



Short Communication

Effect of pill mill laws on opioid overdose deaths in Ohio & Tennessee: A mixed-methods case study

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Pill mill laws impose strict regulations on pain management clinics to prevent them from issuing opioid prescriptions without medical indication. To date, little is known about the implementation or effects of these laws on opioid overdose deaths. A previously untested concern is that by restricting access to prescription opioids, pill mill laws could increase overdose from heroin and synthetic opioids, like illicitly produced fentanyl. We evaluated the effects of pill mill laws on opioid overdose deaths in Ohio and Tennessee. Of the 11 total U.S. states with pill mill laws, Ohio and Tennessee were the only two where: (1) the pill mill law was the only state law designed to curb opioid prescribing implemented in a two-year period, one-year pre/post law; and (2) high-quality drug-specific overdose death data were available from CDC. We conducted synthetic control analyses examining differences in post-pill mill law trends in overdose deaths in Ohio and Tennessee compared to weighted combinations of comparison states. We also conducted qualitative interviews with 11 leaders responsible for pill mill law implementation and enforcement in Ohio and Tennessee. Pill mill law enactment had no effects on overall, prescription opioid, heroin, or synthetic opioid overdose deaths in Ohio or Tennessee. Interview results suggest that both states engaged in robust enforcement and implementation of the law. A multi-pronged policy approach, including but not limited to pill mill laws, may be required to effectively address opioid overdose deaths.

1. Introduction

High volume of opioid prescribing is widely acknowledged as a key driver of the U.S. opioid crisis, in which over 275,000 people have died of overdose since 1999 (Volkow and McLellan, 2016). In recent years, the opioid crisis has shifted. From 1999 to 2013, most opioid overdose deaths were caused by prescription opioids; since 2014, the majority of deaths have been caused by non-prescription opioids like heroin and illicit fentanyl (Centers for Disease Control and Prevention, n.d.). Nonetheless, prescription opioids were involved in 40% of opioid overdose deaths in 2017 (Centers for Disease Control and Prevention, n.d.), and nearly 70% of people who use illicit opioids like heroin and fentanyl initiated their opioid use with a prescription opioid (Cicero et al., 2018).

Over the past decade states have enacted laws designed to curb

inappropriate prescribing, including prescription drug monitoring program (PDMP) laws and – the focus of this study – pill mill laws. Relative to PDMP laws, which have received extensive study (Finley et al., 2017), few studies have rigorously evaluated pill mill laws, which place strict regulations on pain management clinics with the goal of preventing ‘rogue’ clinics from dispensing opioids without medical indication (Rutkow et al., 2017). While no nationwide database exists, pill mills have been documented across the U.S. (Rutkow et al., 2017). Common pill mill law provisions include annual licensing requirements; limits on patient/prescriber ratios; and prohibition of on-site opioid dispensing (Rutkow et al., 2017).

Previous studies (Lyapustina et al., 2016; Rutkow et al., 2015) suggest that pill mill laws in Florida and Texas were associated with reductions in opioid prescribing and overdose death. However, the effects of Florida's pill mill law cannot be separated from the effects of the

Abbreviations: PDMP, Prescription Drug Monitoring Program; NAAG, National Association of Attorney Generals; MSPE, mean squared prediction error; CDC, Centers for Disease Control and Prevention

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PDMP, implemented in the same year (Rutkow et al., 2015), and the study of Texas's pill mill law (Lyapustina et al., 2016) did not include a comparison group. An untested concern is that pill mill laws may, by restricting access to prescription opioids, lead individuals with opioid addiction to transition from prescription opioid to heroin or synthetic opioid use, increasing heroin and synthetic opioid overdose deaths as a result (Pitt et al., 2018). No studies have explored the implementation or enforcement of pill mill laws.

Our objectives were to: (1) evaluate the effects of pill mill laws on overall, prescription opioid, heroin, and synthetic opioid overdose deaths; and (2) characterize the implementation and enforcement of pill mill laws using qualitative interviews.

