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### **Research Article**

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# Prescription Drug Monitoring Programs and Opioid Poisoning: Evaluating the Impact of Prescriber Use Mandates on Prescription Opioid Poisoning Emergency Department Visits

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#### ABSTRACT

Background: Mandatory use of prescription drug monitoring program (PDMP) databases by prescribers has been recommended as a way to influence prescription opioid abuse. Methods: this study explored that recommendation by comparing emergency department (ED) visits related to prescription opioid poisoning among individuals  $\geq 12$  years old in a mandatory use state, Kentucky, with a nonmandatory use state, North Carolina. Data from the State Emergency Department Databases (SEDD) and the State Inpatient databases (SID) were used to identify prescription opioid poisoning ED visits among patients. Main findings: the analysis revealed that the odds of having a prescription opioid poisoning ED visit in the mandated use state of Kentucky were 11% to 35% (95% CI= 6.0% - 39.0%) lower than in North Carolina between 2012 to 2014. Conclusion: this study provides evidence that a prescriber use mandate is effective in reducing prescription opioid poisoning ED visits.

Keywords: Emergency department, Poisoning, Drug abuse, Drug monitoring.

#### **INTRODUTION**

The number of prescriptions for opioids in the United States has increased from 76 million in 1991 to 207 million in 2013 [1]. According to the National Survey on Drug Use and Health (NSDUH), approximately two million Americans abuse prescription opioids [2]. Opioid overdose deaths have quadrupled from 2000 – 2014 with half involving prescription opioids [3]. In 2011, more than 360 thousand emergency department (ED) visits were attributed to non-medical use of prescription opioids [4]. The total cost of prescription opioid poisoning has been estimated at \$16 billion per year with emergency department (ED) costs approximating \$800 million [5].

In 2011, the Federal Government identified prescription drug monitoring programs (PDMPs) as one of four key areas of focus to prevent prescription drug abuse [6]. PDMPs are state-run electronic databases that collect and share information on the prescribing and dispensing of prescription opioids and other controlled substances. To be effective in managing opioid abuse, PDMPs must be utilized as intended by prescribing physicians, nurses, and pharmacists. However, utilization of PDMPs is low and highly variable among different states and health care providers [7-10]. PDMP prescriber use mandates have emerged as a recommended best practice.

Prescriber use mandates are "state laws and regulations that require prescribers to view a patient's PDMP data under certain circumstances". 7 States differ widely in how they require prescribers to check PDMPs [11,12]. Some states have comprehensive rules regarding when and how frequently a prescriber should access PDMPs, while others have less stringent requirements. Prescriber mandates have been enacted with the expectation that they will be used more and therefore reduce inappropriate prescribing and adverse health outcomes associated with prescription opioid abuse. Yet, the current literature is limited regarding the impact of prescriber use mandates on prescription opioid abuse-related health outcomes [13-15].

The current study evaluates the effectiveness of PDMPs by comparing ED visits related to prescription opioid poisoning among individuals  $\geq$ 12 years old in a mandatory use state, Kentucky, with a non-mandatory use state, North Carolina. Using Donabedian's structure-process-outcome quality framework, [16] we hypothesized that the existence of a policy mandating PDMP use by prescribers (i.e., structure) will increase PDMP utilization (i.e., process) and reduce ED visits associated with prescription-related opioid poisoning (i.e., outcome).

The study was restricted to patients in Kentucky and North Carolina because they allowed comparison of a prescriber mandate state, Kentucky, with a state that had no prescriber mandate for the years 2011 to 2014. Kentucky was chosen because it implemented a PDMP prescriber use mandate in July 2012, and it had ED data available in the SEDD and the SID.

North Carolina was selected as the comparator state because it did not have PDMP prescriber mandate, is geographically close to Kentucky, and has ED visits data available for the period of the study. The seven neighboring states to Kentucky were excluded for not having HCUP ED visit data over the study period or for implementing a prescriber mandate during that time.

