Epidemic: An Analysis of the Regulatory and Socioeconomic Factors of the Opioid Crisis

by

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Abstract:

The United States is facing one of the greatest public health emergencies in the history of the nation. This study uses state-level opioid overdose data from the Center for Disease Control's Multiple Causes of Death Data in order to determine what regulatory, legal, and socioeconomic factors are associated with overdose deaths in the United States from 2006 – 2015. The major finding is that when accounting for the cultural and regional differences between each state using fixed effects, we see that there is no broad regulation, law, or social factor that explains the variance in overdose deaths.

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Finally, I would like to dedicate this paper for all of those who have lost their lives to the battle against opioid addiction and those who are still fighting that battle to this day.

Introduction:

In 1995 the FDA approved the usage of the opioid painkiller Oxycontin. Since then, the producer of that drug – Purdue Pharmaceuticals – as well as numerous other major pharmaceutical companies have ramped up production, marketing, and sales of opioid painkillers. These companies were able to persuade doctors that their opioid painkillers were not addictive and that drugs like Oxycontin were safe to prescribe as painkillers.[1] According to the CDC, from 1999 to 2014, the number of opioid painkiller prescriptions nearly quadrupled. Around the same time period, from 1999 to 2015, the size of each patient's prescription rose from 180 MME to 640 MME, more than a three times increase.[2] Over time, opioids began to dominate the painkiller market with uses ranging from acute to chronic pain. Slowly, Americans began to become more and more addicted to prescription painkillers and other even more dangerous opioids – such as heroin and fentanyl. Drug addiction rates and overdose deaths have continued to increase from the early-2000s to the mid-2010s[3] and Exhibit A highlights how overdoses per 100,000 people has skyrocketed over the past decade. In 2016 alone there were nearly 64,000 deaths resulting from overdoses – more than those caused by car accidents.[4] The number of deaths is expected to continue to rise for 2017.

Despite the large jump in overdoses, the opioid drug epidemic went largely unnoticed. Throughout the early 2000s and into the 2010s, few people knew about what has become known as the "Opioid Epidemic". A simple Google-Hits Analysis (see Exhibit B) shows that up until

[1] Mettler, Katie. "OxyContin and our opioid crisis". *Washington Post,* Washington Post, 21 Feb. 2018, https://www.washingtonpost.com/graphics/2018/national/amp-stories/oxycontin-how-misleading-marketing-got-america-addicted/.
[2] Center for Disease Control. *Opioid Prescribing,* https://www.cdc.gov/vitalsigns/opioids/index.html.
[3] See Exhibit B
[4] Boudette, Neal. "US Traffic Deaths Rise for a Second Straight Year". *New York Times,* New York Times, 15 Feb. 2017, https://www.nytimes.com/2017/02/15/business/highway-traffic-safety.html.

2015[5], those very words had little to no searches. It wasn't until the 2016 election cycle, did presidential candidates like Hillary Clinton and Donald Trump bring opioid overdoses into the national spotlight. After the election, many states reacted to the epidemic by enacting new restrictions on opioid prescription sizes. Eventually, some states and counties even began to file lawsuits against the major pharmaceutical companies that produce opioid pain relievers. Over 40 states have subpoenaed and over a dozen cities / counties have filed lawsuits against the major players in the prescription opioid painkillers – including: Purdue Pharmaceuticals, Endo Health Solutions, Teva Pharmaceuticals. Johnson & Johnson, and Allegan.[6] These lawsuits aim to win damages for the public health crisis caused by opioids and harken back to the lawsuits against big tobacco during the late-90s. In the lawsuits against the big tobacco companies, state governments were able to reach the Master Settlement Agreement – which would help pay for some of the social costs that cigarettes cause. Similarly, with the recent opioid lawsuits, the plaintiffs – state and local governments – are trying to get these pharmaceutical companies to cover some of the public health costs that opioids have caused. Yet, the major difference between these two cases is that tobacco is not a prescription drug which means that the regulatory profile between tobacco and opioids are not comparable.

Today, this opioid epidemic has become one of the largest public health challenges that America has ever faced. Beyond suing the suppliers of prescription opioids, many states reacted by passing laws and implementing policies meant to slow down the spread of prescription opioid painkillers. Laws that are meant limit the size of prescriptions a single person can receive

[5] See Exhibit A

[6] Whalen, Jeanne, and Sara Randazzo. "Opioid Painkiller Makers Seek to Dismiss State Lawsuit." *The Wall Street Journal*, Dow Jones & Company, 11 Sept. 2017, www.wsj.com/articles/opioid-painkiller-makers-seek-to-dismiss-state-lawsuit-1505169867.

debuted in Massachusetts in 2016 – with 30 of such bills considered in 2016 and 2017.[7] However, the recent nature of this type of legislation makes it difficult for researchers to study the effectiveness of these regulations because of a lack of data. The general population was not alone in its ignorance of the looming epidemic – during the lead up to the opioid crisis there were few state laws being implemented that were meant to directly target prescription opioids. Some of the regulation that indirectly impacts opium overdoses includes the implementation of prescription drug monitoring programs (PDMPs) and Naloxone availability laws. In the past, researchers have focused on these types of programs when it comes to determining the factors that drive opioid overdose.