2. Methods

2.1. Quantitative study

2.1.1. Approach & study design

We used the synthetic control method to compare overdose rates in Ohio and Tennessee before and after pill mill law implementation to overdose rates over the same time period in comparison states that did not implement the policy of interest (Abadie et al., 2010; Abadie et al., 2015). The synthetic control method compares outcomes after a law is enacted in a single intervention state to outcomes in a weighted combination of comparison states, or the “synthetic control.” In other words, to evaluate the effects of Ohio's pill mill law, this method combines data from eligible comparison states to create a “synthetic Ohio” with similar demographic characteristics and pre-law trends in opioid overdose deaths (Abadie et al., 2010; Abadie et al., 2015).

As of February 2019, 11 U.S. states have pill mill laws. For this study, we selected states meeting two criteria. First, a state had to implement a pill mill law and no other potentially confounding laws (see Appendix Table 1) designed to address opioid prescribing or overdose during a minimum of a two-year period, one year pre- and one-year post-law. Eight total potentially confounding laws included voluntary and mandatory PDMP laws, opioid prescribing cap laws, naloxone access laws, good Samaritan laws, physical exam laws, mandatory pharmacy ID laws, and doctor-shopping laws (McGinty et al., 2018; Kolodny et al., 2015). Second, a state had to report $\geq 80\%$ of drug-specific overdose deaths during the study period; many states significantly under-report this information (Rudd et al., 2016). Ohio and Tennessee were the only two states that met these criteria, Tennessee with a three-year study period (July 1, 2009–June 30, 2012, with pill mill law effective July 1, 2011) and Ohio with a four-year study period (January 1, 2010–December 31, 2013, with pill mill law effective January 1, 2012). Tennessee's study period ended in 2012 and was limited to three years because of that state's implementation of a potentially confounding mandatory PDMP law on January 1, 2013.

Control states (1) had no pill mill law; (2) reported $> 80\%$ of drug-specific overdose deaths during the study period; and (3) had the same opioid policy environment as the treatment state – with the exception of the pill mill law – for the entire study period. Both Ohio and Tennessee had voluntary PDMP (i.e., no required registration or use), physical exam, and doctor-shopping laws in place for their entire respective study periods; eligible control pool states had the same three laws, but no pill mill law or other potentially confounding laws, in place for the same periods. Control states for Ohio were Colorado, Iowa, Minnesota, New York, Nevada, Oklahoma, and Virginia. For Tennessee, control states included these same states, except Minnesota. Minnesota enacted a voluntary PDMP law on January 1, 2010, during Tennessee's study period. In contrast, Minnesota's voluntary PDMP law was in effect for the entirety of Ohio's study period and was therefore included in Ohio's control pool.

2.1.2. Data and measures

Data were set-up at the month level. The pill mill law measure was a

dichotomous measure that “turned on” from zero to one in the month the law went into effect. The outcome variable of interest was the rate of opioid overdose deaths per 100,000 state population. We used restricted CDC multiple cause of death data to identify the number of overall, heroin, prescription, and synthetic opioid overdoses. Overdose deaths in these categories were identified using an algorithm created by CDC (Rudd et al., 2016).

Covariates included time-varying annual measures of the state population's household median income; income inequality (Gini index), the proportion of the state population that was: female, black; Hispanic, aged 0–14, 15–29, 30–44, 45–59, or 60+; unemployed; living below the federal poverty level; covered by Medicaid; and whose educational attainment was categorized as no diploma, a high school diploma, some college, associate/bachelor degree, or a graduate degree. These measures were obtained from the American Community Survey (US Census Bureau, n.d.). We also accounted for the proportion of residents in rural areas, obtained from the 2010 U.S. census data (US Census Bureau, 2010), and number of physicians per state population, per year obtained from the Area Health Resource Files (Health Resources and Services Administration, 2014).