## STUDY DATA AND METHODS

#### Data

Data for this study came from the Healthcare Cost and Utilization Project (HCUP) State Emergency Department Databases (SEDD) and the State Inpatient Databases (SID) [17]. The SEDD contains state-specific information on all treat-and-release and transfer ED visits that do not result in a hospital admission at a community hospital. The SID contains state-specific data on ED visits that resulted in community hospital admissions. ED visit data from the SEDD was combined with SID data to identify prescription opioid poisoning ED visits among patients at community hospitals in Kentucky and North Carolina.

### Study sample

Patients had to be at least 12 years of age and residents of Kentucky and North Carolina to be included in this study. ED visits with any listed diagnosis of prescription opioid poisoning were included (ICD-9-CM codes: 965.00, 965.02, and 965.09). Prescription opioid poisoning ED visits with any intent were considered eligible for inclusion (E-codes: E850.1 E850.2, E950.0, and E980.0). Patients were excluded if they had a pre-existing diagnosis of cancer (Single level Clinical Classifications Software (CCS): 11 - 45), fatal prescription opioid poisoning, or heroin-related visits.

#### Measures

The main outcome measure was the occurrence of prescription opioid poisoning ED visits (a binary variable). The main predictor variable was an interaction term of state with time relative to policy implementation.

All final regression models included the predictors: age, gender, race, income, primary payer, number of chronic conditions, a pre-existing diagnosis of drug abuse, a preexisting diagnosis of depression, and an interaction term between age and number of chronic conditions.

#### Study design

ED visits were compared within Kentucky before and after prescriber use mandates implementation using a pre-post study design. In addition, ED visits were compared between Kentucky and North Carolina using a controlled pre-post study design.

#### Study setting

All prescription opioid poisoning ED visits in Kentucky and North Carolina for the years 2011 to 2014.

#### Statistical analyses

Prevalence estimates of prescription opioid poisoning ED visits were calculated for Kentucky and North Carolina. Descriptive statistics were used to describe basic sociodemographic and clinical characteristics of prescription opioid poisoning ED visits in each state over the 2011 – 2014 period.

Multivariable logistic regression analysis was used to examine the impact of prescriber use mandates on prescription opioid poisoning ED visits in Kentucky. Three models were created to compare ED visits before and after prescriber use mandates implementation in Kentucky. The

mandates policy became effective in July 2012 with the first set of comparisons being made for the years 2011 and 2012. The subsequent set of comparisons included the years (2011, 2013) and (2011, 2014).

A difference in difference (DID) framework was applied to analyze the casual effect of prescriber use mandates policy on prescription opioid poisoning ED visits.

The DID framework is a common analytical technique used to evaluate the impact of policy change [18,19]. It estimates the difference in changes of an outcome variable over time between the intervention and control group. Three sets of comparison models were conducted including the years (2011, 2012), (2011, 2013), and (2011, 2014). Each model compared the occurrences of prescription opioid poisoning ED visits in Kentucky and North Carolina. (see Appendix Exhibit A1 for more explanation of the DID model)."To access the Appendix, click on the Appendix link in the box to the right of the article online."

#### STUDY RESULTS

Sociodemographic, clinical characteristics, and prevalence estimates

Sociodemographic and clinical characteristics:

The study populations in Kentucky and North Carolina shared similar sociodemographic characteristics over the period 2011 to 2014. The mean age of individuals poisoned by opioids was 43 years (SD=15.9) and 44.5 years (SD =17.2) in Kentucky and North Carolina, respectively.

ED visits were more common in adults >50 years old (33.5% and 39.0%), female (54.1% and 56.6%), white (93.9% and 81.4%), and those with low income (34.4% and 31.2%). Medicare was the largest payer for prescription opioid poisoning ED visits (29.1% and 29.2%). ED visits for patients from urban areas were more common compared to rural (51.9% and 65.8%). More than one third of

prescription opioid poisoning ED visits involved people with five or more chronic conditions. Approximately one quarter of ED visits were related to patients with pre-existing depression.

