Prescription Drug Monitoring and Dispensing of Prescription Opioids

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ABSTRACT

Objective. In the United States, per-capita opioid dispensing has increased concurrently with analgesic-related mortality and morbidity since the 1990s. To deter diversion and abuse of controlled substances, most states have implemented electronic prescription drug monitoring programs (PDMPs). We evaluated the impact of state PDMPs on opioid dispensing.

Methods. We acquired data on opioids dispensed in a given quarter of the year for each state and the District of Columbia from 1999 to 2008 from the Automation of Reports and Consolidated Orders System and converted them to morphine milligram equivalents (MMEs). We used multivariable linear regression modeling with generalized estimating equations to assess the effect of state PDMPs on per-capita dispensing of MMEs.

Results. The annual MMEs dispensed per capita increased progressively until 2007 before stabilizing. Adjusting for temporal trends and demographic characteristics, implementation of state PDMPs was associated with a 3% decrease in MMEs dispensed per capita ($p=0.68$). The impact of PDMPs on MMEs dispensed per capita varied markedly by state, from a 66% decrease in Colorado to a 61% increase in Connecticut.

Conclusions. Implementation of state PDMPs up to 2008 did not show a significant impact on per-capita opioids dispensed. To control the diversion and abuse of prescription drugs, state PDMPs may need to improve their usability, implement requirements for committee oversight of the PDMP, and increase data sharing with neighboring states.

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During the past decade, the distribution of controlled substances in the United States, particularly opioid analgesics (e.g., methadone, oxycodone, and hydrocodone), markedly increased. From 1991 to 2010, the annual number of prescriptions for opioid analgesics in the U.S. almost tripled, from approximately 76 million to almost 210 million.[1] Per-capita retail dispensing of opioid analgesics increased 402% from 73.6 to 369.2 milligrams (mg) per person from 1997 to 2007.[2] In 2010, an estimated 12 million Americans aged 12 years and older reported nonmedical opioid analgesic use in the prior year.[3]

Use of opioid analgesics increased in tandem with morbidity due to prescription drugs. Nonmedical use of prescription drugs accounted for 1.2 million emergency department (ED) visits in 2009.[4–6] From 2004 to 2008, ED visits for nonmedical use of opioid analgesics rose 111%, from almost 150,000 visits to more than 305,000 visits a year.[6] While all age groups have been affected by the epidemic of prescription drug misuse, the health consequences of opioid analgesic misuse are particularly striking in adolescents and young adults. Hospitalizations for opioid analgesics in adults aged 18–24 years rose 122% from 1999 to 2008, and neonatal abstinence syndrome tripled from 2000 to 2009.[7,8]

Increases in mortality due to prescription drugs have also been observed. Unintentional drug overdose deaths almost tripled, from 12,000 in 1999 to 32,000 in 2009.[9–11] Opioid analgesics were responsible for the majority of prescription drug-related morbidity and mortality, with prescription drug overdose deaths exceeding overdose deaths from heroin or cocaine combined.[3]

As a policy intervention in response to the epidemic of opioid analgesic misuse, state prescription drug monitoring programs (PDMPs) are intended to support the appropriate use of controlled substances, detect and deter diversion of controlled substances, and inform public health interventions to prevent drug abuse.[12–14] In 2002, under the Harold Rogers Prescription Drug Monitoring Program and in conjunction with technical assistance provided by the National Alliance for Model State Drug Laws, the U.S. government began issuing grants to help support states in planning, establishing, or enhancing statewide electronic databases to monitor the dispensing of controlled substances. As of June 12, 2012, 50 states (including the District of Columbia [DC]) had enacted laws establishing PDMPs, and 40 states had operational PDMPs.

Evidence for the effect of state PDMPs on prescription drug dispensing and outpatient insurance claims is inconsistent.[15–17] A study of outpatient prescription drug claims of commercially insured individuals found that rates of claims for prescription opioids differed significantly by state, and that the presence of a state PDMP was associated with significantly lower county-level Schedule II opioid claims.[17] A recent study suggests that state PDMPs are effective in reducing opioid abuse and misuse.[18] However, other studies found that state PDMPs had a minimal effect on the overall dispensing of opioids and overdose mortality.[15,16,19] Most of the studies were based on data from earlier time periods and did not consider statutory variations in state PDMPs. Using dispensing as a surrogate marker for consumption, this study assessed the impact of PDMP implementation on the dispensing of prescription opioids nationally and at the state level for the years 1999–2008 and explored whether specific PDMP characteristics are associated with a greater impact.