2.1.3. Analyses

The algorithm used to create the synthetic control has been described elsewhere (Abadie et al., 2010; Abadie et al., 2015). The vector of weights minimized the mean squared prediction error (MSPE) between the opioid overdose death rates and all covariates described above in Ohio and Tennessee, respectively, and the weighted vector of opioid overdose rates and the same covariates in the control pool states during the pre-law period. For more detail regarding synthetic control construction, see Appendix Table 2. Four out of six control states received nonzero weights to create the synthetic control for Ohio (Iowa = 0.058, Nevada = 0.183, New York = 0.594, Oklahoma = 0.166) and Tennessee (Iowa = 0.101, Nevada = 0.144, New York = 0.469, Oklahoma = 0.286).

Following Abadie et al. (2010) and Abadie et al. (2015), the “effect” of the pill mill law was measured as the post-law difference in opioid overdose deaths in a treatment state versus its synthetic control. We conducted a permutation-based test, also called a placebo or falsification test, similar to the Fischer exact test, in which the synthetic control analysis conducted for a given treatment state was repeated for all states in the control pool. To assess statistical significance, we calculated the proportion of control pool states with an estimated post-law “effect” on opioid overdose deaths that was as extreme or more extreme than the estimated effect in the treatment state (Abadie et al., 2010; Abadie et al., 2015). This proportion is comparable to and reported as a *p*-value. All analyses were performed using the STATA/IC version 14.2. synth package.

2.2. Qualitative study

2.2.1. Sample, recruitment, and instrument

We conducted semi-structured telephone interviews with key stakeholders involved in the implementation and enforcement of pill mill laws in Ohio and Tennessee, including state regulators, law enforcement leaders, and medical professional organization staff. Recruitment occurred in three steps: (1) contacting the person with primary responsibility for law implementation, (2) using National Association of Attorney Generals (NAAG) partners to identify additional stakeholders (purposive sampling), and (3) contacting individuals suggested by the previous stakeholder group (snowball sampling) (Miles et al., 1994). Potential interviewees were contacted with an email explaining the study's purpose and goals, followed by two follow-up emails (one week apart) for non-responders. Additional interviews were conducted until no new information was obtained (i.e., data saturation) (Strauss and Corbin, 1990).

Interviews were conducted by one study member over telephone

and were digitally recorded and transcribed. Oral consent was completed at the beginning of each interview. Interviews included questions focused on characterizing the perceptions, implementation, and enforcement of pill mill laws. Interviews lasted between 9 and 34 min (median:16 min).

Analysis. Interviews were coded using a combination inductive/deductive approach based on themes identified in the summary notes (Miles et al., 1994). Final organization and analysis of key themes was done using an iterative process.

3. Results

3.1. Descriptive statistics

In Ohio, the overall opioid overdose rate in the two-year pre-law period was 9.42 per 100,000, and in the post-law period was 12.1 per 100,000. In Tennessee, the opioid overdose death rate in the two-year pre-law period was 9.9 per 100,000, and in the post-law period was 11.2 per 100,000. Trends in the monthly opioid overdose death rate in Ohio and Tennessee as well as each control pool state are shown in Appendix Fig. 1.

3.2. Synthetic control results

Pill mill laws had no effect on rates of overall opioid overdose in Ohio ($p = 0.43$) or Tennessee ($p = 0.66$) (Fig. 1). Furthermore, there was no impact of pill mill laws on overdose rates for prescription opioids, synthetic opioids, and heroin (see Appendix Fig. 2). The low MSPE in both Ohio (0.128) and Tennessee (0.107) indicated good model fit (Abadie et al., 2010; Abadie et al., 2015).

3.3. Qualitative interview results

We initially contacted seventeen individuals for interviews, eight in Ohio and nine in Tennessee; interviews were completed with six stakeholders in Ohio and five in Tennessee, between February and August 2018 (Table 1). Interviewees in Ohio and Tennessee described fairly similar and robust implementation and enforcement of pill mill laws. In both states, agencies with medical expertise (State Board of Pharmacy and State Board of Medicine in Ohio and the Department of Health in Tennessee) were the primary implementers and enforcers of the law.

