Opioid-Overdose Laws Association with Opioid Use and Overdose Mortality

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Supplementary Appendix

I. Timing of Law and Program Implementation

Figure S1 shows the geographic dispersion and enactment year of jurisdictions that have implemented a naloxone access law and/or Good Samaritan law. There is wide variation in both the geographic and temporal dispersion of law implementation. Table S1 provides further detail on each state's enactment date for both the broader overdose mortality prevention laws and each provision examined.

II. Opioid Mortality Classification Strategy

Opioid-overdose deaths were classified using the *International Classification of Diseases, Tenth Revision* (ICD-10). For cases with drug overdose coded as the underlying cause of death, the type of opioid involved was indicated by the following ICD-10 multiple cause-of-death codes: opioids (T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6); natural and semisynthetic opioids (T40.2); methadone (T40.3); synthetic opioids, other than methadone (T40.4); and heroin (T40.1). We included cases for which the underlying cause of death was coded as unintentional (X40–44), homicide (X85), or undetermined intent (Y10–Y14) and removed cases coded as suicide (X60–64).

III. Model

To identify the effect of the overdose mortality prevention laws on opioid mortality and use, we use a standard difference-in-differences (DID) approach in which states that have implemented laws are members of the exposure group and those that have not implemented the measures are the comparison group. The differential time and geographic implementation of the measures provides a natural experiment that allows us to control for a number of potential cofounders. In particular, the wide range of law enactment dates and similarities in increases in opioid use across the exposure and comparison groups help account for any potential bias due to these laws being implemented in response to changes in opioid use. Additionally, the comparison occurs both between exposure and comparison groups and also within the exposure group before and after implementation. As such, we are comparing the outcomes for the same population before and after implementation, accounting for such issues as population distribution.

The negative binomial model is preferred to a linear model because of the count nature of overdose mortality and the relatively low frequency of deaths. Hausman tests indicated that state and/or county random effects appropriately accounted for unobserved heterogeneity. The basic formula each regression model takes is as follows:

(1) $m_{at} = \alpha + \beta Treat_{at-1} + \tau_a + \gamma_t + \ln(POP_{at}) + \epsilon_{at} + \mu_a$

Where m_{at} is the mortality count of area *a* (either state or county, depending on if the exposure is a law or program, respectively) in year *t,* α is the intercept, and the coefficient of interest is β, the estimate of the association of area *a* having implemented a law in the previous year. The variable τ_a is an indicator variable for the treatment status of area *a*, that is equal to 1 if they ever implemented a law and zero otherwise, and γ_t is a vector of indicator variables for the year of observation. The inclusion of these variables in a regression framework serves to make the explanatory variable of interest, $Treat_{at-1}$, a DID measure. The natural log of the relevant population is included as an exposure variable. The error term is divided into two parts, the first being ϵ_{at}, the idiosyncratic error for area *a* in year *t* and the second, μ_a being the random effect for area *a*. In these estimations, heteroskedasticity robust errors are clustered at the state level to control for serial correlation within geographic areas.

We follow a similar approach to examine the relationship between naloxone laws, overdose Good Samaritan laws, and nonmedical opioid use. Because of the binary nature of the outcome and the relatively few individuals who report using opioids nonmedically, the logit model is the preferred estimation strategy. We modify equation 1 to reflect the individual level of the NSDUH data, giving it the following form:

(2) $u_{iat} = \alpha + \beta Treat_{iat-1} + \Gamma \mathbf{X_{iat}} + \xi_a + \gamma_t + \mathrm{T_a} + \epsilon_{iat}$

Where u_{iat} is an indicator that equals 1 if respondent *i* in geographic state area *a* in year *t* used opioids nonmedically in the past month and zero otherwise. Likewise, $Treat_{iat-1}$ is an indicator variable if that individual lived in a jurisdiction with a law in the previous year. The vector $\mathbf{X_{iat}}$ contains individual-level controls, including age, sex, race/ethnicity, education, and income. The ξ_a, γ_t, *and* T_a vectors represent area indicators, year indicators, and state-specific linear time

trends, respectively. As with the exposure group and year indicators in the mixed-effects negative binomial models, the inclusion of area and year indicators makes the estimate of β a DID measure. Finally the errors, represented by ϵ_{iat} are adjusted for complex survey design, which may introduce serial correlation.