#### Prevalence estimates

Over the four-year period, a total of 7,419 and 12,598 prescription opioid poisoning ED visits were reported in Kentucky and North Carolina, respectively. The total (four year) prevalence rate of prescription opioid poisoning ED visits was 199.6 and 151.94 per 100,000 population in Kentucky and North Carolina, respectively. In Kentucky, there was a 26.1% decrease in the prevalence of prescription opioid poisoning ED visits from 2011 to 2014, while in North Carolina, the prevalence increased by 3.2%.

Annual prevalence rate, prevalence rate by age group, and prevalence rate per 100,000 ED visits are available in Appendix Exhibits A2, A3, and A4. "To access the Appendix, click on the Appendix link in the box to the right of the article online."

## Prescription opioid poisoning ED visits pre and post use mandates in Kentucky (multivariable logistic regression)

In the three regression models that compared the years 2012, 2013, and 2014 to 2011, all covariates had a significant relationship with opioid poisoning ED visits (i.e. p-value<0.05). Holding all other variables constant, the odds of having a prescription opioid poisoning ED visit in 2012 was 11% (95% CI= 6.0% - 17.0%) less compared to 2011. These odds decreased to 33% (95% CI= 28.0% - 37.0%) and 35.0% (95% CI= 30.0% - 39.0%) in 2013 and 2014, respectively, as compared to 2011 (results of the three regression models are available in Appendix Exhibit A5. "To access the Appendix, click on the Appendix link in the box to the right of the article online."

## Prescription opioid poisoning ED visits in Kentucky and North Carolina (difference in difference model):

All covariates, including the main predictor variable, were significantly associated with prescription opioid poisoning ED visits (i.e. p-value <0.05). Holding all other variables constant, the odds of having an opioid poisoning ED visit in Kentucky compared to North Carolina was 9% (95% CI= 1% - 16%) less in 2012 compared to 2011. These odds decreased to 30% (95% CI= 24% - 35%) in 2013 and 2014 (Exhibit 1).

The regression models showed that the odds of having an opioid poisoning ED visit were significantly higher for those less <50 years old, white, male, Medicaid, and self-paid patients. However, patients with private insurance had lower odds of developing a poisoning event compared to patients covered with Medicare. In addition, patients with five or more chronic conditions, or had a pre-existing condition of depression or drug abuse had higher odds of having an opioid poisoning ED visit (EXHIBIT 1).

#### DISCUSSION

This is the first study to examine the impact of a PDMP prescriber use mandates on prescription opioid poisoning ED visits using a controlled pre-post study design.

This research focused on the impact of comprehensive prescriber use mandates. Prescription opioid poisoning ED visits were compared between Kentucky and North Carolina using three comparison models for the years 2012, 2013, and 2014 as compared to 2011.

This study found that the prevalence rate of prescription opioid poisoning ED visits in 2014 was 43.82 per 100,000 residents for Kentucky and 37.45 per 100,000 residents for North Carolina. In the same year, the Agency for Healthcare Research and Quality (AHRQ) estimated the national rate of opioid related ED visits to be 177.7 per 100,000 residents [20]. However, this national estimate included all heroin and non-heroin related ED visits for all age groups. A recent report by the CDC found that the rate of opioid overdose ED visits among those aged 11 years and older decreased by 15% in Kentucky, and increased by 30% in North Carolina from July 2016 to September 2017 [21]. Our study estimated a 26.1% reduction in the rate of prescription opioid poisoning ED visits in Kentucky and 3.2% increase in North Carolina from 2011 to 2014.