Interviewees in both states described dissemination of information – through publicizing and issuance of guidance – related to the legislation's implementation. Enforcement of pill mill laws in Ohio and Tennessee included both complaint- and investigation-based activities.

4. Discussion

Although both states reported robust enforcement and implementation, enactment of a pill mill law did not affect the rate of overdose deaths for any opioid category in Ohio or Tennessee. While we found no protective effects of the law, we also found no evidence suggesting that the law increased overdoses from heroin or synthetic opioids (Pitt et al., 2018). It is possible that pill mills were not significant contributors to opioid overdose deaths in Ohio or Tennessee during the time periods studied. Data on the number of pill mills operating in Ohio and Tennessee pre/post law implementation is not available, and enforcement data is also limited. Ohio reports issuing 15 disciplinary actions for violation of the state pill mill law during the 2010–2013 study period (Ohio State Board of Pharmacy, 2011); while Tennessee interviewees reported robust enforcement during the July 2009–June 2012 study period, the state did not begin tracking pill mill enforcement actions until 2013 (Smith and Hughes-Toombs, 2014). It is also possible that during the period studied Ohio and Tennessee residents increasingly initiated opioid use with heroin or illicitly produced synthetic opioids like fentanyl, a trend observed nationwide (Cicero et al., 2018) but for which state-specific data is not available.

Our study is limited to Ohio and Tennessee; effects of pill mill laws in other states may differ depending upon the scope of the pill mill problem, implementation, and enforcement in those states. The CDC restricted multiple cause of death data used in this study did not include decedent-level demographic information; our models used aggregate state-level demographic data consistent with the synthetic control approach (Abadie et al., 2010; Abadie et al., 2015). As a result, we were unable to stratify analyses by decedents' demographic characteristics. Finally, this study focuses on pill mill laws' effects on fatal opioid overdose. These laws' effects on other outcomes, such as non-fatal overdose and harms related to injection drug use (e.g., hepatitis C infection) need future study.

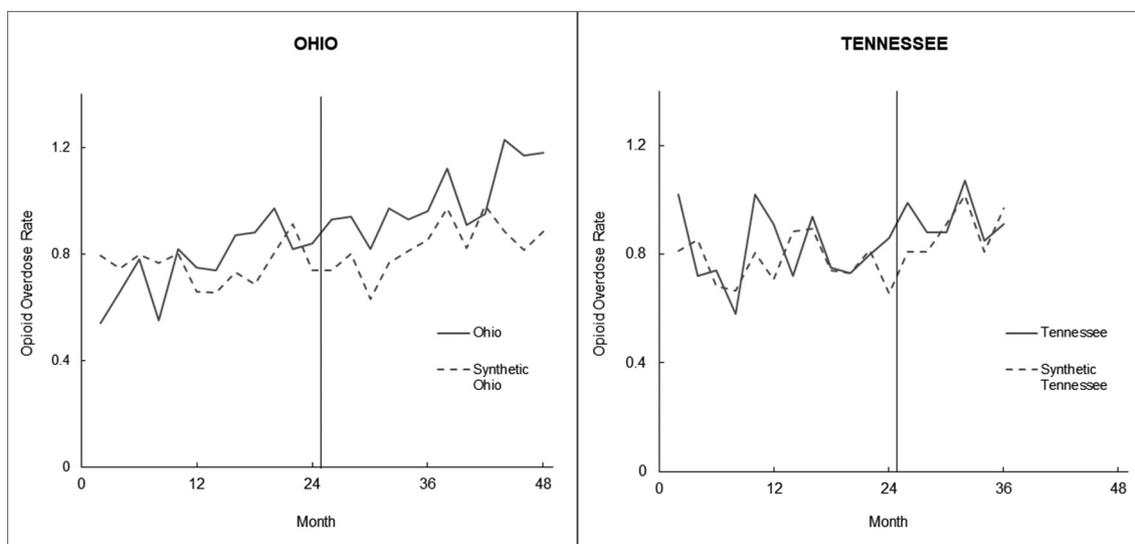


Fig. 1. Rates of Opioid Overdose Pre and Post Pill Mill Law in Ohio and Tennessee. Note. Differences in opioid overdose rates between the treatment state (solid line) and synthetic control (dashed line). The vertical line indicates when the pill mill law was enacted. For Ohio – RMSPE: 0.128, Law Enacted: 7/1/11, Study period: 7/1/09–6/30/13. For Tennessee – RMSPE: 0.107, Law enacted: 1/1/12, Study period: 1/1/10–12/31/12.