METHODS

Data sources

Data on distributed opioids came from the Automation of Reports and Consolidated Orders System (ARCOS), a data system maintained by the Office of Diversion Control of the U.S. Drug Enforcement Administration.[20] The Controlled Substances Act of 1970[21] mandates that manufacturers and distributors track and report the dissemination of controlled substances from their manufacture to their sale or dispensing.[20] Quarterly data on the amount of opioids distributed (in grams) during 1999–2008 were tabulated for each state using ARCOS retail drug summary reports.[22] Information recorded in ARCOS includes drug name and the amount of drug distributed in grams. This study included data for the seven most commonly distributed opioid analgesics: fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, and oxycodone. Consistent with previous studies, we did not include codeine dispensed in the analysis.[15,16] To account for the relative potency of these drugs, the amount of each drug distributed was converted into morphine mg equivalents (MMEs) using the following multipliers: fentanyl-75, hydrocodone-1, hydromorphone-4, meperidine-0.1, methadone-7.5, morphine-1, and oxycodone-1.[16,23,24]

Annual state-, race-, and age group-specific population data came from the bridged-race intercensal and postcensal population estimates, developed jointly by the U.S. Census Bureau and the National Center for Health Statistics. We used annual state-specific population estimates for the July 1 resident population to calculate the MMEs distributed per capita. We used race- and age group-specific population estimates to calculate the percentage of the population identifying as white and the percentage of the population that was aged 35–54 years.[25] White people disproportionately receive prescription opioids for pain relief and are more likely than other races to be illicit abusers of these pain medications.[26,27] Studies have found that white people have an increased risk of nonmedical use of prescription drugs and overdose, and that death rates from poisoning are highest for individuals aged 45–54 years.[28–30] Groupings of states into geographic regions were defined according to the U.S. Census Bureau.[31]

The date by which a state PDMP was implemented was ascertained from the U.S. Drug Enforcement Administration, and PDMP characteristics were collected from an evaluation conducted by the Kentucky All Schedule Prescription Electronic Reporting (KASPER) Program Evaluation Team.[14,32] The implementation date of a state PDMP refers to the quarter and year when electronic prescription drug data collection began.[32] We assessed three characteristics of PDMPs that were outlined by the KASPER Program Evaluation Team: (*1*) type of governing agency (e.g., Department of Health, Board of Pharmacy, or other [mostly offices related to public safety and drug control]); (*2*) statutory requirement for committee oversight (i.e., statutory requirement for a PDMP to work with an advisory committee task force or working group during the program's implementation, monitoring, and evaluation) (yes or no); and (*3*) explicit provision that imposes no expectation on practitioners to access the statewide electronic database of dispensed prescriptions before prescribing or dispensing (yes or no).

Statistical analysis

The unit of analysis was the state quarter, where quarters were grouped into four three-month intervals: January–March, April–June, July–September, and October–December. If a state had an operational electronic PDMP at any time during a quarter, the state quarter was coded as having a PDMP. From January 1999 to December 2008, there were 2,040 state quarters ($10 \times 4 \times 51$; DC was included as a state). PDMP implementation dates varied across states. Of the 2,040 state quarters, 31 states and 619 state quarters had operational PDMPs. We examined the association between PDMP implementation and MMEs distributed by comparing data for state quarters with and without PDMPs.

We performed multivariable analyses to estimate the effect of state PDMPs on MMEs of opioid analgesics distributed. To account for non-normality, the natural logarithm of MMEs distributed was modeled as the dependent variable. We used generalized estimating equations to account for repeated measurements over time and correlation within states.[33,34] Robust standard errors (SEs) calculated using an empirical variance estimator were used and the independence working covariance matrix was selected as the best working covariance, because models with this covariance structure had the lowest quasi-likelihood under the independence model criterion.[35]

