Mitigating the Opioid Crisis: The Effect of Naloxone Access Laws (NALs) on Reducing Opioid Deaths

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Abstract: From 1999–2020, almost 500,00 people in the U.S. died from an opioid overdose, and opioid mortality is increasing overtime and is exacerbated by the COVID-19 pandemic. Originally, the rise in opioid mortality was caused by excessive opioid prescribing. Thus, to address this problem and save lives, states enacted laws to limit the prescribing of opioids. However, most opioid deaths are caused currently by synthetic opioids, particularly illegally made fentanyl. Since 2001, states have enacted naloxone access laws (NALs) to increase the access of naloxone, an opioid antagonist, to laypeople and save lives. However, there has been little research done on NALs' effectiveness of reducing opioid mortality, in addition to the existing literature being mixed. This paper analyzes the effect of NALs on drug and opioid mortality from 1999–2020 using a two-stage difference-in-differences analysis. The analysis reveals a large negative association between NALs and drug and opioid mortality. Further research is needed to assess whether this negative association is causal.

Introduction

The opioid crisis has continued disrupting communities and claiming lives since its origins in the 1990s caused by the increased prescribing of opioids (Centers for Disease Control and Prevention, 2021b). Opioids are pain-relieving drugs that interact with opioid receptors

(Centers for Disease Control and Prevention, 2021a). Examples include fentanyl, oxycodone, morphine, and hydrocodone. A fatal opioid overdose is when an excessive dosage of an opioid, or opioids plural for combined drugs, is taken that the resulting body poisoning leads to death. Federal and state government, along with nonprofits, businesses, and residents, have worked together to try and mitigate the consequences of the opioid crisis. For example, states have enacted laws to limit the prescribing of opioids, such as day and dosage limits. However, the number of opioid deaths in the U.S. is continuing to increase and is exacerbated by the COVID-19 pandemic, up 44 percent from 2019 to 2020. Because opioid mortality is increasing at a rapid rate, current policy actions must be evaluated to assess their effectiveness at decreasing opioid deaths. One current state policy that has not been thoroughly researched is naloxone access laws (NALs).

Naloxone is a medicine that reverses opioid overdose (Substance Abuse and Mental Health Services Administration, 2021). It is an opioid antagonist: it binds to opioid receptors and can reverse and block the effects of opioids. Naloxone is administered after a person takes a dosage of opioids and is currently showing signs of an opioid overdose. Signs of opioid overdose include slowing or stopping of breathing or heartbeat, discoloration of fingernails or lips, and vomiting. When naloxone is administered to a person who is overdosing on opioids, naloxone temporarily treats the person, so further medical help is still needed. However, naloxone buys the person experiencing an opioid overtime time to receive further medical help that can permanently stop and reverse the opioid overdose. Its effects can last anywhere from 30 to 90 minutes (National Council for Mental Wellbeing, n.d.). Naloxone can be administered in many different forms—intranasal spray, intramuscular, subcutaneous, or intravenous injection—meaning that non-medical personnel can administer naloxone (Substance Abuse and Mental

Health Services Administration, 2021). For example, family members of the opioid user or bystanders can administer naloxone and then call 911 to save someone's life. However, training is required to administer naloxone properly. This training includes how to identify someone who is possibly overdosing instead of being very high, how to safely administer naloxone, and how much naloxone to give, and this training can be conducted by practitioners, pharmacists, or advocacy groups.

Naloxone is also a prescription drug, meaning that a prescription is required to obtain naloxone (Davis, 2015). This prescription requirement is a barrier to accessing naloxone, especially for those most at risk of an opioid overdose. NALs are state regulations and statutes that increase access to naloxone. NALs vary greatly in how they increase access to naloxone, such as allowing for third party prescriptions or providing civil, criminal, and professional immunity to prescribers and dispensers. NALs were first enacted in April 2001 by New Mexico (Prescription Drug Abuse Policy System, 2022).

In this paper, I analyze whether a state having a NAL causes a reduction in drug and opioid deaths in the state, including measuring and quantifying the policy effect. Ideally, the specific types of NALs would also be analyzed to see if certain types are more effective than others. However, different types of NALs are enacted in the state at the same time, so measuring the impact of all of them separately is a methodological challenge. Thus, this paper will analyze only the effect of a state enacting their first NAL. The purpose of this paper is to educate policy makers on the impact of NALs on opioid deaths. Specifically, the research will identify whether NALs are effective at reducing opioid deaths and quantity the effect size, which will allow policy makers to conduct a more accurate cost-benefit analysis of NALs.

To conduct my analysis, I use time-series data from 1999–2020. The unit of analysis is county-year, and the data includes all counties and county equivalences, e.g., parishes, independent cities, boroughs, and census areas, in the fifty U.S. states and D.C. To quantity the effect sizes of NALs, I run two-stage difference-in-differences (DiD) analyses with two-way fixed effects (2FE) for county and year.

Review of the Literature

Because NALs are a relatively new policy intervention and vary drastically across states, as well as time, there has been little research done on their effectiveness of reducing opioid mortality. However, the existing literature on NALs' effect on mortality is mixed with literature finding a positive (Erfanian et al., 2019), negative (Abouk et al., 2019; McClellan et al., 2018; Rees et al., 2019), or no relationship (Doleac & Mukherjee, 2018) between NALs or a type of NALs and mortality. Even among studies that found a statistically significant decrease in opioid deaths, they have different effect sizes, with some variation explained by differences in NAL components and time period analyzed. Most studies are consistent with using a difference-in-differences (DiD) regression analysis to establish the relationship between NALs, or a specific NAL component, and mortality. This is a strength of the literature because quantitative analysis is better than qualitative analysis at establishing relationships and quantifying the effect size. Additionally, a DiD analysis helps establish relationships better than a basic regression because it mitigates extraneous variables and selection bias.