More recently, at the federal level, President Trump declared the epidemic a 'public health emergency' in late October of 2017.[8] Talks have even begun in Congress with the hopes of creating a framework for a national approach to addressing the epidemic that has spread to much of the nation. Given the high financial costs – nearly $500 billion a year according to some estimates[9] - and the large death toll it Congress is eager to try to implement some sort of national solution. Senator Elizabeth Warren has even called for a large federal response – similar to the one directed at the AIDs epidemic – in order to slow the increases in opioid related overdose deaths.[10] Yet, this begs the question: are there certain policies, regulations, or social conditions that are universally effective in preventing overdose deaths? For many policymakers the answer to this question lies in dealing with the epidemic as a public health issue. They call for increasing

[7] National Conference of State Legislatures. *Prescribing Policies: States Confront Opioid Overdose Epidemic,* 5 Apr. 2018, http://www.ncsl.org/research/health/prescribing-policies-states-confront-opioid-overdose-epidemic.aspx.
[8]Davis, Julie Hirschfeld. "Trump Declares Opioid Crisis a 'Health Emergency' but Requests No Funds." *The New York Times,* The New York Times, 26 Oct. 2017, www.nytimes.com/2017/10/26/us/politics/trump-opioid-crisis.html.
[9] The Council of Economic Advisors, *The Underestimated Cost of the Opioid Crisis,* Nov. 2018, https://www.whitehouse.gov/sites/whitehouse.gov/files/images/The%20Underestimated%20Cost%20of%20the%20Opioid%20Crisis.pdf.
[10] LeBlanc, Steve. "Warren calls for new federal approach to opioid crisis." *The Washington Times,* The Washington Times, 6 Apr. 2018, https://www.washingtontimes.com/news/2018/apr/6/warren-to-call-for-new-federal-approach-to-opioid-/.

treatment and rehabilitation programs covered by government healthcare. On the other side of the aisle, lawmakers have also cited public health programs such as Medicaid as a contributory factor to the rise in overdoses since it gives the opportunity for people to get prescriptions for opioids. They want to treat the problem as a law and order issue and address it with better policing.

From the academic standpoint, some economists have labeled opioid overdoses as 'deaths of despair' (Case and Deaton, 2015)[11] and cite the epidemic as a result of the decline in economic and social wellbeing. They attribute the overall declines in life expectancies of poorer educated non-Hispanic white Americans to drug overdoses – as well as alcohol and suicides. Taking a look at a heat map of overdoses in 2015 in Exhibit C, we can see that the issue main affects areas in the 'rust belt' – which has been hit especially hard by globalization and the 2008 economic recession.[12] The deaths of despair explanation seems to fit well into the narrative of a declining opportunities in Appalachia and in some parts of the Midwest – leading people to turn to drugs and alcohol. There could exist some kind of connection to the rising number of opioid overdoses and the decline in economic wellbeing in some parts of the United States. However, other economists argue that after running statistical analysis on county level overdose data (Ruhm, 2018)[13] that the main contributory factors are related to drug usage in generals. They argue that the economic explanation – though appealing – overlooks factors that lead to an increase in drug usage. Similar to the divide amongst policymakers, this disagreement between academics lies in their perspective on how to view the opioid epidemic.

[11] Case A, Deaton A. *Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century*. Proc Natl Acad Sci 2015;112:15078–83.
[12] See Exhibit C
[13] Ruhm C. *Deaths of Despair or Drug Problems?* National Bureau of Economic Research 2018: 24188. *(2018)*

Although many social scientists and economists have addressed portions of the opioid epidemic in their research – including PDMPs (Finklea, Sacco, Bagalman 2014; Rutkow, Chang, Daubresse, et al., 2015)[14][15] Medical Marijuana laws (Bachhuber, Saloner, Cunningham, et. al 2014; Powell, Pacula, Jacobson, 2015)[16][17], and economic despair (Case and Deaton, 2015)[18] – there has not been much research looking at a compilation of factors affecting the epidemic. At the same time there is a divide within the academic community and among politicians based on which perspective the opioid overdose epidemic should be looked upon. This paper will examine how to bridge that divide. By looking at state-level opioid overdose death data against a wide array of regulatory and socioeconomic factors, this paper will try to pinpoint whether the opioid epidemic is more of a regulatory issue or a socioeconomic one.

<u>The Data and Variables:</u>

<u>Quantifying the Magnitude of the Epidemic:</u>

When analyzing the opioid epidemic, overdose deaths is the figure that is most likely to be brought up. For this paper, data concerning opioid overdose deaths was collected from each of the fifty states and the District of Columbia for the 2006 – 2015 time period. The CDC tracks the causes of deaths on the deaths certificates of all residents in the United States on its *CDC*

[14] Finklea K, Bagalman, E, Sacco L. *Prescription Drug Monitoring Programs.* Journal of Dug Addiction, Education, and Eradication 2012. 143-164. *(2012)*
[15] Rutkow L, Chang H, Daubresse M, et al. *Effect of Florida's Prescription Drug Monitoring Program and Pill Mill Laws on Opioid Prescribing Use.* https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2429105. *(2014)*
[16] Bachhuber M, Saloner B, Cunningham C, et al. *Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States* . JAMA Intern Med. 2014;174(10):1668-1673. doi:10.1001/jamainternmed.2014.4005
[17] Powell D, Pacula RL, Jacobson M. *Do medical marijuana laws reduce addictions and deaths related to pain killers?* J Health Econ. 2018 Mar;58:29-42. doi: 10.1016/j.jhealeco.2017.12.007. Epub 2018 Feb 3.
[18] Case A, Deaton A. *Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century*. Proc Natl Acad Sci 2015;112:15078–83.

Wonder Multiple Causes of Death application.[19] The deaths are classified under the International Statistical Classification of Disease and Related Health Problems (ICD-10) codes. For all opioid overdoses the corresponding ICD-10 codes are T40.0, T40.1, T40.2, T40.3, T40.4, and T-40.6. This list includes overdose deaths related to drugs including: opium, heroin, 'other opioids', methadone, 'other synthetic narcotics', and 'other unspecified narcotics'. From here, deaths can be converted into deaths per 100,000 people in order to achieve a mortality rate which is comparable across states regardless of population size. This results in a set of cross sectional data set of overdose deaths across the United States over the 1999 – 2006 period.

Factors that Affect Drug Market Dynamics:

Despite their deadly and illegal nature opioids, can be analyzed from an economic perspective like any other good. In any market, there are supply and demand factors that drive production and consumption, and that is no different in the market for opioids. There could be a direct connection between the strength of the opioid market and the number of opioid deaths. Some economists argue that this connection along with the increasing strength of the market for opioids is what is driving the overdose crisis in the United States. At a high level, their argument is that the more opioids that the more opioids that a user consumes, the greater the likelihood that the user would eventually overdose.