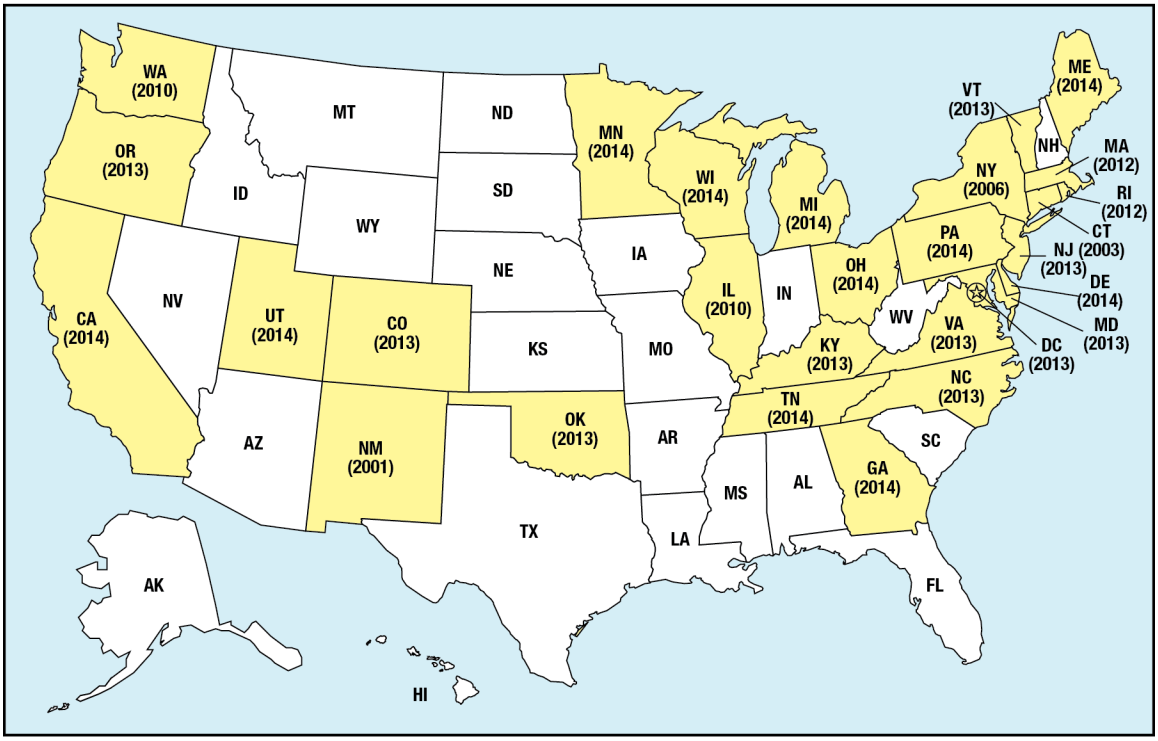
All models are estimated using Stata software, version 14.1. The mixed-effects negative binomial models are estimated with the 'menbreg' command and the survey adjusted logit models are estimated with the 'logit' command with the 'svy' prefix.

IV. Analysis of Contemporaneous Interventions

For all models, we considered the inclusion of measures for other contemporaneous interventions such as the implementation of Prescription Drug Monitoring Programs (PDMP) laws. PDMP law definitions were coded following prior literature (Ali, Dowd, Classen, Mutter, & Novak, 2017). However, using a chi-square analysis of the relationship between overdose mortality prevention laws and PDMP laws, we found no association between the two ($P>0.19$ for all measures). These results can be found in Table S2. This indicates that PDMP laws are not a potential confounding factor of overdose mortality prevention laws and therefore their inclusion in the model is not appropriate.