Literature Limitations

A major weakness of the research on NALs using a DiD framework is that every state enacted a NAL by the end of 2017 (Prescription Drug Abuse Policy System, 2022), meaning that the time period analyzed cannot extend beyond 2017 when analyzing the effect of a state having a NAL. This is because there would be no states to serve as counterfactuals for states that have NALs. In the literature, the most recent year analyzed is 2016. Not analyzing data after 2016 is problematic because the dispensing of naloxone experienced an eight-fold increase from the fourth quarter of 2015 to the second quarter of 2017, with 70 percent of this growth caused by the intranasal naloxone spray NARCAN (Freeman et al., 2018), which was approved by the FDA in November 2015 (*Narcan Nasal Spray*, 2016). NARCAN makes it easier for laypeople to administer naloxone because it requires significantly less training to administer as compared to other forms, such as an intravenous injection. Additionally, there might be another increase in naloxone dispensing because the FDA granted final approval of the first generic NARCAN in 2019 (*FDA Approves*, 2019), which might decrease the price of NARCAN and allow more people to afford and buy it.

Methodology

The research design for this paper uses time-series data from 1999–2020 for all fifty states and D.C. with a unit of analysis of county-year. The purpose of the research design is to quantity the effect NALs have on drug and opioid mortality, if any. My study seeks to fill the time gap in the literature by using a two-stage DiD regression, which was created by Gardner (2021). A two-stage DiD regression uses never treated units and yet to be treated units to estimate the control on which the treated units can be compared to. There is a large literature that shows that standard 2FE models that only have unit and time fixed effects can be problematic in settings with staggered treatment adoption or time-variant treatment effects (Athey & Imbens, 2022; Baker et al., 2022; Borusyak et al., 2022; de Chaisemartin & D'Haultfœuille, 2020; Goodman-Bacon, 2021; Imai & Kim, 2020; Sun & Abraham, 2021). Gardner's approach is one solution to these problems. With the two-stage DiD regression, I use 2FE for county and year to control for county-level differences and time effect in the regression analysis. Additionally, I run event studies to analyze whether there is a lag between when the law was enacted and when the policy effect occurred.

Data

Dependent Variables—Opioid Death Rate and Drug Death Rate

In my analysis, I run two different models for the two-stage DiD regression and event-study regression, one with opioid death rate as the dependent variable and another with drug death rate as the dependent variable. The variable opioid death rate is measured as the number of people who died from a fatal opioid overdose in a certain county for a certain year out of 10,000 residents. Data for opioid mortality come from the CDC restricted mortality files, which includes data on all deaths in the U.S. at the individual level (Centers for Disease Control and Prevention, 2016). In the data, opioid deaths are identified as having an International Classification of Diseases revision 10 (ICD-10) code of T40.0 (poisoning by opium), T40.1 (heroin), T40.2 (natural/semisynthetic opioids), T40.3 (methadone), T40.4 (synthetic opioids other than methadone), and T40.6 (other and unspecified narcotics) as immediate or contributory causes of death (Rudd et al., 2016). Thus, the total number of opioid deaths by county and year is a summation of the number of individuals who have at least one of these three ICD-10 codes as a contributing cause of death who resided in that specific county and died in that specific year.

The CDC mortality data are based on death certificates, so the cause and contributing causes of death are recorded by the medical examiner or coroner on the death certificate. However, the specific drug that caused the drug death is not always recorded. From 1999–2015, 23 percent of fatal overdoses did not specify a specific drug (Ruhm, 2018). Thus, opioid mortality is most likely underreported nationally. Ruhm (2018) estimates that opioid mortality is 21–35 percent higher than reported opioid mortality. These supposed underreported opioid deaths are included as drug deaths, so I use the drug death rate as an additional dependent variable in the regression analysis for robustness.

Independent Variable—NALs

Data on NALs come from the Prescription Drug Abuse Policy System (PDAPS) (Prescription Drug Abuse Policy System, 2022). PDAPS collected data on each state's and D.C.'s NALs across thirty-three indicators from January 1, 2001–January 1, 2022. The independent variable is a dichotomous variable representing whether the state has at least one currently effective NAL, as of January 1st of that year. This classification does not consider the type of NALs nor the future enactment of more NALs after the initial first law.

Results

Drug and Opioid Mortality Trends

U.S. drug mortality has continued to increase over the entire 1999–2020 time period (Fig. 1). In 1999, 16,849 Americans died of a drug death. In 2020, drug mortality was 91,799 deaths, more than four times the number of drug deaths in 1999. This increase has been steady over time with a 30 percent from 2019 to 2020, most likely caused by the pandemic. This brings the century total to 915,520 drug deaths. Within drug mortality, most of the deaths currently involve opioids, with 70 percent of the drug deaths in 2020 involving opioids (Fig. 2). However, this has been a recent development, as the percentage of drug deaths that involve opioids has increased since 1999. In 1999, only 24 percent of drug deaths involve opioids, the lowest during this period. In 2016, 50 percent was reached, meaning that one in two drug deaths involved opioids. In 2020, the percentage increased 7 percent from 2019 and reached a high of 70 percent. This increase in the percentage of drug deaths that involve opioids is caused by the increase in opioid mortality over this period. From 1999–2020, U.S. opioid mortality has followed a similar trend as drug mortality. Opioid mortality steadily increased from 4,030 deaths in 1999 to 64,306 deaths in 2020, almost 1,500 times more deaths than in 1999. Opioid mortality has steadily increased since 1999 with a substantial increase in 2016. From 2015 to 2016 and 2016 to 2017, opioid mortality increased by almost 1,000 deaths, a 44 and 23 percent increase, respectively. Another substantial increase in opioid mortality occurred in 2020, when opioid mortality increased from 44,624 deaths to 64,306 deaths from 2019 to 2020, a 44 percent increase. These patterns show that drug and opioid mortality are still increasing and are exacerbated by the pandemic.