When examining the opioid market from the supply side we can analyze the factors that affect the impact the number of opioids in the market. The CDC has compiled state-level prescription data of opioids taken from the *QuintilesIMS Transactional Data Warehouse (TDW).* This database tracks approximately 59,000 retail pharmacies which dispense around 88% of all

[19] "CDC WONDER." *Centers for Disease Control and Prevention,* Centers for Disease Control and Prevention, wonder.cdc.gov/.

retail prescriptions for the US. From here, the CDC uses census population data in order calculate a prescribing rate per 100 people.[20] This number is then multiplied by 1,000 in order to calculate the rate per 100,000 population – so that the data is at an apples to apples basis with the overdose data collected. This prescribing rate data for each of the 50 states and the District of Columbia was then compiled for the 2006 – 2015 testing period.

A common practice in the prescription opioids market is ‘double dipping’, or going to multiple doctors to get a prescription for opioids from each. The amount of prescriptions in places like Williamson, West Virginia – where there are enough opioids prescribed so that each resident could have a supply of 6,500 pills – highlights this problem. A regulatory initiative which could decrease the supply of opioids to these ‘double dippers’ is through the implementation of a Prescription Drug Monitoring Program (PDMP). These programs essentially allow doctors to view the prescribing history of their patients which could prevent those who have already received prescriptions for opioid painkillers from getting another one. The problem with this sort of qualitative legislative data is how to apply it to a quantitative statistical analysis. A ‘dummy variable’ – which is a binary variable (1 being yes, the law exists and 0 being no, the law does not exist) – must then be used which can be ‘toggled on’ whenever a certain institutes a PDMP. From here we can quantify this sort of legislative data for our own uses. The PDMP data was compiled from the Prescription Drug Monitoring Program Training and Technical Assistance Center. Economists have already looked at the effectiveness of these monitoring programs (Rutkow, Chang, Daubresse, et al., 2015) specifically within the state of Florida. Their study found that there was some decreases in the supply of opioids in Florida attributable to the

[20] Center for Disease Control, *US Prescribing Rate Maps, https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html.*

implementation of a PDMP.[21] In this paper rather than focusing on a specific state, PDMP effectiveness will be analyzed across the United States.

This paper will not address state limitations on the amount of opioids a single person can be prescribed, due to the fact that there is not enough historical data to conduct accurate statistical analyses on their effectiveness. Since these laws debuted in 2016 and this study will focus on overdoses from 2006 – 2015 there is no overlap between our analysis on the new prescription limitation laws. Thus, even though limits on days prescriptions per patient could move the needle when it comes to overdose deaths, this variable will be ignored in this paper. However, this set of regulations could be analyzed in a future paper as a potential deterrent to opioid overdoses once more data is compiled.

On the other side of the economic equation, when we think about the demand for opioids if we assume that opioids are a normal good we can then extrapolate that with a decrease in income there would be a decrease in demand. From here we can take a proxy for state level income which also can be compared across varying population – gross domestic product (GDP) spending per 100,000 population. Assuming that opioids are a normal good, some predict that the higher the GDP per 100,000 population in a state the higher the demand / consumption of opioids. Many people would argue that drugs that are as addictive as opioids have inelastic demand – which is broadly supported by academic literature on drug usage.[22] However, others may counter that drugs probably are not perfectly inelastic and thus there would still be some sort of demand side effect with regards to income shifts. State level GDP data during the testing

[21] Rutkow L, Chang H, Daubresse M, et al. *Effect of Florida's Prescription Drug Monitoring Program and Pill Mill Laws on Opioid Prescribing Use.* https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2429105. *(2014)*
[22] National Drug Research Council. *Assessment of Two Cost-Effectiveness Studies on Cocaine Control Policy.* Washington (DC): National Academies Press (US) ISBN-10: 0-309-06477-5. *(1999)*

period was compile from the Bureau of Economic Analysis.[23] From here Census data on state populations was used in order to calculate GDP per 100,000 population.

When thinking about demand for any good another factor to consider are substitute goods. The presence of a substitute painkiller would impact opioid demand. From a microeconomics standpoint the more of this substitute is available the fewer opioids would be consumed. Recently, medical marijuana has been considered as a potential alternative painkiller. Some biotechnology firms have even started going through the FDA approval process with their marijuana base painkillers. Potentially, medical cannabis could be a substitute and the varying legality across states makes medical marijuana legislation an interesting test variable. As with prescription drug monitoring programs a dummy variable will be utilized with medical marijuana laws. After testing the relationship between medical marijuana laws and opioid overdoses, academics conclude that at a national level such laws do not have a significant impact on overdoses (Powell, Pacula, Jacobson, 2015).[24]

Factors that Affect Socioeconomic Dynamics:

Beyond the market for prescription painkillers, another set of factors that would directly affect overdose deaths include the policies meant to curb overdoses and reduce addiction. One specific example is the drug Naloxone, which is a drug that can immediately stop overdoses. Yet, despite the effectiveness of this drug in combating overdoses up until even 2016 several states lacked Naloxone Access Laws. These laws allowed non-medical personnel to get access to Naloxone and thus administer it to prevent an overdose. The state level variation of the

[23] Bureau of Economic Analysis, *Regional Economic Accounts, https://www.bea.gov/regional/downloadzip.cfm.*
[24] Powell D, Pacula RL, Jacobson M. *Do medical marijuana laws reduce addictions and deaths related to pain killers?* J Health Econ. 2018 Mar;58:29-42. doi: 10.1016/j.jhealeco.2017.12.007. Epub 2018 Feb 3.