Table 1
Stakeholder perceptions of pill mill law implementation and enforcement in Ohio and Tennessee.

State	Implementation and Enforcement Activities During the Study period ^a	Illustrative quotations
Ohio (6 interviewees)	Implementation	
	<ul style="list-style-type: none"> – Licensing of pain management clinics by State Board of Pharmacy^b – Rulemaking for physician-owners of pain management clinics by State Medical Board[†] – Press conferences and announcements about law in conjunction with Governor's Cabinet Opiate Action Team (GCOAT) 	<p><i>"The pill mill bill really requires that the state board of pharmacy license pain management clinics and so that way we have a way to regulate them. Then as part of that, the state medical board of Ohio had to adopt rules that established standards for physicians who operated pain management clinics."</i> – OH-01</p> <p><i>"It was between two agencies so you had the med board and the pharm board that were working together. So you essentially had to have two separate independent administrative agencies signing off and in some essence double checking their work."</i> – OH-05</p>
	Enforcement	
	<ul style="list-style-type: none"> – Complaint- and investigation-based enforcement by State Board of Pharmacy (clinics) and State Medical Board (physicians)^b – Active mining of prescription drug monitoring program (PDMP) data by State Board of Pharmacy^b – Board of Pharmacy and State Medical Board coordinate with law enforcement agencies (e.g. Office of the Attorney General) when necessary^b 	<p><i>"So anytime someone submits an application [the board of pharmacy] can go in and inspect, which is different from other healthcare regulatory boards ... because [pain management clinics] are potentially high-risk entities we wanted to be able to regularly and practically inspect them."</i> – OH-02</p> <p><i>"[The board of pharmacy] has upwards of 40 actual field staff to do inspections... inspectors are specifically related to investigating drug diversion and inspecting facilities like pain management clinics, pharmacies, and hospitals."</i> – OH-02</p>
Tennessee (5 interviewees)	Implementation	
	<ul style="list-style-type: none"> – Rules promulgated by the Commissioner of the Department of Health with input from taskforce of licensing entity representatives^b – Department of Health disseminated guidance on regulation through website and other education efforts 	<p><i>"The legislature enacted it and the department of health was responsible to implement by licensing pain management facilities. They did get the word out to have these clinics licensed as pain management clinics, so a lot of the education was done from the department of health."</i> – TN-05</p> <p><i>"There was a taskforce formed of members of the board of medical examiners, osteopathic examination, board of nursing, and physician assistant committee ... that met and reviewed draft rules to give input from those licensing entities to the commissioner [of the department of health]."</i> – TN-01</p>
	Enforcement	
	<ul style="list-style-type: none"> – Complaint- and investigation-based enforcement by Department of Health^b – Tennessee Bureau of Investigations and Drug Enforcement Administration involvement for clinics operating outside of the scope of the law (i.e. unlicensed clinics) 	<p><i>"All of the clinics now have to, as they apply for a license, they have to have an inspection initially and then there's an inspection that occurs, it used to be purely random in the statute, but starting this past July, requires it to be once within the licensure renewal cycle."</i> – TN-01</p> <p><i>"The health-related boards have authority over [the pain management clinics]. They do have inspections and they do have investigators that go out and inspect."</i> –TN-03</p>

^a For Ohio, the study period was 7/1/09–6/30/13. For Tennessee, the study period was 1/1/10–12/31/12.

^b Indicates required by legislation.

5. Conclusion

Our study found no effects of pill mill laws on prescription opioid, heroin, or synthetic opioid overdose deaths in Ohio and Tennessee.

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Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ypmed.2019.05.024>.

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