Fig. 1: U.S. Drug and Opioid Mortality, 1999–2020

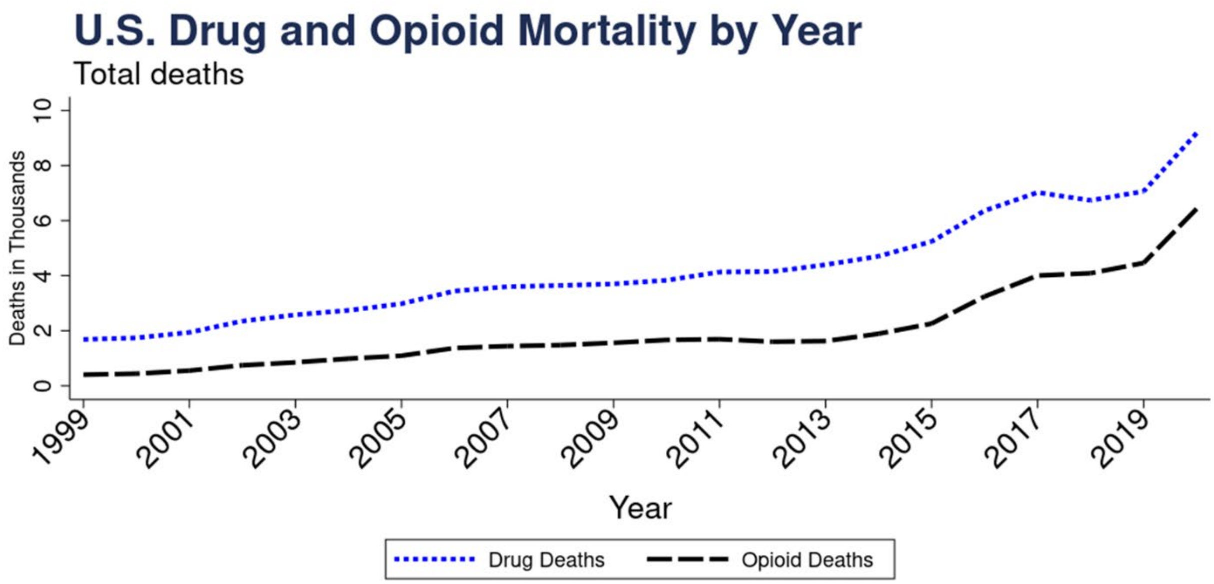
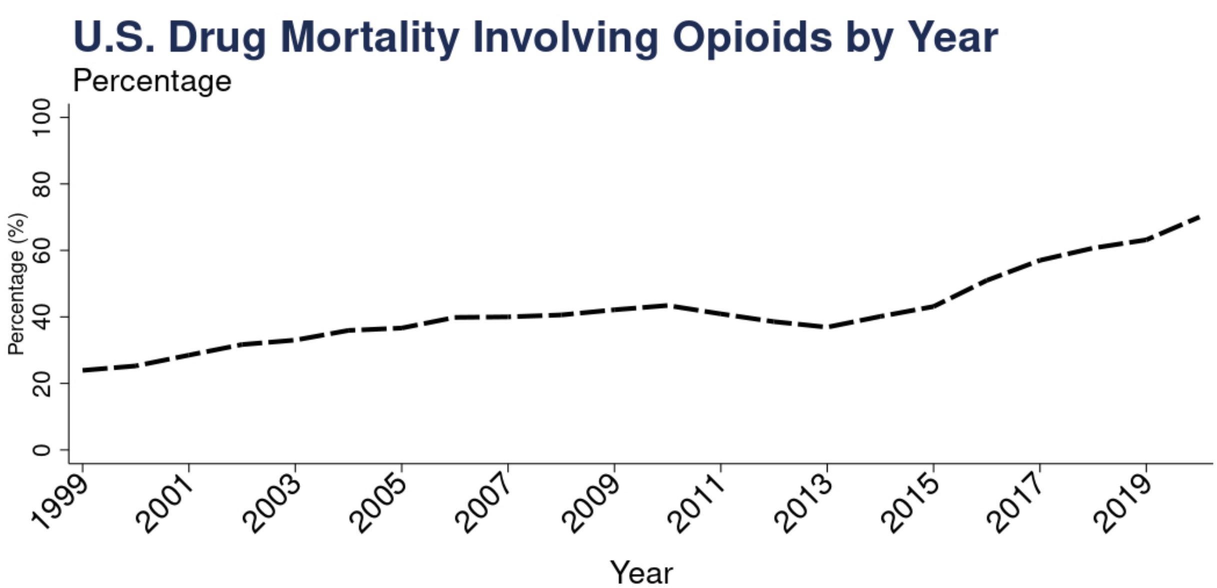


Fig. 2: Percentage of U.S. Drug Mortality Involving Opioids, 1999–2020



In the U.S., not every community, township, city, nor state is affected equally by the opioid crisis or drugs generally. Counties on the West Coast and in Arizona and New Mexico were hit the hardest and have the most drug deaths per capita in 1999 (Fig. 3). Alternatively, counties in the Appalachian Mountains and Northeast, as well as select counties in and surrounding New Mexico, have the most drug deaths per capita in 2020 (Fig. 5). The Appalachian Mountains is the worst hit area in 2020. The three counties with the highest drug deaths per capita in 2020 all reside in West Virginia—McDowell, Logan, and Summers county, respectively. Of the top ten worst counties, six counties are in West Virginia.