This study found evidence to support prescriber use mandates and how this differed in Kentucky and North Carolina. Prescriber use mandates implemented in Kentucky in July 2012 were associated with a moderate, but significant, reduction in prescription opioid poisoning ED visits in 2012 as compared to 2011, controlling for North Carolina in the model. An even greater reduction in opioid related ED visits was seen in 2013. The impact of the policy has leveled off in 2014, as no further reduction was seen in prescription opioid poisoning ED visits (EXHIBIT 2). The impact of the policy cannot be isolated from pain clinic regulations, which were part of the House Bill 1 (HB1) legislation implemented in Kentucky in 2012. Also, Kentucky and North Carolina differ in the adoption of other policies, which could impact the assessment of prescriber use mandates. In 2011, North Carolina implemented a state-wide program called Project Lazarus. The program aimed to combat the prescription opioid abuse epidemic and related health outcomes. When first initiated in Wilkes county in 2008, Project Lazarus reduced overdose deaths and opioid abuse related ED visits by 69% and 15%, respectively [22]. Despite the initiative in North Carolina, our study found a significant reduction in prescription opioid poisoning ED visits in Kentucky compared to North Carolina. This finding further supports the effectiveness of prescriber use mandates.

Results of this study expand the growing body of evidence on PDMP effectiveness. It differs with Maughan et al. who did not find a statistically significant difference in prescription opioid misuse related ED visits between states with and without PDMPs [23]. One explanation for the non-significant results reported by the authors was the low and variable utilization of PDMPs by prescribers at the time of their study [24-39]. PDMP use was much greater in Kentucky during the period of our study.

The few studies specific to prescriber use mandates are generally supportive of them. In New York, prescription opioid related ED visits leveled off following prescriber use mandate implementation [13]. New York also saw a significant reduction in opioid prescribing after prescriber use mandates [40]. A national study by Dowell reported significant reduction in prescription opioid related deaths following prescriber use mandates [14]. Only one study found nonsignificant impact of prescriber use mandates on opioid prescribing [15].

### **Study limitations**

This study has several limitations. The intended study population was abusers who obtained their prescription opioids from doctors although the data did not allow us to verify this. Physicians are only one source of prescription opioids. According to National Survey on Drug Use and Health (NSDUH), half of non-medical users (50.5%) obtained their opioid from a friend or relative for free, 22.1% got it from one doctor, and 11% bought it from a friend or relative [41].

Prescription opioid poisoning is also not limited to prescription opioid abusers. Accidental poisoning due to polypharmacy, defined as taking five or more medications [42] can be another cause. The current study found that more than one third of opioid-related ED visits were attributed to patients with 5 or more chronic conditions indicating that polypharmacy might be a cause. Furthermore, this study could not control for patient's living condition (i.e. homelessness), marital status, education, and employment which are potential confounders.

Evidence from the existing literature supports the relationship between these variables and opioid abuse; [43,44] however, no information on these variables were available in the SEDD and the SID for the period of the study. Other data limitations are related to the ICD-9-CM codes; there are no specific codes that identify prescription opioid poisoning and thus, the analyses of this study may overestimate the occurrences of prescription opioid poisoning ED visits.

Other state level unobserved factors may affect the findings of this study. There may be local policies or interventions that were implemented at similar time to prescriber use mandates, which could impact the estimated effect of the policy. These may include other opioid-related prescriber mandates, regulations of naloxone access, and others.

Lastly, findings of the current study may not be generalizable to all states. This is due to differences among the states in conditions under which a prescriber is required to check the state PDMP.

States without prescriber use mandates policy should consider its adoption. To maximize prescriber use of PDMPs, other policies or practices should also be considered. Prescribers and other intended users of PDMPs should be educated about the importance of using the system and how to use it appropriately. In addition, prescriber should be given the right to authorize other staff, such as nurses to use the PDMP. This will save time for prescribers, hence enhancing PDMPs utilization. Proactive reports are another important practice; sending unsolicited reports to prescribers will notify them about high risk patients, and encourage them to coordinate care with other healthcare providers. In addition to these practices, states must adopt laws that specifically provide immunity to prescribers and other intended users for accessing the system and impose sanctions on those who fail to use it.

