glenview, IL: American Pain Society.

———. 2004. *Guideline for the Management of Cancer Pain in Adults and Children.* Glenview, IL: American Pain Society.

Clancy, M. A. 2000. "Down East High; Washington County Pill Addicts Have Health Officials Worried." *Bangor Daily News* May 13.

Clark, D. O., M. Von Korff, K. Saunders, W. M. Baluch, and G. E. Simon, 1995. "A Chronic Disease Score with Empirically Derived Weights." *Medical Care.* 33 (8): 783–95.

Clines, F. X., and B. Meier. 2001. "Cancer Painkillers Pose New Abuse Threat." *New York Times* February 9, p. A1.

Controlled Substances Act of 1970. Pub L No. 91-513, 84 Stat 1242.

Cox, E. R., B. R. Motheral, R. R. Henderson, and D. Mager. 2003. "Geographic Variation in the Prevalence of Stimulant Medication Use among Children 5 to 14 Years Old: Results from a Commercially Insured US Sample." *Pediatrics* 111 (2): 237–43.

Department of Justice. 2000. "A Closer Look at State Prescription Monitoring Programs" [accessed on August 4, 2003]. Available at http://www.deadiversion.usdoj.gov/pubs/program/rx_monitor/summary.htm

Diehr, P., K. Cain, F. Connell, and E. Volinn. 1990. "What Is Too Much Variation?" *Health Services Research* 24 (6): 741–71.

Drug Enforcement Administration. 2002. "Drug Intelligence Brief: OxyContin: Pharmaceutical Diversion, March 2002" [accessed on September 2, 2005]. Washington, DC: Drug Enforcement Administration. Available at http://www.usdoj.gov/dea/pubs/intel/02017/02017p.html

Drug Facts and Comparisons 2002: Pocket Version. 2002. 6th Edition. St. Louis, MO: Facts and Comparisons

Dubois, R. W., E. Batchlor, and S. Wade. 2002. "Geographic Variation in the Use of Medications: Is Uniformity Good News or Bad?" *Health Affairs* 21 (1): 240–50.

Gilson, A. M., K. M. Ryan, D. E. Joranson, and J. L. Dahl. 2004. "A Reassessment of Trends in the Medical Use and Abuse of Opioid Analgesics and Implications for Diversion Control: 1997–2002." *Journal of Pain and Symptom Management* 28 (2): 176–88.

Gold, D. 2000. "A Prescription for Crime: Abuse of 2 Painkillers Blamed for Rise in Violence in Maine's Poorest County." *Boston Globe* May 21, p. D22.

Gornick, M. 1982. "Trends and Regional Variations in Hospital Use under Medicare." *Health Care Financing Review*. 3 (3): 41–73.

Graettinger, D. 2000. "Down East High: Tribal Officials Seek to Stem Flow of Pills to Reservations." *Bangor Daily News* May 15.

Huber, P. J. 1967. "The Behavior of Maximum Likelihood Estimates under Non-Standard Conditions." In *Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability*, pp. 221–33. Berkeley, CA: University of California Press.

Joranson, D. E., K. M. Ryan, A. M. Gilson, and J. L. Dahl. 2000. "Trends in Medical Use and Abuse of Opioid Analgesics." *Journal of the American Medical Association* 283 (13): 1710–4.

Legler, J., N. Breen, H. Meissner, D. Malec, and C. Coyne. 2002. "Predicting Patterns of Mammography Use: A Geographic Perspective on National Needs for Intervention Research." *Health Services Research* 37 (4): 929–47.

Lopez, J., J. Meier, F. Cunningham, and D. Siegel. 2004. "Antihypertensive Medication Use in the Department of Veterans Affairs: A National Analysis of Prescribing Patterns from 2000 to 2002." *American Journal of Hypertension* 17 (12, part 1): 1095–9.

McPherson, K., P. M. Strong, A. Epstein, and L. Jones. 1981. "Regional Variations in the Use of Common Surgical Procedures: Within and between England and Wales, Canada and the United States of America." *Social Science and Medicine* 15 (3, part 1): 273–88.

O'Connor, G. T., H. B. Quinton, N. D. Traven, L. D. Ramunno, T. A. Dodds, T. A. Marciniak, and J. E. Wennberg. 1999. "Geographic Variations in the Treatment of Acute Myocardial Infarction: The Cooperative Cardiovascular Project." *Journal of the American Medical Association* 281 (7): 627–33.

Ordway, R. O. 2000. "Narcotics Abuse on Rise: Pharmaceutical Drug Fraud, Misuse Worry Officials." *Bangor Daily News* April 6, 2000.

Pain and Policy Studies Group. 2003. "States with Prescription Monitoring Programs" [accessed on September 2, 2005]. Available at http://www.medsch.wisc.edu/painpolicy/domestic/PMP_matrix.pdf

Parker, J. P., J. S. McCombs, and E. A. Graddy. 2003. "Can Pharmacy Data Improve Prediction of Hospital Outcomes? Comparison with a Diagnosis-Based Comorbidity Measure." *Medical Care* 41 (3): 407–19.

Pocock, S., D. Cook, and S. Beresford. 1981. "Regression of Area Mortality Rates on Explanatory Variables: What Weighting Is Appropriate?" *Applied Statistics* 30 (3): 286–95.