Fig. 3: Logged Number of Drug Deaths per 10,000 People by U.S. County, 1999

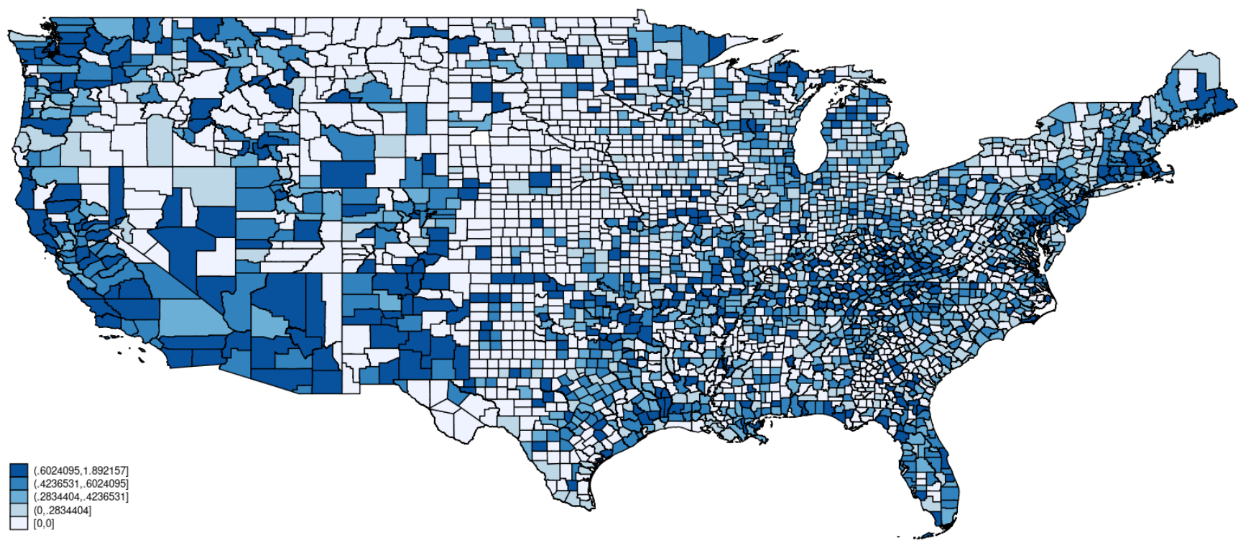


Fig. 4: Logged Number of Drug Deaths per 10,000 People by U.S. County, 1999

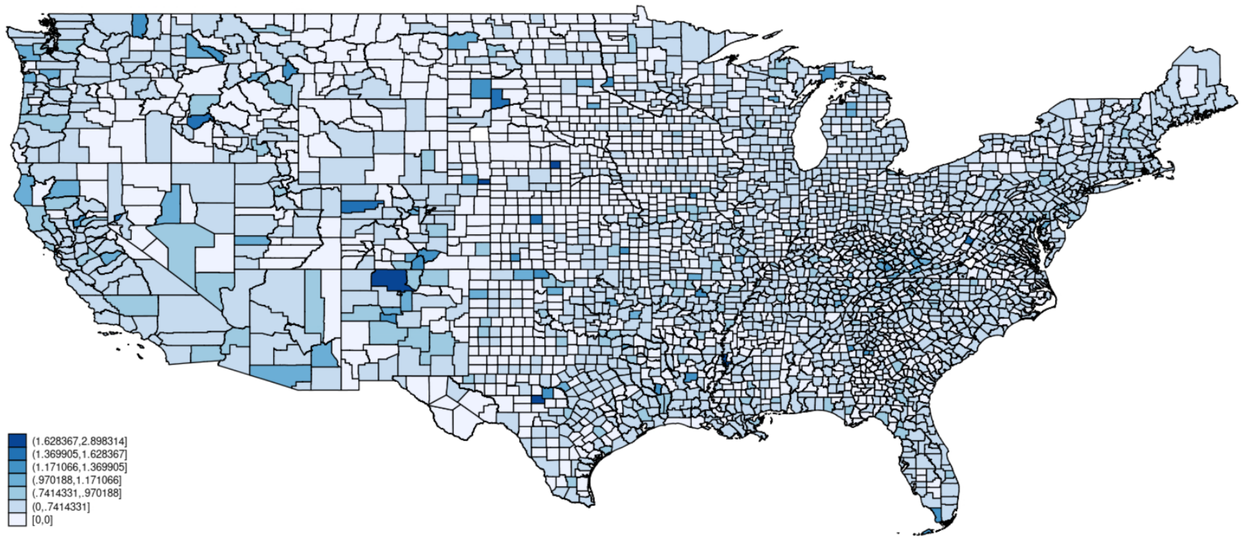
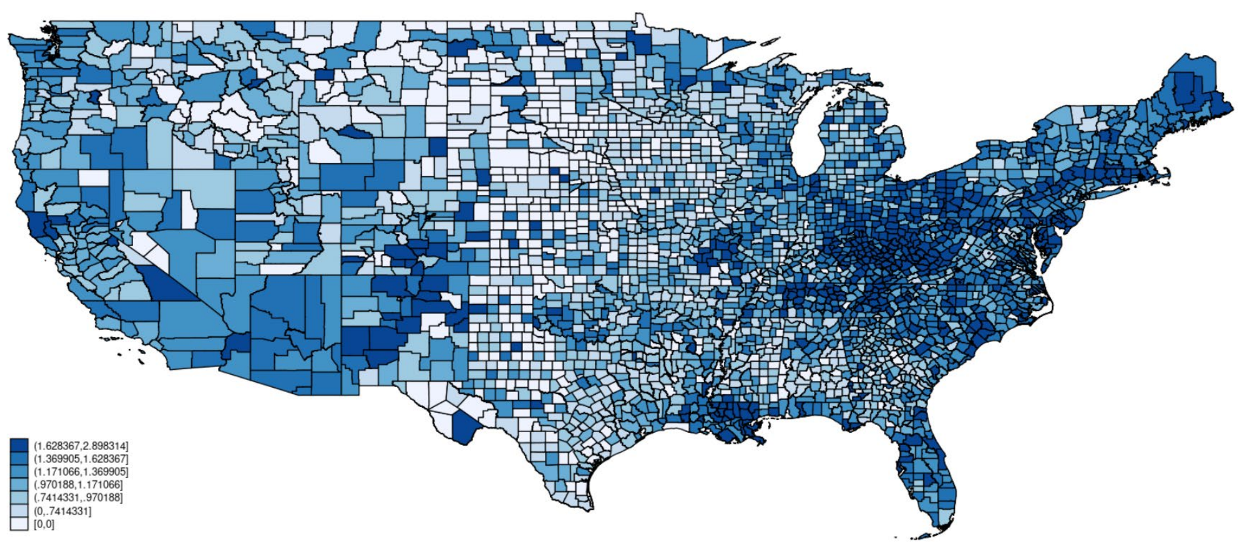