implementation of this legislation could have potentially impacted the number of overdose deaths. Using *Prescription Drug Abuse Policy System* which tracks when Naloxone Access laws were passed across the 50 states and the District of Columbia, a dummy variable could be set up for these laws and applied to our statistical analysis.[25] From a regulatory standpoint the government could also prevent overdoses by promoting the reporting of these events to the proper authorities. Once reported, professional emergency medical attention could be administered to potentially prevent death. One set of laws meant to accomplish this goal is known as 'Good Samaritan Laws'. These laws safeguard those who administer medical treatment to someone overdosing or those who report overdoses from liability and reduces possible legal punishment. The Network for Public Health Law compiled a database on state Good Samaritan Laws, and this was also converted into dummy variable form to fit the statistical analysis.[26]

The opioid epidemic could also be approached from a public health standpoint. Many argue that the best way to end the crisis is through more effective drug rehabilitation programs. Due to the strong withdrawal symptoms that opioid addicts deal with whenever trying to quit their addiction, many patients end up relapsing during the rehabilitation process. A treatment program that is said to be effective in preventing this is known as methadone detoxification. In this treatment regimen, methadone or buprenorphine is given to patients as an alternative to heroin or prescription opioids so that that person can slowly detox and ween off of opium. The Substance Abuse and Mental Health Data Archive conducted surveys of rehabilitation and treatment facilities across each state and the District of Columbia in order to determine if they

[25] Prescription Drug Abuse Policy System. *Naloxone Overdose Prevention Laws*, 1 Jul. 2017, http://pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139.

[26] The Network for Public Health Law, *Leal Interventions to Reduce Overdose Mortality: Naloxone Access and Overdose Good Samaritan Laws.*

provided methadone or buprenorphine treatment programs. Using the yes responses in each state as a proxy for the general availability of these types of treatment programs in the state, these results were then converted into aggregate per 100,000 population data. However, since the survey stopped being conducted after 2011, the 2011 ratio per 100,000 population was assumed to have held constant through the rest of the testing period.

Beyond rehabilitation programs, general public health investment arguably has an impact on opioid overdoses. For instance, certain states may have better hospitals due to higher public health investment in drug treatment programs. State level Medicaid expenditures will be used as a proxy for public health. The rationale behind using this variable is that since Medicaid is meant to improve the populations' access to healthcare, it should reflect the level of investment in public health initiatives. The National Association of State Budget Officers tracks state-level Medicaid spending during the 2006 – 2015 time period.[27] This expenditure data was then converted into millions of dollars of spending per 100,000 population so that it could be comparable with the other variables in the analysis. Intuitively a greater investment in public health would correlate with a lower number of opioid overdoses. However, increasing access to healthcare could actually be detrimental when it comes to the opioid epidemic because opioid painkillers are prescribed as medication. Potentially, people who would never have been prescribed opioids would get prescriptions due to their access to healthcare.

Another set of socioeconomic factors to consider is associated with law and order. Since opioids are an illegal substance, one view on how to reduce consumption is to increase punishment for opioid related crimes. The economic model for crime created by Gary Becker

[27] National Association of State Budget Officers, *Archive of State Expenditure Report,* https://www.nasbo.org/mainsite/reports-data/state-expenditure-report/state-expenditure-archives.

includes a variable for potential punishment for committing crime. (Becker, 1974)[28] Essentially, the more likely someone is to receive a penalty for a crime the less likely one will commit such a crime because this penalty reduces the expected payout of the crime. For opioids, a user who is more likely to be caught and punished would be less likely to use opioids – leading to fewer opioid deaths. Therefore, a potential deterrent to opioid overdoses is stricter punishment and more investment in law and order. In order to test this, incarceration rate will be used as a proxy for these law enforcement factors. The Bureau of Justice statistics tracks state level incarceration data, which was converted into population per 100,000 for 2006 – 2015.

One last variable which was already touched upon in the discussion on opioid market factors which is also part of the socioeconomic dynamic is income. While income is a factor that affects the consumption of normal goods, it also plays into the narrative of "deaths of despair". For the latter, states with lower income would actually have higher opioid consumption and overdoses since those areas are presumably worse off economically. The populations in these states would then turn to drugs due to their economic despair. This actually contradicts the idea that opioids are normal goods and consumption and thus positively related to income. Instead, income from the standpoint of a socioeconomic factor would be negatively correlated with opioid overdose deaths.

At a high level, we can bucket the predictor variables into the socioeconomic factors and drug usage factors. Though, interestingly, there are some variable – such as income – that can even be bucketed into both categories. From the standpoint of the analysis, this split between the variables will not only allow for the deduction of which variables specifically have an impact on

[28] Becker G. *Crime and Punishment: An Economic Approach*, Essays in the Economics of Crime and Punishment, National Bureau of Economic Research 1974, ISBN: 0-87014-263-1.

opioid overdoses, but it also helps determine which categories of variables move the needle more when it comes to overdose deaths.

The Statistical Methodology:

To answer the major questions posed, this paper will focus on conducting statistical regression analysis on the cross sectional data that has been collected. This dataset encompasses 50 states in the United States as well as Washington DC during the 2006 – 2015 time period with the aforementioned variables.

Selecting a Dependent Variable:

The dependent variable for the regression analysis is the number of opioid deaths caused by drugs including: opium, heroin, ‘other opioids’, methadone, ‘other synthetic narcotics’, and ‘other unspecified narcotics’. The number of overdose deaths was chosen as the outcome variable of the regression because the analysis is meant to try to determine potential reasons could help explain the variation of overdoses across various states and periods of time.

Potentially the number of opioid deaths could have been further sorted into categories such as overdoses caused by heroin, opioid pain relievers, or non-synthetic opioid pain relievers. However, this kind of further bifurcation in order to run multiple regressions was not conducted because of the risk of type-II error. Sorting opioid deaths in general into numerous sub variables would increase the likelihood of a false acceptance of the null hypothesis. Ultimately, focusing on the broadest category of opioid overdoses will make the statistical analysis comprehensive while ensuring robustness.