In the multivariable statistical analysis, we considered the following covariates: calendar year, demographic characteristics (percentage of the population that was male, aged 35–54 years, and white), and geographic region (Northeast, Midwest, South, and West). Natural logarithms of state population counts were included as a covariate in the multivariable regression model. We considered covariates at the $p<0.05$ level when adjusting for PDMP status to be significant and included them in the final adjusted model. For state-level PDMP estimates, we estimated the effect of PDMP separately for each state that implemented a PDMP in the study period. In addition to aggregated analyses, we estimated the effects of individual state PDMPs on opioid dispensing by models based on data for state quarters with and without an operational PDMP for a given state that implemented a PDMP, along with those without an operational PDMP throughout the study period (Alaska, Arkansas, DC, Delaware, Florida, Georgia, Iowa, Kansas, Maryland, Minnesota, Missouri, Montana, Nebraska, New Hampshire, New Jersey, Oregon, South Dakota, Vermont, Washington, and Wisconsin). We conducted data analysis using SAS® version 9.2 and Stata® version 11.2.[36,37]

RESULTS

Overall

From 1999 to 2008, the annual MMEs dispensed per capita increased fivefold, from 163.1 to 827.0 (Figure). During the 10-year study period, more than 1.3 billion MMEs were dispensed and 41.5% were dispensed in the 619 state quarters with operational PDMPs (data not shown). Overall, when not accounting for the time trend, more MMEs per capita were dispensed in state quarters with PDMPs than in state quarters without PDMPs (510.16 vs. 427.09) (Table 1). However, when the data were examined by year, fewer MMEs per capita were dispensed in state quarters with PDMPs than in state quarters without PDMPs (Figure). The greater overall MMEs per capita in state quarters with PDMPs than in state quarters without PDMPs (Table 1) was the result of the confounding effect due to the increase in opioids dispensed during the study period and the differential distributions of state quarters with PDMPs and without PDMPs over time (a larger portion of state

Table 1. Annualized MMEs of opioid analgesics[a] distributed per capita, by PDMP implementation status and characteristics: U.S., 1999–2008

PDMP status/characteristic	*State quarters* N	*MMEs per capita (SE)*
Without PDMP	1,421	427.09 (6.74)
PDMP program, but not yet implemented	621	367.48 (8.71)
No PDMP program during the study period	800	500.54 (9.70)
With active PDMP	619	510.16 (12.84)
PDMP governing agency		
Department of health	163	434.39 (22.99)
Board of pharmacy	315	678.27 (17.51)
Other	141	478.01 (29.56)
Statutory requirements for committee oversight		
Yes	152	551.02 (25.66)
No	467	494.27 (14.80)
Explicit laws that impose no expectation on practitioners		
Yes	176	531.25 (23.80)
No	443	504.72 (15.26)

[a]The seven most common opioid analgesics are fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, and oxycodone.

MME = morphine milligram equivalent

PDMP = prescription drug monitoring program

SE = standard error

quarters with PDMPs being distributed in late years of the study period).

When considering the characteristics of PDMPs, the amount of MMEs dispensed per capita was less in state quarters with PDMPs governed by state health departments than in state quarters with PDMPs governed by state boards of pharmacy or other agencies; less in state quarters with PDMPs with no statutory requirements for committee oversight than in state quarters that have statutory requirements for committee oversight; and less in state quarters without laws that explicitly impose no expectation on practitioners to access statewide electronic PDMP data than in state quarters with laws that explicitly impose no burden on practitioners to access PDMP data (Table 1).

Overall effect of state PDMPs

Multivariable modeling revealed that there was no statistically significant difference in MMEs dispensed in state quarters with and without PDMPs (difference of −3%, SE=0.07, p=0.68) (Table 2). When considering characteristics of state PDMPs, the seven states with PDMPs governed by a state department of health dispensed nearly 18% fewer MMEs per capita than state quarters without PDMPs (−17.9%, SE=0.09, p=0.06). The 12 states with a statutory requirement for committee oversight of the PDMP (−5.3%, SE=0.10, p=0.60) and the 11 states with an explicit provision that imposes no expectation on practitioners to access PDMP data (–6.9%, SE=0.11, p=0.52) were not significantly associated with changes in the MMEs dispensed per capita (data not shown). In unadjusted and adjusted models, the MMEs distributed per capita increased throughout the study period, and the MMEs dispensed per capita were lower in the Midwest than in the Northeast (unadjusted results not shown; adjusted results shown in Table 2).