Fig. 5: Logged Number of Drug Deaths per 10,000 People by U.S. County, 2020



Effect of NALs on Drug and Opioid Mortality

The two-stage DiD regressions for the effect of NALs on drug and opioid mortality show the same trend; NALs are associated with an increase in both drug and opioid mortality (Table 1). Starting with opioid mortality, NALs are associated with a 0.698 increase in opioid deaths per

10,000 people or 128 percent increase in the mean opioid death rate. For drug mortality, NALs are associated with a 0.834 increase in drug deaths per 10,000 people or a 72 percent increase in the mean drug death rate.

Table 1: Two-Stage DiD Regressions of Effect of NALs

	Opioid Death Rate	Drug Death Rate
NAL	0.698^{***}	0.834^{***}
	(0.166)	(0.183)
N	69075	69075

Standard errors in parentheses
* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

The event studies show the same positive association from the two-stage DiD regressions (Figs. 6 and 7). Before NALs are implemented, the association of NALs on drug and opioid mortality is small and not statistically discernable from zero. However, after NALs are effective, the association of NALs on drug and opioid mortality increases considerably and is statistically discernable from zero. In one year, NALs are associated with a 0.636 increase in opioid deaths per 10,000 people or a 116 percent increase in the mean opioid death rate, as well as a 0.829 increase in drug deaths per 10,000 people or a 72 percent increase in the mean drug death rate.

In comparison to the mean, the association of NALs on drug and opioid mortality is staggering as NALs are associated with almost a doubling of the number of drug deaths and over a doubling of the number of opioid deaths in a county. These results question the effectiveness of NALs at reducing drug and opioid mortality by showing that NALs might substantially increase drug and opioid mortality. If NALs increase drug and opioid mortality, NALs must be repealed and replaced with new policy solutions to help combat the rising increase in drug and opioid mortality and save lives.