Figure S1: Enactment Year of Naloxone Laws and Good Samaritan Laws through December 31, 2014, by State.

1a: Naloxone Access Laws by State



1b: Good Samaritan Laws by State

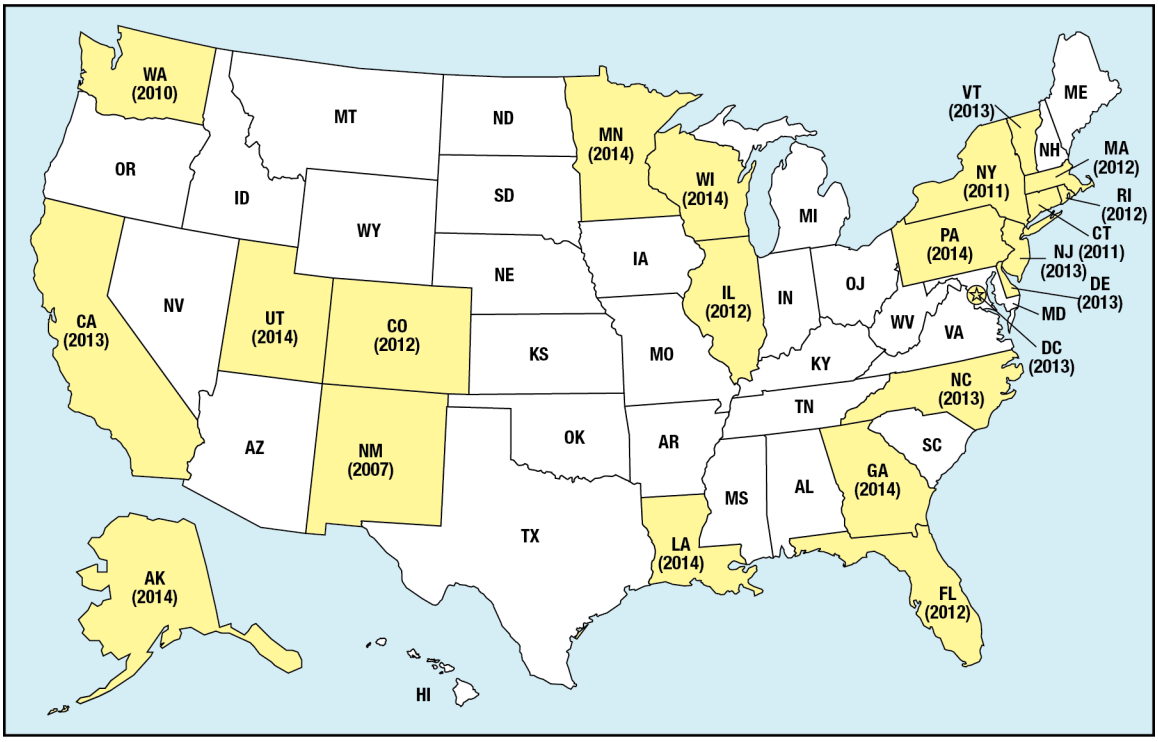


Table S1. Enactment Year of Naloxone Laws and Regulations through December 31, 2014, by State.									
	Naloxone law provisions						Good Samaritan laws		
State	Any naloxone law	Third party	Standing order	Possession	Prescriber immunity	Dispenser immunity	Any Good Samaritan law	Good Samaritan law possession	Good Samaritan law probation
Alabama	-	-	-	-	-	-	-	-	-
Alaska	-	-	-	-	-	-	2014	-	-
Arizona	-	-	-	-	-	-	-	-	-
Arkansas	-	-	-	-	-	-	-	-	-
California	2014	2014	2014	-	2014	2014	2013	2013	-
Colorado	2013	-	-	-	2013	2013	2012		-
Connecticut	2003	-	-	-	2003	2012	2011	2011	-
District Of Columbia	2013	-	-	2013			2013	2013	2013
Delaware	2014	-	2014	-	2014	2014	2013	2013	2013
Florida	-	-	-	-	-	-	2012	-	-
Georgia	2014	2014	2014	-	2014	2014	2014	2014	2014
Hawaii	-	-	-	-	-	-	-	-	-
Idaho	-	-	-	-	-	-	-	-	-
Illinois	2010	2010	2010	2010	-	-	2012	-	-
Indiana	-	-	-	-	-	-	-	-	-
Iowa	-	-	-	-	-	-	-	-	-
Kansas	-	-	-	-	-	-	-	-	-
Kentucky	2013	2013	2013	-	-	-	-	-	-
Louisiana	-	-	-	-	-	-	2014	-	-
Maine	2014	2014	-	-	-	-	-	-	-
Maryland	2013	2013	-	-	-	-	-	-	-
Massachusetts	2012	2014	2014	2012	-	-	2012	-	-
Michigan	2014	2014	-	2014	2014	2014	-	-	-
Minnesota	2014	-	2014	-	2014	2014	2014	-	2014
Mississippi	-	-	-	-	-	-	-	-	-

Missouri	-	-	-	-	-	-	-	-	-
Montana	-	-	-	-	-	-	-	-	-
Nebraska	-	-	-	-	-	-	-	-	-
Nevada	-	-	-	-	-	-	-	-	-
New Hampshire	-	-	-	-	-	-	-	-	-
New Jersey	2013	2013	2013	-	-	2013	2013	2013	2013