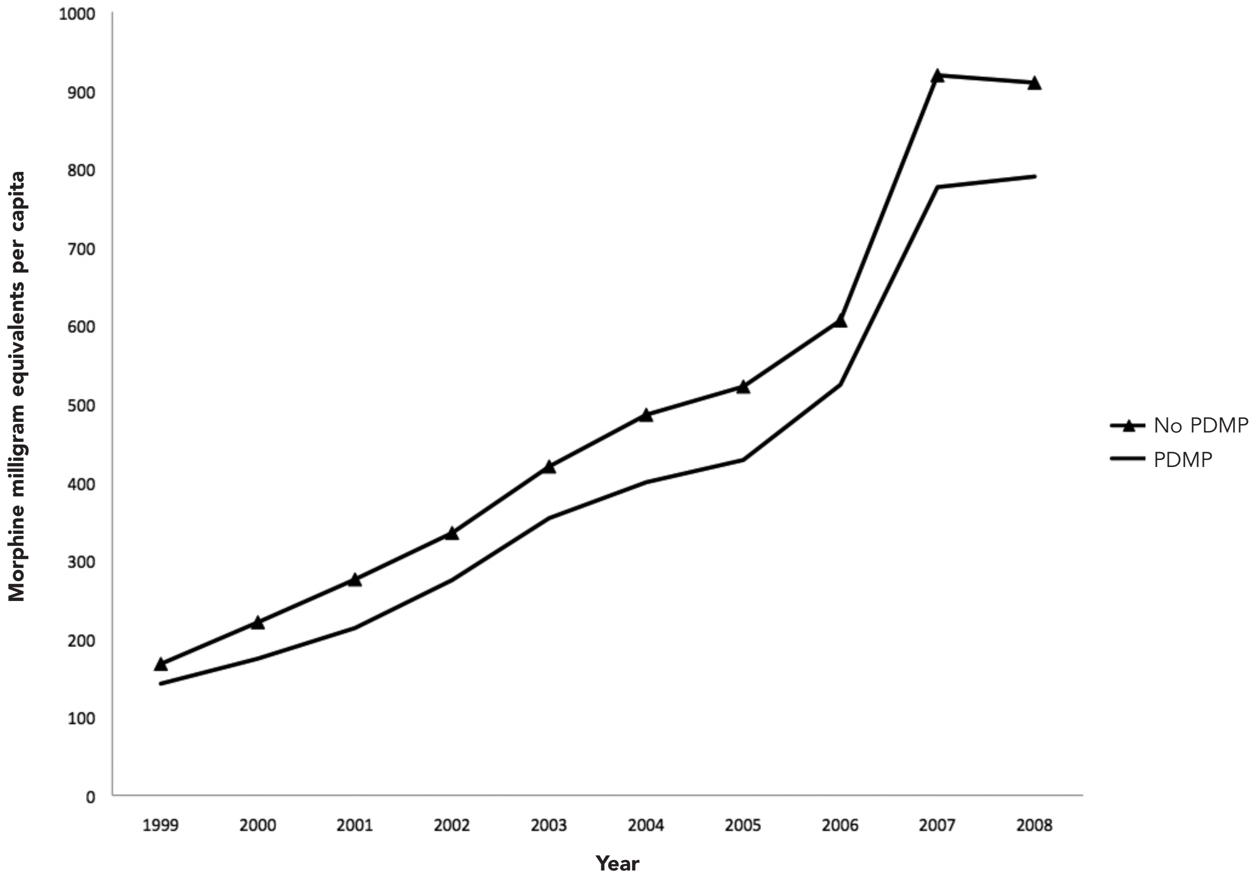
Effect of individual PDMPs

The effect of PDMPs on MMEs dispensed per capita varied markedly across the states (Table 3). The implementation of PDMPs was associated with significantly fewer MMEs dispensed per capita in nine states, no significant effect in 14 states, and a significant increase in the MMEs dispensed per capita in eight states. The greatest percentage decrease in MMEs dispensed per capita (−66.4%, SE=13.3, p<0.0001) associated with PDMP implementation was in Colorado, and the greatest percentage increase in MMEs dispensed per capita (60.6%, SE=9.4, p<0.0001) was in Connecticut.

DISCUSSION

Results of this study indicate that through 2008, state PDMPs had no discernible impact on the overall MMEs dispensed per capita. A previous study by Paulozzi et al.,[16] which analyzed annual state-level drug-dispensing data from 1999 to 2005, found that PDMPs were not associated with decreased dispensing of overall opioids per capita. An earlier study by Simeone and Holland

Figure. Morphine milligram equivalents of opioids dispensed per capita, by year and PDMP status: U.S., 1999–2008



PDMP = prescription drug monitoring program

found that PDMPs were associated with significantly lower dispensing of Schedule II opioids from 1997 to 2003. However, this analysis did not include the use of hydrocodone.[15] From 1999 to 2003, hydrocodone accounted for an average of 21.4% of the MMEs distributed among the seven most commonly reported opioids.[38] We analyzed data from 1999 to 2008 and, like the Paulozzi et al. study,[16] we included the use of hydrocodone.