Fig. 6: Event-Study Regression of Effect of NALs on Opioid Death Rate

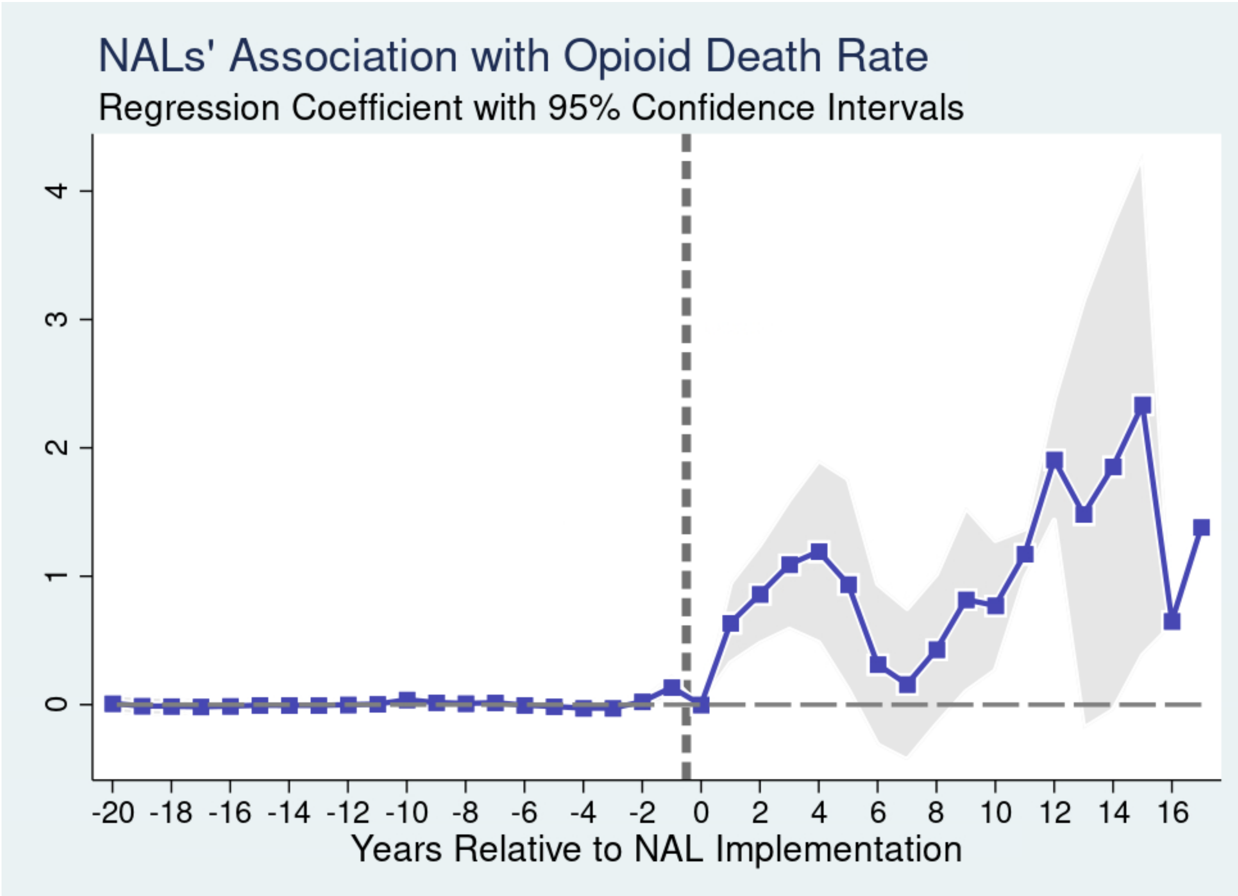
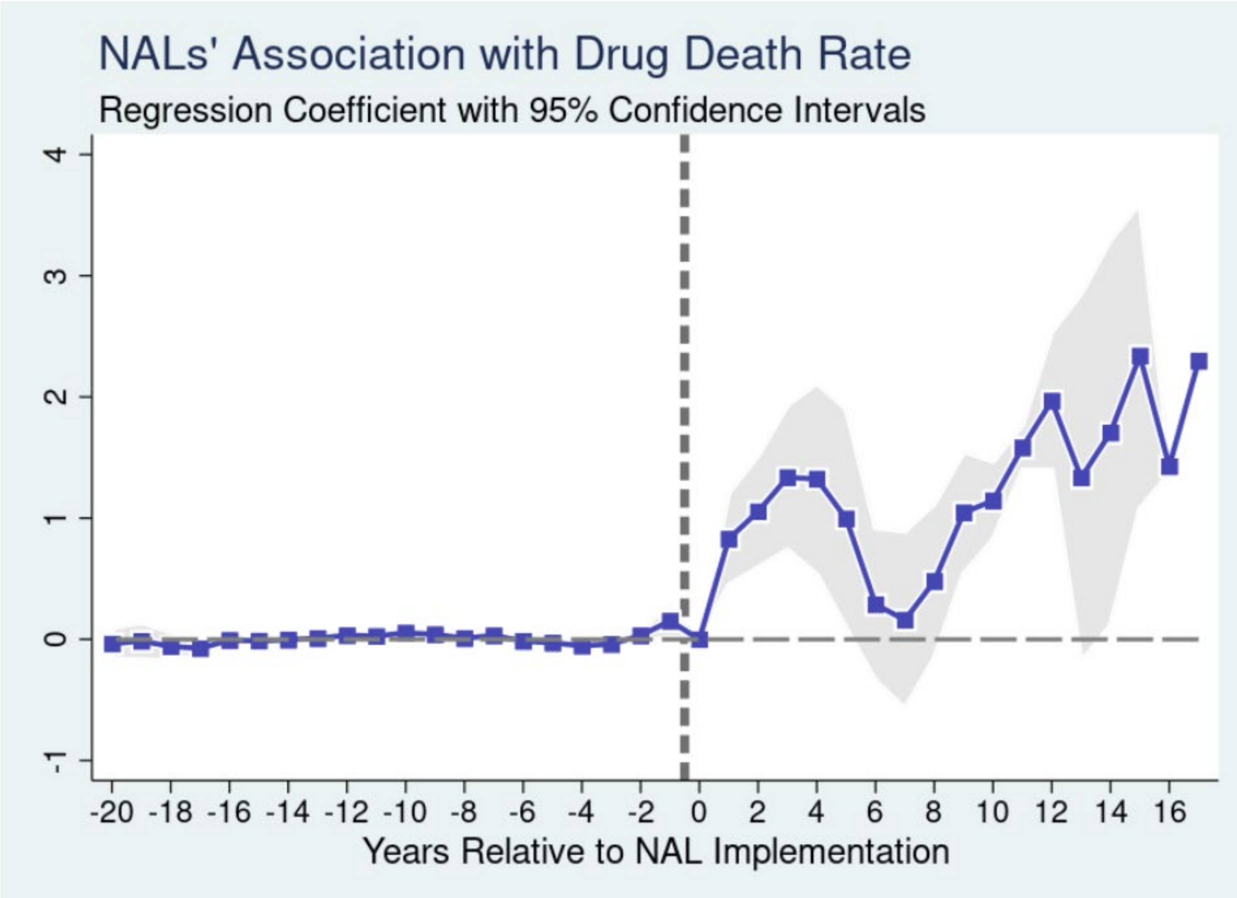


Fig. 7: Event-Study Regression of Effect of NALs on Drug Death Rate



<u>Limitations</u>

A major methodological limitation of this analysis is that the state adoption of NALs is not random. States that experience the most opioid deaths may implement NALs to reduce opioid mortality, while other states wait to implement NALs. Alternatively, other factors may affect the adoption of NALs, such as characteristics of the state legislature and geographical location. Thus, states that have not yet implemented NALs are not good counterfactuals, thus violating the parallel trends assumption of DiD analysis. Therefore, even though the two-stage DiD regressions show a statistically significant positive relationship between NALs and drug and opioid mortality, these results should not be used as evidence for causality. Rather, there is a positive association between NALs and drug and opioid mortality; states that implemented NALs experienced an increase in the drug and opioid mortality compared to states that did not implement NALs.