The Fixed-Effects Regression:

One issue with testing cross-sectional data is omitted variable bias. This occurs when there are certain variables that are not accounted for, but are inherent within either the time period analyzed or the various samples being analyzed. These unaccounted for variations impact both sides of the regression. Utilizing a fixed effects regression could potentially mitigate this issue. Fixed effects works by creating a dummy variable for each sample that is fixed. This would then control for the variation between the samples. Theoretically, with the dataset in this paper either the individual state or the time period could be fixed through this technique.

For this analysis, the state is the variable that was fixed because each state may have unique characteristics that would impact the predictor variables as well the dependent variable. Fixed effects essentially reflects how much variation in opioid overdose death rates is caused by factors unique to each state – such as culture and regional differences. Using this statistical treatment will give each state its own coefficient. Once the fixed effects regression was run, the R-squared for the regression went from 0.3506 to 0.8286 – which reflects how the model is better fitted into the regression.

Addressing Endogeneity and the Two-Staged Lee Squared Regression:

For predictor variables, a possible issue when running regression analysis is endogeneity. Endogeneity is when the explanatory variable is correlated with both the dependent variable and the error term. When this occurs, there will be a circular causality between the independent and dependent variable where it is unknown whether the independent variable causes the dependent one or vice versa. The way to address endogeneity is through the usage of instrumental variables and a two-stage least square regression. Instrumental variables are those that are correlated with the explanatory variable, but not correlated with the error term. From here using any instrumental variables that have been collected a two-stage least squared (2SLS) regression is run.

Two-Stage Least Square Equation:

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots \beta_k x_k + u$$

$$x_1 = \pi_0 + \pi_1 z + \pi_2 x_2 + \ldots \pi_k x_k + v$$

This 2SLS regression will produce an adjusted variable, which allows multiple instrumental variables to be converted into a single instrument to be used in the regression analysis. The first stage uses instrumental variables and the original explanatory variable in order to create an adjusted variable. From here the second stage works like any regression, except instead of the original explanatory variable this adjusted variable – that factors in the instrumental variables – is used in its place.

Endogeneity could potentially occur with the inmates per 100,000 populations variable. Intuitively, since opioid usage is illegal, the states with more overdoses and usage would have more people going to jail for committing these offenses all else being equal. Thus, there would be a circularity loop of causality between the inmates per 100,000 population variable and the dependent variable. In order to deal with this endogeneity problem, the first step is to identify potential instrumental variables. The two that are going to be used are national security grants given to each state by the Department of Homeland Security (DHS) as well as state level transportation spending. The data for the first instrument was collected using data from the

Statistical Abstract of the United States and converted into grant spending per 100,000 population.[29] However, since data was only collected for the 2006 – 2010 period the 2010 ratio was assumed to be constant for the missing years of the analysis. The second variable – transportation / capital spending – was collected by the National Association of State Budge Officers. The data was converted into spending per 100,000 population. It is likely that neither of these variables are strongly correlated with opioid overdoses. However, intuitively they would be related potentially to law enforcement spending and thus the number of people who are in jail in a state. The next step would be to use the two instruments as well as jail variable to run the first stage of a two-stage least squares regression. Below, is the output for the first stage of the regression:

Two-Stage Least Squares Regression – Jail Variable

```
Call:
lm(formula = Jail ~ Transpo + Sec, data = pnl1)

Residuals:
    Min      1Q  Median      3Q     Max
-290.96 -103.38  -10.68   74.26  473.91

Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept) 457.37455   15.38477  29.729  < 2e-16 ***
Transpo       0.54754    0.21488   2.548   0.0111 *
Sec          -0.11583    0.02781  -4.165 3.67e-05 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

The key takeaway is that since both transportation spending and national security grants allocated are significant these two are viable instruments for the jail variable. From here an

[29] United States Census Bureau, *Statistical Abstracts of the United States, https://www.census.gov/library/publications/time-series/statistical_abstracts.html.*

adjusted jail variable was created. This adjusted variable can then be used in the statistical analysis in order to mitigate the endogeneity issue.

Results:

After running the various statistical analyses, the results of the regressions that are run have been outputted in Exhibit D. The analysis highlights that in the clean regression – without 2SLS or fixed effects treatment – there are numerous significant variables that help explain the variation in overdose deaths. With the clean regression some of the variables aligned with their initial predictions. For instance, for the jail variable for every 1 increase in the incarceration per 100,000 there was a .001 decrease in overdoses per 100,000 population. One interpretation of this result is that every additional 100,000 people that are incarcerated results in 100 fewer overdoses. Another variable that somewhat aligned with the predictions is GDP. For this variable for every 1 increase in GDP per 100,000 population there was a .0007 increase in overdoses. With the prescription rate variable there was a positive relationship with opioid overdoses – aligning with the prediction that opioid market supply increases overdoses. Increases in Medicaid spending per 100,000 population predicted increases in opioid overdoses. With regards to the Medicaid expenditure per 100,000 population variable a 1% increase in would correlate to a 0.0142% increase in overdoses per 100,000 population. The variables that contradicted the prediction for the initial analysis included medical marijuana laws, Good Samaritan Laws, and Naloxone Laws. For these variables where a dummy variable was implemented – Good Samaritan Laws, and Naloxone Laws – the positive and significant coefficient highlights how the existence of these laws actually does the opposite of deterring overdoses according to this model.

Given the need to address endogeneity, a two-stage least squared regression, with transportation and homeland security grants as instruments for the jail variable, is completed to derive an adjusted jail variable. After applying this treatment and re-running the regression the key takeaway is that the jail variable remains significant at the 5% level.

Afterwards, fixed effects treatment is applied to the regressions given the significant immeasurable cultural and regional differences between each state. There are significant overlaps when analyzing the highest and lowest coefficients for the individual states in Exhibit E and comparing that to the 2015 overdose heat map in Exhibit C. Especially striking is that to the most part list of states with the highest coefficients matches up with the states that have the highest rate of overdose deaths. The higher coefficient signifies that there are certain cultural factors in that state that increases the propensity for those that live in the state to use opioids and – unfortunately – overdose from them.

Once the fixed effects treatment is applied some of the variables drop out. Most importantly, the inmates per 100,000 adjusted variable loses its significance. The explanation for this is that there is likely some unmeasured cultural difference between the states that accounted for the original significance of the jail variable. Ultimately this means the 'lock-em-up' approach would not prevent opioid overdoses according to this analysis. Another variable that drops out is legalization of medical marijuana – which no longer is significant. The variables that survive the fixed effects treatment without losing their significance or changing signs includes: Medicaid expenditures, GDP, and Naloxone Laws. For the SAMHDA survey, these treatments cause the variable to become significant, but would seem to imply that the factor has an adverse effect on overdose deaths. The final major takeaway is that the prescription rate variable switched directions, but remained significant at the 5% level. This is interesting because it would seem as though after accounting for the cultural differences among the states that the number of prescriptions supplied within the state is not positively related to overdoses – which would invalidate t the original hypothesis.

Potential Explanations:

Major Regional and Cultural Differences Across Each State