The overall ineffectiveness of state PDMPs to significantly reduce the amount of opioids distributed per capita is likely related to several factors not examined in this study. First, there has been little interstate data sharing.[39] In an effort to thwart prescription drug monitoring, some individuals procure controlled substances from multiple states, particularly neighboring states.[40] Thus, developing mechanisms to support interstate data sharing is now increasingly a priority. By 2010, standardized requirements for data sharing were developed and there were two independent entities with operational servers for interstate data sharing.[41] Further, Kentucky and Ohio currently exchange prescription drug-dispensing information and have plans to expand to data sharing with other states. Second, prescription drug-dispensing information is often not available to state PDMPs in real time.[42–44] Availability of prescription drug-dispensing information in PDMP databases may take up to a month after a prescription is dispensed. It is evident that more timely availability of prescription drug-dispensing information may improve the detection of drug diversion.[45,46] Finally, the lack of awareness about PDMP data, restrictions on PDMP access, and the lack of technological interoperability and standardization might have further limited the utility of the PDMPs.[47–50]

The current study shows marked variations in the effect of PDMPs on MMEs distributed across states, with Colorado, Texas, and Wyoming having the greatest reduction in total MMEs distributed after PDMP implementation. Although state PDMPs are similar in basic elements of electronically transmitted prescription data, many characteristics of these programs vary from state to state. This study examined three characteristics of PDMPs and found that having a department of health as the governing agency had a significant protective effect on MMEs dispensed. However, there are other differences in state PDMPs, such as variations in the drug schedules monitored and whether health-care providers can access PDMP data, which may influence the overall effectiveness of PDMPs.[51,52] Understanding the impact of state PDMPs can inform case studies of PDMPs and aid in guiding additional research in determining and isolating which characteristics of PDMPs are most effective. This information may then be used to ensure that new and existing PDMPs implement program components associated with increased effectiveness.

There is a paucity of research examining the relative utility of state PDMPs for surveillance and detection of aberrant prescribing patterns and even less research on the effectiveness of individual state PDMPs on reducing rates of MMEs dispensed and overdose deaths per capita.[53–55] Separate investigations of the effects of PDMPs in Massachusetts and California studied individuals who obtained the same medication from multiple providers. These studies found that visiting multiple providers was associated with prescriptions for short-acting opioids, specifically oxycodone.[53,54] A small study examining how a PDMP affected prescribing behaviors in an Ohio ED found that access and review of patients' controlled substances prescription histories resulted in a change in prescribing for 41% of patients with non-traumatic pain; 61% of these patients received fewer opioids and 39% received more.[56]

Table 2. Adjusted coefficient and standard error of morphine milligram equivalents according to PDMP implementation status and other variables: U.S., 1999–2008

Variable	*Adjusted coefficient*[a] *(SE)*	P*-value*
PDMP implemented		
No	Ref.	
Yes	−0.03 (0.07)	0.68
Calendar year		
1999	Ref.	
2000	0.25 (0.05)	<0.0001
2001	0.43 (0.07)	<0.0001
2002	0.62 (0.06)	<0.0001
2003	0.89 (0.05)	<0.0001
2004	1.04 (0.04)	<0.0001
2005	1.17 (0.05)	<0.0001
2006	1.27 (0.06)	<0.0001
2007	1.65 (0.07)	<0.0001
2008	1.65 (0.07)	<0.0001
Region		
Northeast	Ref.	
Midwest	−0.21 (0.10)	0.04
South	0.19 (0.09)	0.04
West	0.18 (0.12)	0.12
Percent aged 35–54 years	0.05 (0.10)	0.08
Percent white	0.01 (0.00)	0.04

[a]Adjusted for the natural log of the quarterly population

PDMP = prescription drug monitoring program

SE = standard error

Ref. = reference group

Limitations

This study was subject to several important limitations. First, this study was observational and, therefore, susceptible to information bias and unmeasured confounding. Second, while this study attempted to account for correlation over time, it did not account for spatial correlation across states (e.g., data from neighboring states may be more highly correlated than data from states that are geographically distant). There are increasing concerns about cross-state trade of prescription opioids and dispensing prescriptions from neighboring states.[56,57] Third, we examined only a few characteristics of state PDMP programs and did not take into account other differences among PDMP programs that may influence opioid dispensing, such as the lag between a prescription being dispensed and recorded in the PDMP database and barriers to accessing the PDMP data. Fourth, this study used data for the years 1999–2008 and the findings of this study may not be generalizable to more recent years, as PDMP implementation has greatly expanded and there have been widespread reforms in state PDMPs since 2008.