#### STUDY CONCLUSION

The prescriber use mandate policy is effective in reducing prescription opioid poisoning ED visits and their associated costs. PDMP use mandates are one of several policies that can increase prescribers and pharmacists use of the system, thereby support PDMPs effectiveness. Decision makers should consider ways to maximize the implementation of prescriber use mandates, and adopt other policies or practices that enhance the effectiveness of PDMPs.

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### APPENDIX

### Exhibit A1: The difference in difference (DID) model.

The logistic regression analysis with DID framework can be explained by the following equation:

Logit (poisoning indicator=1) =  $\beta 0 + \beta 1$  mandates +  $\beta 2$  post+  $\beta 3$  (mandates\*post) +  $\beta (4-n) X(4-n)$ 

- Poisoning\_indicator is a dummy variable for prescription opioid poisoning ED visit (1= prescription opioid poisoning ED visit, 0= other ED visit)

- Mandates is a dummy variable for prescriber mandates (1= Kentucky, 0= North Carolina).

- Post is a dummy variable for post mandates period (1= post mandates (i.e. 2012, 2013 and, 2014), 0= pre-mandates (i.e. 2011).

-  $\beta$ 3 is the DID estimator which represents the true effect of mandates:

 $\beta$ 3= (KY post - KY pre) - (NC post - NC pre).

- X (4 - n) are the potential confounders considered in the final model.

- N= number of confounders.

#### Exhibit A2: Annual prevalence rate of prescription opioid-poisoning ED visits (per 100,000 population) by state.

State	KY	NC
2011	59.31	36.29
2012	54.94	37.68
2013	41.67	39.49
2014	43.82	37.45
Percent change 2011 - 2014	-26.12	3.20

Source/Notes: SOURCE [Authors' analysis of the data from the State Emergency Department Databases and the State Inpatient Databases, Kentucky and North Carolina 2011 – 2014.] Notes [KY= Kentucky; NC = North Carolina].

Exhibit A3	: Annual and tota	al prevalence rate	e of prescrip	tion opioid p	oisoning ED	visits (per	100,000	popula	tion) by a	age group	) by state	<b>!</b> .
							-			_	·	-

State	Age	2011	2012	2013	2014	Percent change 2011	Total prevalence rate
	(in years)					- 2014	
KY	12 - 17	19.00	14.00	12.56	11.71	-38.40	14.25
	18 - 25	62.15	58.3	32.2	34	-45.3	46.50
	26 - 34	94	77	48.3	54.2	-42.3	68.43
	35 - 50	78	69	58	56.3	-27.8	65.46
	>50	43	46.5	39	43.3	0.7	43.00
NC	12 - 17	12.7	14.0	11.1	14.7	15.7	13.12
	18 - 25	41.9	38.6	37.2	38.3	-8.6	39.00
	26 - 34	43.0	39.7	45.5	44.5	3.5	43.18
	35 - 50	41.1	42.4	44.6	40.3	-1.9	42.12
	>50	34.3	39.2	41.6	41.2	20.1	39.14

Source/Notes: SOURCE [Authors' analysis of the data from the State Emergency Department Databases and the State Inpatient Databases, Kentucky and North Carolina 2011 – 2014.] Notes [KY= Kentucky; NC = North Carolina].

Exhibit A4: Annual	prevalence rate of	prescription	opioid	poisoning !	ED visits	(per 10	00,000 ED	visits) by state.
	1					<b>A</b>	/	<i>, .</i>

State	KY	NC
2011	117	86.8
2012	109.4	87.1
2013	87.2	90.5
2014	86.5	86.8
Percent change 2011 - 2014	-26.1	0

Source/Notes: SOURCE [Authors' analysis of the data from the State Emergency Department Databases and the State Inpatient Databases, Kentucky and North Carolina 2011 – 2014.] Notes [KY= Kentucky; NC = North Carolina].