The United States of America is known as the melting pot of the world, and one of the unique characteristics of the nation made up of people from around the world is the diversity within the various states. From California to Missouri to Maine, no two states have the same culture, demographics, or even geography. This extreme regional difference within the United States drives the reasoning behind the need to utilize fixed effects in the statistical analysis in order to account for those variations. There are too many hidden cultural variables that are unaccounted for that could drive a regression that is analyzing state level data astray.

Once fixed effects were implemented in the regression analysis, there were major impacts on some of the key predictor variables. Firstly, the variable measuring law enforcement – inmates per 100,000 – lost its significance. Secondly, the variable measuring the supply and availability of prescription opioids – prescriptions per 100,000 population – remained significant by changed directions away from what was expected. These two major impacts as well as the lack of deterrence in the other regulations and social factors that were tested highlights that the regional differences between the states is driving opioid overdose deaths.

Though there have been past papers and case studies that have highlighted the success of certain regulations for certain states, according to the statistical model in this paper the success can only be applied to the state being tested. Therefore, a law preventing opioid usage that may work in Florida cannot be necessarily applied across the country in North Dakota given the vast cultural and regional differences between the two states. Within the context of our analysis, this means that among the variables that were tested as potential predictors for opioid overdose deaths, there are none that could be implemented on the broad national level in order to prevent opioid overdoses. Rather, like many issues that the US faces, the solution will fall on state and even local legislatures to craft laws that fit the cultures of the regions that they govern. It would seem that the broad nationwide approach to identify a universal silver bullet fix to the opioid epidemic may not bear fruit.

Opioids as a Normal Good

Though opioids are extremely deadly and illegal, ultimately they can be looked at like any other economic good. This statistical model highlights that opioids can be considered a normal economic good, which has increased demand when the income of a population increases. For the statistical analysis in this paper, the predictor variable of GDP per 100,000 population was used as a proxy for income. Ultimately, the results of the analysis was that even with fixed effects there was positive explanatory significance at the 5% level for the income variable. The result confirms that opioids – though dangerous and highly illegal – can be considered normal goods.

It was mentioned earlier that income could be looked at as either a drug market dynamic or socioeconomic factor. From the standpoint of this dichotomy, this result would seem to signify that the economic and market dynamic explanation for opioids overpowers the products of despair narrative. If the latter were true, opioids would likely be an inferior good that people would turn to whenever their income decreased. This explanation is not the case, as the model highlights the directionally positive relationship between income (GDP) and opioid overdoses.

Additional Endogeneity Issues

Although the endogeneity issue for the incarceration variable was addressed using a two-stage least squares analysis and instrumental variables, there are other variables that could have been endogenous with opioid overdoses. Specifically with Naloxone Availability Laws, the states that have higher overdoses may have implemented the law to reduce overdose deaths. Yet, the question is whether the overdose deaths caused the law to be implemented or if the Naloxone Law ended up affecting opioid related deaths. A similar sort of endogeneity issue exists with Medicaid expenditures, Naloxone Laws, and the SAMHDA survey – all of which were significant in the 2SLS regression with fixed effects. Ultimately these variables positively explain overdose deaths – meaning more Medicaid spending translates to more deaths, the implementation of Naloxone Laws drove up overdoses, and the states with more methodone treatment programs had higher overdose deaths.

Logically, the endogeneity issue would be driving these variables to be positively related to opioid deaths if the causation is being controlled by overdoses. However, these variables actually deter overdose deaths and have a negative relationship with the independent variable. Further testing should be conducted to see if using instrumental variable and a two-stage least squared regression analysis with these predictor variables if the coefficients would remain significant or if the direction of the coefficients would stay positive.

Omitted Variable Bias