Additionally, this study evaluated the possible impact of implementing PDMPs on the dispensing of opioids only. PDMPs may be effective in identifying other indications of drug misuse, such as decreasing "doctor shopping" (i.e., visiting multiple physicians to obtain controlled substances), detecting aberrant prescribing practices, or changing prescribing practices.[13,18,54,56] The magnitude of the prescription drug misuse epidemic will likely require other interventions to prevent misuse, such as proposed Medicaid and other payment restrictions to decrease doctor shopping, augmenting health-care provider training on pain management, implementing evidence-based guidelines for pain management, improving access to drug treatment, and expanding community-based harm-reduction programs.[58–61]

Table 3. Adjusted coefficient and standard error of morphine milligram equivalents associated with PDMP implementation, by state: U.S., 1999–2008

State	*Adjusted coefficient (SE)*[a]	*P-value*	*State*	*Adjusted coefficient (SE)*[a]	*P-value*
Colorado	−0.66 (0.13)	<0.0001	Pennsylvania	0.01 (0.10)	0.94
Texas	−0.54 (0.12)	<0.0001	Mississippi	0.01 (0.07)	0.88
Wyoming	−0.48 (0.09)	<0.0001	Tennessee	0.04 (0.09)	0.66
North Carolina	−0.44 (0.10)	<0.0001	Rhode Island	0.10 (0.07)	0.21
Idaho	−0.41 (0.11)	0.0004	West Virginia	0.13 (0.08)	0.11
Illinois	−0.32 (0.12)	0.01	California	0.15 (0.16)	0.33
South Carolina	−0.30 (0.08)	0.0002	Michigan	0.17 (0.11)	0.14
New York	−0.29 (0.12)	0.02	Maine	0.19 (0.07)	0.01
North Dakota	−0.23 (0.11)	0.03	Nevada	0.29 (0.07)	<0.0001
New Mexico	−0.21 (0.11)	0.05	Indiana	0.36 (0.10)	0.0004
Virginia	−0.17 (0.09)	0.05	Alabama	0.36 (0.07)	<0.0001
Arizona	−0.15 (0.10)	0.14	Louisiana	0.37 (0.08)	<0.0001
Massachusetts	−0.12 (0.09)	0.18	Oklahoma	0.42 (0.08)	<0.0001
Utah	0.00 (0.23)	0.99	Ohio	0.47 (0.12)	<0.0001
Hawaii	0.00 (0.15)	0.99	Connecticut	0.61 (0.09)	<0.0001
Kentucky	0.00 (0.09)	0.96			

[a]To calculate the state-level PDMP estimates, for a given state that implemented a PDMP, models compared state quarters that had an operational PDMP with state quarters that did not have a PDMP along with those without an operational PDMP throughout the study period (Alaska, Arkansas, Washington, D.C., Delaware, Florida, Georgia, Iowa, Kansas, Maryland, Minnesota, Montana, Missouri, Nebraska, New Hampshire, New Jersey, Oregon, South Dakota, Vermont, Washington, and Wisconsin). Models were adjusted for calendar year, geographic region, percent of the population aged 35–54 years, percent of the population that was white, and for the natural log of the quarterly population. Then the models were estimated separately for each state.

PDMP = prescription drug monitoring program

SE = standard error

CONCLUSIONS

This study indicates that the number of prescription opioids dispensed increased until 2007 and then stabilized. Through 2008, implementation of state PDMPs had no measurable overall impact on prescription opioid distribution. However, the effect of PDMP implementation on opioid dispensing varied from state to state. The wide variability in the design and functioning of PDMP programs likely affects their impact on opioid dispensing. The overall lack of effectiveness may be related to health-care providers' limited access to, and use of, PDMP data systems, as well as barriers to interstate data sharing. Improving the effectiveness of state PDMPs may include education about such programs and improvements in integrating PDMPs into clinical and pharmacy routines.

The study was deemed exempt from review by the Columbia University Medical Center Institutional Review Board.

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