Conclusion

In this paper, I examine the effect NALs have on drug and opioid mortality using time-series data on all fifty states and D.C. over the span of 1999–2020. To estimate the relationship, I run two-stage DiD and event-study regressions with two-way fixed effects for county and year. A two-stage DiD regression was created by Gardner (2021) and uses never treated units and yet to be treated units to estimate the control on which the treated units can be compared to. There is a large literature that shows that standard two-way fixed effects models that only have unit and time fixed effects can be problematic in settings with staggered treatment adoption or time-variant treatment effects (Athey & Imbens, 2022; Baker et al., 2022; Borusyak et al., 2022; de Chaisemartin & D'Haultfœuille, 2020; Goodman-Bacon, 2021; Imai & Kim, 2020; Sun & Abraham, 2021). Gardner's approach is one solution to these problems.

The regressions reveal a positive relationship between NALs and drug and opioid mortality, meaning that NALs are associated with an increase in drug and opioid mortality. NALs are associated with a 0.698 increase in opioid deaths per 10,000 people or 128 percent increase in the mean opioid death rate. Additionally, NALs are associated with a 0.834 increase in drug deaths per 10,000 people or a 72 percent increase in the mean drug death rate. On its face, these results support that NALs encourage riskier opioid abuse behavior. Doleac and Mukherjee (2018) propose that increase naloxone access may unintentionally increase opioid abuse by reducing the risk of death per use, thus making riskier opioid use more appealing, and saving the lives of active drug users, who survive to continue abusing opioids. However, further research is needed to support this causal claim that NALs cause an increase in drug and opioid mortality because of the limitations of current DiD analyses. Most importantly, the adoption of NALs is not random, so states that have not yet implemented NALs are not good counterfactuals, which violates the parallel trends assumption DiD analysis.

In addition to further research investigating whether the found association is causal, further research is needed to explore the effect of NALs on subsets of opioid mortality, such as mortality caused by prescription opioids, synthetic opioids, natural opioids, or heroin. Also, future research should utilize a different time span in the analysis to find if the effect is consistent across the three waves of the opioid crisis. Because type or broadness of NALs were not considered in the analysis, future research is needed to explore the effect of different types of NALs, such as standing orders and prescriber and dispenser immunity, on opioid mortality.