New Mexico	2001	-	-	-	2001	2001	2007	-	-
New York	2006	2006	2014	2014	-	-	2011	2011	-
North Carolina	2013	2013	2013	-	2013	-	2013	-	-
North Dakota	-	-	-	-	-	-	-	-	-
Ohio	2014	2014	-	-	2014	2014	-	-	-
Oklahoma	2013	2013	-	-	-	-	-	-	-
Oregon	2013	2013	2013	-	-	-	-	-	-
Pennsylvania	2014	2014	2014	-	2014	2014	2014	-	2014
Rhode Island	2012	2014	2014	2014	-	-	2012	-	-
South Carolina	-	-	-	-	-	-	-	-	-
South Dakota	-	-	-	-	-	-	-	-	-
Tennessee	2014	2014	-	-	2014	2014	-	-	-
Texas	-	-	-	-	-	-	-	-	-
Utah	2014	2014	-	-	2014	2014	2014	-	-
Vermont	2013	2013	2014	2013	2013	2013	2013	2013	2013
Virginia	2013	-	2013	-	2013	2013	-	-	-
Washington	2010	2010	-	-	-	-	2010	-	-
West Virginia	-	-	-	-	-	-	-	-	-
Wisconsin	2014	2014	2014	2014	2014	2014	2014	-	-
Wyoming	-	-	-	-	-	-	-	-	-

Table S2. Are Prescription Drug Monitoring Program Laws Associated with Naloxone/Good Samaritan Laws?

	Naloxone and PDMP	Good Samaritan Law and PDMP
	P value	
2000	-	-
2001	0.58	-
2002	0.58	-
2003	0.40	-
2004	0.37	-
2005	0.61	-
2006	0.32	-
2007	0.48	0.28
2008	0.67	0.36
2009	0.19	0.46
2010	0.51	0.61
2011	0.69	0.91
2012	0.26	0.19
2013	0.46	0.84
2014	0.89	0.80

References

Ali, M. M., Dowd, W. N., Classen, T., Mutter, R., & Novak, S. P. (2017). Prescription drug monitoring programs, nonmedical use of prescription drugs, and heroin use: Evidence from the National Survey of Drug Use and Health. *Addictive behaviors,* 69, 65-77.

Wheeler, E., Jones, T. S., Gilbert, M. K., Davidson, P. J., Centers for Disease, C., & Prevention. (2015). Opioid Overdose Prevention Programs Providing Naloxone to Laypersons - United States, 2014. *MMWR Morb Mortal Wkly Rep,* 64(23), 631-635.