Variable OR (95% CI)		OR (95% CI)		OR (95% CI)	OR (95% CI)		
		(2011, 2012)		(2011, 2013)	(2011, 2014)		
Post							
2012	0.89	(0.83-0.94)	-	-	-		
2013	-	-	0.67	(0.63-0.72)	-		
2014	-	-	-	-	0.65	(0.61-0.70)	
2011&	-	-	-	-	-	-	
Age(in years)							
12 -17	2.57	(1.06-6.22)	3.90	(1.84-8.27)	2.61	(1.16-5.85)	
18 - 25	2.87	(2.06-4.01)	2.16	(1.45-3.21)	2.17	(1.51-3.13)	
26 -34	3.27	(2.68-3.98)	3.02	(2.30-3.53)	2.53	(2.05-3.12)	
35 -50	2.34	(2.06-2.65)	2.41	(2.12-2.74)	2.06	(1.81-2.34)	
$\geq 50^{\&}$	-	-	-	-	-	-	
Gender							
Female <sup>&amp;</sup>	-	-	-	-	-	-	
Male	1.23	(1.16-1.31)	1.20	(1.12-1.28)	1.21	(1.13-1.29)	
Race							
White <sup>&amp;</sup>	-	-	-	-	-0.33	-	
Black	0.30	(0.25-0.35)	0.33	(0.27-0.39)	0.94	(0.28-0.39)	
Hispanic	0.57	(0.38-0.87)	1.20	(0.95-1.53)	0.73	(0.70-1.27)	
Other	0.95	(0.71-1.26)	0.70	(0.45-1.10)		(0.51-1.05)	
Primary expected							
payer							
Medicare <sup>&amp;</sup>	-	-	-	-	-	-	
Medicaid	1.29	(1.17-1.42)	1.20	(1.08-1.34)	1.33	(1.20-1.47)	
Private insurance	0.97	(0.88-1.07)	0.90	(0.80-1.00)	0.96	(0.86-1.06)	
Self-pay	1.35	(1.22-1.50)	1.35	(1.21-1.50)	1.42	(1.26-1.60)	
Other	1.46	(1.28-1.66)	1.28	(1.11-1.48)	1.38	(1.19-1.61)	
Median household income							
First quartile							
Second quartile	1.17	(1.07-1.29)	1.06	(0.96-1.17)	1.09	(0.99-1.20)	
Third quartile	1.02	(0.93-1.13)	0.95	(0.86-1.05)	0.94	(0.85-1.04)	
Fourth quartile <sup>&amp;</sup>	0.90	(0.83-0.99)	0.89	(0.81-0.99)	0.85	(0.77-0.94)	
	-	-	-	-	-	-	

Exhibit A5: Adjusted logistic regression for prescription opioid poisoning ED visits (Kentucky 2011-2014).

No. of chronic conditions						
0						
1	0.19	(0.15-0.23)	0.20	(0.16-0.25)	0.19	(0.15-0.24)
2	0.26	(0.21-0.33)	0.26	(0.20-0.33)	0.24	(0.19-0.30)
3	0.38	(0.31-0.46)	0.36	(0.28-0.44)	0.33	(0.27-0.42)
4	0.49	(0.40-0.60)	0.51	(0.42-0.63)	0.46	(0.37-0.56)
$\geq 5^{\&}$	0.78	(0.66-0.94)	0.82	(0.69-0.99)	0.70	(0.59-0.85)
	-	-	-	-	-	-
Drug abuse						
No	0.05	(0.01-0.20)	0.05	(0.01-0.20)	0.51	(0.19-1.36)
Yes <sup>&amp;</sup>	-	-	-	-	-	-
Depression						
No	0.40	(0.37-0.44)	0.40	(0.37-0.43)	0.40	(0.37-0.44)
Yes <sup>&amp;</sup>	-	-	-	-	-	-

Source/Notes: SOURCE [Authors' analysis of the data from the State Emergency Department Databases and the State Inpatient Databases, Kentucky and North Carolina 2011 – 2014.] Notes [post: main independent variable that compares ED visits in the post and pre-mandates period in Kentucky, OR: odds ratio; CI: confidence interval, &: reference category].