Appendix

Fig. 1: NAL Policy Implementation Year by State

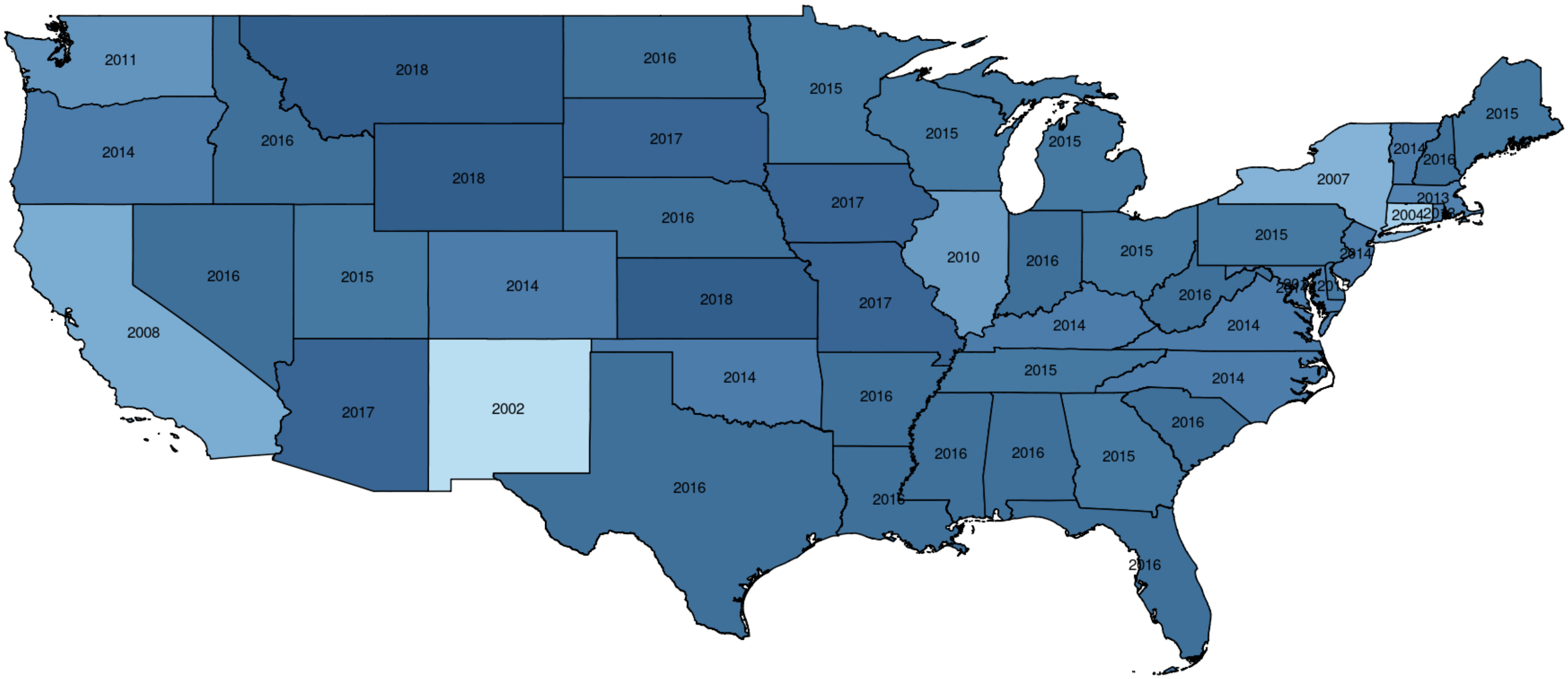


Table 1: NAL Policy Implementation Year by State

State	NAL Year
Alabama	2016
Alaska	2017
Arizona	2017
Arkansas	2016
California	2008
Colorado	2014
Connecticut	2004
Delaware	2015
District of Columbia	2014
Florida	2016
Georgia	2015
Hawaii	2017
Idaho	2016
Illinois	2010
Indiana	2016
Iowa	2017
Kansas	2018
Kentucky	2014
Louisiana	2016
Maine	2015
Maryland	2014
Massachusetts	2013
Michigan	2015
Minnesota	2015
Mississippi	2016
Missouri	2017
Montana	2018
Nebraska	2016
Nevada	2016
New Hampshire	2016
New Jersey	2014
New Mexico	2002
New York	2007
North Carolina	2014
North Dakota	2016
Ohio	2015
Oklahoma	2014
Oregon	2014
Pennsylvania	2015
Rhode Island	2013
South Carolina	2016
South Dakota	2017

State	NAL Year
Tennessee	2015
Texas	2016
Utah	2015
Vermont	2014
Virginia	2014
Washington	2011
West Virginia	2016
Wisconsin	2015
Wyoming	2018

Table 2: State NAL Policy Implementation by Year

NAL Year	State
2002	New Mexico
2004	Connecticut
2007	New York
2008	California
2010	Illinois
2011	Washington
2013	Massachusetts Rhode Island
2014	Colorado District of Columbia Kentucky Maryland New Jersey North Carolina Oklahoma Oregon Vermont Virginia
2015	Delaware Georgia Maine Michigan Minnesota Ohio Pennsylvania Tennessee Utah Wisconsin
2016	Alabama Arkansas Florida Idaho

NAL Year	State
	Indiana
	Louisiana
	Mississippi
	Nebraska
	Nevada
	New Hampshire
	North Dakota
	South Carolina
	Texas
	West Virginia
2017	Alaska
	Arizona
	Hawaii
	Iowa
	Missouri
	South Dakota
2018	Kansas
	Montana
	Wyoming

Table 3: Event-Study Regressions of Effect of NALs

Years Relative to NAL Implementation	Drug Death Rate	Opioid Death Rate
-20	-0.0362	0.00919
	(0.0657)	(0.0375)
-19	-0.0141	-0.00985
	(0.0770)	(0.0403)
-18	-0.0589	-0.0120
	(0.0603)	(0.0383)
-17	-0.0743**	-0.0164
	(0.0292)	(0.0215)
-16	-0.00765	-0.0111
	(0.0229)	(0.0144)
-15	-0.0123	-0.00438
	(0.0139)	(0.00901)
-14	-0.00372	-0.00487
	(0.0134)	(0.00660)
-13	0.00863	-0.00541
	(0.0183)	(0.0101)
-12	0.0333**	-0.000259
	(0.0161)	(0.00982)
-11	0.0259	0.00442
	(0.0178)	(0.0118)
-10	0.0535	0.0387
	(0.0343)	(0.0272)
-9	0.0403**	0.0170
	(0.0177)	(0.0142)
-8	0.00923	0.00960
	(0.0299)	(0.00929)
-7	0.0312	0.0158

Years Relative to NAL Implementation	Drug Death Rate	Opioid Death Rate
	(0.0229)	(0.0127)
-6	-0.0144	-0.00386
	(0.0223)	(0.0104)
-5	-0.0293***	-0.0141
	(0.0114)	(0.00960)
-4	-0.0533***	-0.0271***
	(0.0129)	(0.00787)
-3	-0.0390**	-0.0272**
	(0.0169)	(0.0124)
-2	0.0312	0.0237
	(0.0241)	(0.0170)
-1	0.152**	0.134***
	(0.0688)	(0.0506)
1	0.829***	0.636***
	(0.190)	(0.156)
2	1.055***	0.861***
	(0.231)	(0.192)
3	1.335***	1.092***
	(0.298)	(0.252)
4	1.323***	1.194***
	(0.394)	(0.354)
5	0.996**	0.937**
	(0.453)	(0.409)
6	0.288	0.314
	(0.316)	(0.313)
7	0.160	0.159
	(0.365)	(0.294)
8	0.479	0.430

Years Relative to NAL Implementation	Drug Death Rate	Opioid Death Rate
	(0.319)	(0.292)
9	1.046***	0.819**
	(0.251)	(0.358)
10	1.144***	0.772***
	(0.162)	(0.253)
11	1.582***	1.174***
	(0.0930)	(0.0976)
12	1.967***	1.908***
	(0.285)	(0.235)
13	1.333*	1.483*
	(0.759)	(0.831)
14	1.706**	1.855**
	(0.793)	(0.946)
15	2.340***	2.337**
	(0.629)	(0.972)
16	1.428***	0.650***
	(0.0325)	(0.0162)
17	2.298***	1.382***
	(0.0325)	(0.0162)
N	69075	69075

Standard errors in parentheses
* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

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