Rogers, P. 2001. "Prescription for Death." *People Weekly* August 13, pp. 50–5.

Rosenberg, D. 2001. "How One Town Got Hooked." *Newsweek* April 9, pp. 48–51.

Sigler, K. A., B. G. Guernsey, N. B. Ingrim, A. S. Buesing, J. A. Hokanson, E. Galvin, and W. H. Doutre. 1984. "Effect of a Triplicate Prescription Law on Prescribing of Schedule II Drugs." *American Journal of Hospital Pharmacy* 41 (1): 108–11.

Simoni-Wastila, L. 2000. "The Use of Abusable Prescription Drugs: The Role of Gender." *Journal of Women's Health and Gender-Based Medicine* 9 (3): 289–97.

Simoni-Wastila, L., G. Ritter, and G. Strickler. 2004. "Gender and Other Factors Associated with the Nonmedical Use of Abusable Prescription Drugs." *Substance Use & Misuse* 39 (1): 1–23.

Simoni-Wastila, L., D. Ross-Degnan, C. Mah, X. Gao, J. Brown, L. E. Cosler, T. Fanning, P. Gallagher, C. Salzman, and S. B. Soumerai. 2004. "A Retrospective Data Analysis of the Impact of the New York Triplicate Prescription Program on Benzodiazepine Use in Medicaid Patients with Chronic Psychiatric and Neurologic Disorders." *Clinical Therapeutics* 26 (2): 322–36.

Simoni-Wastila, L., and G. Strickler. 2004. "Risk Factors Associated with Problem Use of Prescription Drugs." *American Journal of Public Health* 94 (2): 266–8.

Strom, B. L. 2001. "Data Validity Issues in Using Claims Data." *Pharmacoepidemiology and Drug Safety* 10 (5): 389–92.

Tough, P. 2001. "The Alchemy of OxyContin: From Pain Relief to Drug Addiction." *New York Times Magazine* July 29, pp. 32–7, 52, 62–3.

Von Korff, M., E. H. Wagner, and K. Saunders. 1992. "A Chronic Disease Score from Automated Pharmacy Data." *Journal of Clinical Epidemiology* 45 (2): 197–203.

Wagner, A. K., S. B. Soumerai, F. Zhang, C. Mah, L. Simoni-Wastila, L. Cosler, T. Fanning, P. Gallagner, and D. Ross-Degnan. 2003. "Effects of State Surveillance on New Post-Hospitalization Benzodiazepine Use." *International Journal for Quality in Health Care* 15 (5): 423–31.

Wastila, L. J., and C. Bishop. 1996. "The Influence of Multiple Copy Prescription Programs on Analgesic Utilization." *Journal of Pharmaceutical Care in Pain and Symptom Control* 4 (3): 3–19.

Weintraub, M., S. Singh, L. Byrne, K. Maharaj, and L. Guttmacher. 1991. "Consequences of the 1989 New York State Triplicate Benzodiazepine Prescription Regulations." *Journal of the American Medical Association* 266 (17): 2392–7.

Welch, W. P., M. E. Miller, H. G. Welch, E. S. Fisher, and J. E. Wennberg. 1993. "Geographic Variation in Expenditures for Physicians' Services in the United States." *New England Journal of Medicine* 328 (9): 621–7.

Wennberg, J. E. 1996. *The Dartmouth Atlas of Health Care, 1996.* Chicago: American Hospital Publishing.

Wennberg, J., and A. Gittelsohn. 1973. "Small Area Variations in Health Care Delivery." *Science* 183 (117): 1102–8.

Wennberg, J., and D. Wennberg. 2000. "Practice Variations and the Use of Prescription Drugs" [accessed on April 21, 2005]. In *Dartmouth Atlas of Health Care in Michigan.* Detroit, MI: Blue Cross Blue Shield of Michigan and Blue Care Network. Available at http://www.bcbsm.com/atlas/practice.shtml

West, S. L., and B. L. Strom. 2000. "Validity of Pharmacoepidemiology Drug and Diagnosis Data." In *Pharmacoepidemiology*, 3d Edition, edited by B. L. Strom. Sussex, UK: John Wiley.

White, H. 1980. "A Heteroskedasticity-Consistent Covariance Matrix Estimator and a Direct Test for Heteroskedasticity." *Econometrica* 48 (4): 817–30.

World Health Organization. 2000. *The Use of Essential Drugs: Ninth Report of the WHO Expert Committee (Technical Report Series 895).* Geneva: World Health Organization.

Wright, D. 2002. *State Estimates of Substance Use from the 2000 National Household Survey on Drug Abuse: Volume I. Findings* (DHHS Publication No. SMA 02-3731, NHSDA Series H-15). Rockville, MD: Substance Abuse and Mental Health Services Administration.

Zipinfo.com Website [accessed on September 2, 2005]. Available at http://www.zipinfo.com/

Zito, J. M., D. J. Safer, S. dosReis, L. S. Magder, and M. A. Riddle. 1997. "Methylphenidate Patterns among Medicaid Youths." *Psychopharmacology Bulletin* 33 (1): 143–7.