One of the variables which ultimately positively predicts opioid overdoses was Medicaid spending. However, the data that was taken was total expenditures and not a more bifurcated version – which may lead to a different result. For instance, Medicaid spending on opioid prescriptions may lead to increases in opioid overdose deaths. At the same time, Medicaid spending on drug treatment programs may lead to reductions in overdose deaths. By using total Medicaid spending as the predictor variable the model may be mislabeling all parts of a very large and broad program as contributing to opioid overdose deaths. There may be a missing variable – like Medicaid prescriptions for opioids – which is driving the overall Medicaid variable to positively predict opioid overdoses. Even though utilizing fixed-effects with the regression diminishes the likelihood of omitted variable bias, it does not completely eliminate this threat. Potentially, looking into a more granular breakdown of Medicaid expenditures could allow policy makers to strip out an eliminate parts of the program that contribute to overdose deaths and increase budgets of programs that accomplish the opposite.

Conclusions:

Ultimately, the biggest takeaway from this paper is that from the standpoint of opioid overdose prevention there are few national remedies that can be effective in addressing overdoses. Once the cultural and regional differences between the states is accounted for the only set of regulations that seemed like they could potentially translate to fewer overdoses – increased incarceration and crime deterrence or decreasing prescription availability – dropped out or changed directions. This shows that the various regional and cultural differences play a major role on the drug consumption and overdose deaths of each state. Unlike other public health issues – like a flu outbreak – for the opioid epidemic, there is not a single ‘vaccine’ that can be prescribed as an effective treatment. From a regulatory standpoint this means that there may be few broad nation-wide initiatives that would be effective in combating the crisis.

Another important finding is that opioids – despite their unique characteristics – are considered a normal good. Thus the narrative that those people who have been ravaged by the economic downturn have a propensity to turn to opioid painkillers to cope is countered by this statistical model. In reality falling incomes would lead to less opioid consumption and fewer overdose deaths.

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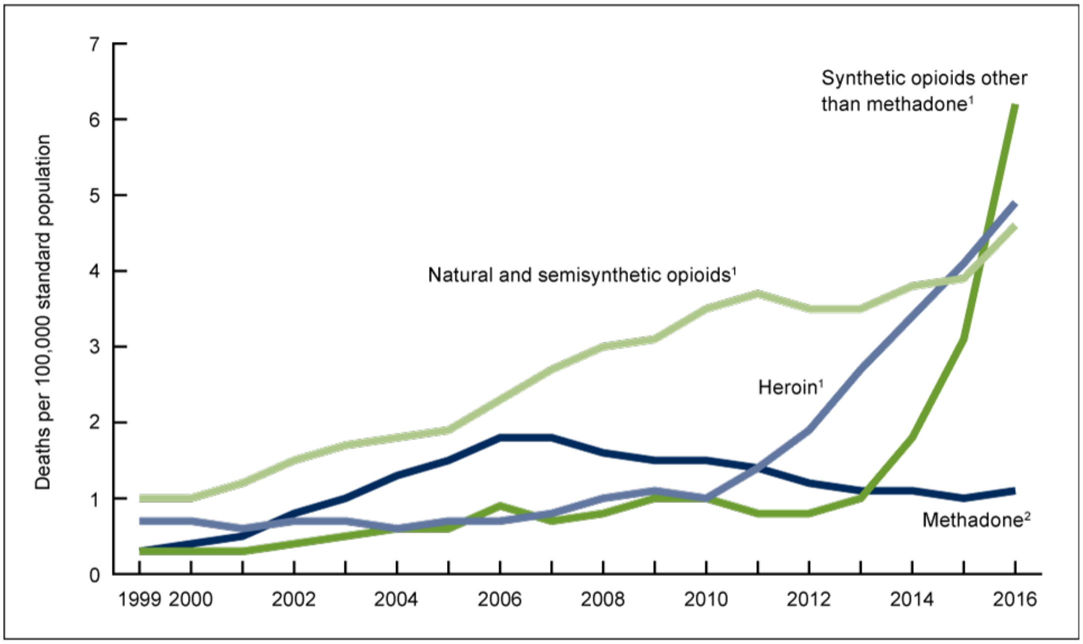
Appendix

Exhibit A[30]:
Opioid Overdose Rates from 1999 – 2016

The figure tracks overdose death rates for various types of opioids from 1999 – 2016 in the United States. The death rates are recorded in deaths per 100,000 population. The data was compiled using the CDC *Wonder* database.



[1] Significant increasing trend from 1999 to 2016 with different rates of change over time, $p < 0.05$.
[2] Significant increasing trend from 1999 to 2006, then decreasing trend from 2006 to 2016, $p < 0.05$.
NOTES: Deaths are classified using the *International Classification of Diseases, Tenth Revision*. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug overdose deaths involving selected drug categories are identified by specific multiple-cause-of-death codes: heroin, T40.1; natural and semisynthetic opioids, T40.2; methadone, T40.3; and synthetic opioids other than methadone, T40.4. Deaths involving more than one opioid category (e.g., a death involving both methadone and a natural or semisynthetic opioid) are counted in both categories. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, with ranges of 75%–79% from 1999 to 2013, and 81%–85% from 2014 to 2016. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db294_table.pdf#4.
SOURCE: NCHS, National Vital Statistics System, Mortality.

[30] Center for Disease Control, *Drug Overdose Deaths in the United States, 1999 – 2016,* Dec. 2017, https://www.cdc.gov/nchs/products/databriefs/db294.htm.

Exhibit B:

Google Hits Analysis of the phrase: "Opioid Epidemic"

The figure tracks the number of Google search hits of the phrase: "Opioid Epidemic". The hits are displayed graphically in millions and the data spans from 2004 – 2016.

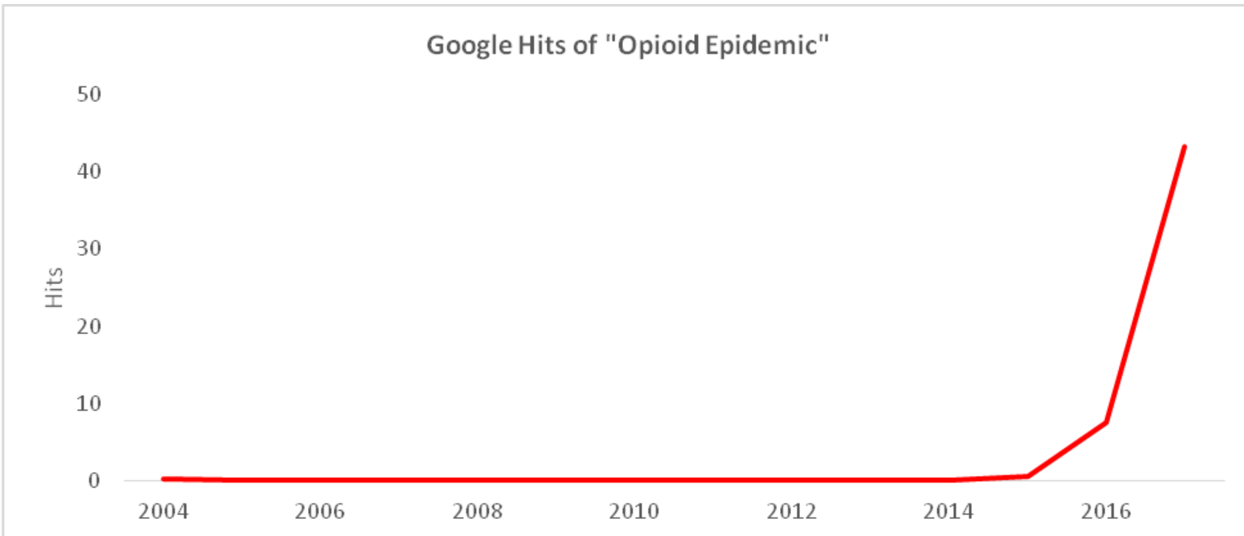


Exhibit C:
Heat Map of Overdose Death Rates in 2015
The figure is a heat map of state level opioid overdose mortality rates. The darker the colors correspond with a higher overdose death rate. The CDC used its *Wonder* database of causes of deaths to identify deaths rates caused by all types of opioids.

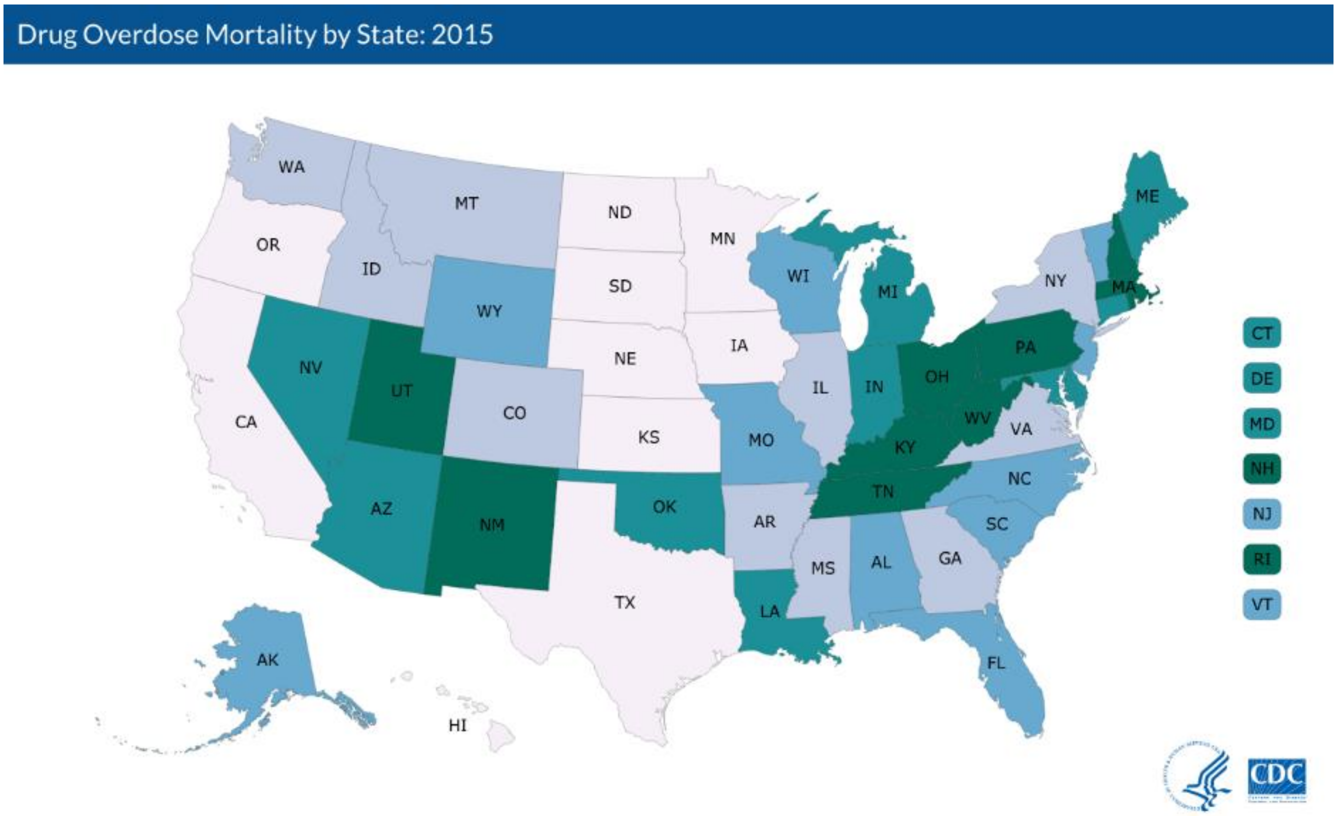


Exhibit D:
Regression Output

The table highlights the coefficients on the various independent variables for each type of regression. The asterisks call out significance variables at the 1%, 5%, and 10% level.

Dependent Variable: Opioid Deaths

	Standard	**Fixed Effects**	**2SLS**	**2SLS with Fixed Effects**
Prescription Rate	0.0001***	-0.0007***	0.0017***	-0.0001***
Prescription Drug Monitoring Program	-0.2348	-0.4475	-42.1843**	-0.5030
Medicaid	0.0142***	0.0227***	0.8890***	0.0231***
Legalization of Medical Marijuana	2.6159***	2.5534***	-14.3919	2.53571
GDP	0.0007***	0.0017***	0.0066*	0.0016***
Good Samaritan Laws	1.2210*	-0.1655	13.4910	-0.09708
Naloxone Laws	2.4092***	1.1171***	-19.6390	1.1516***
SAMHDA Survey	0.04247	0.5902***	0.0090	0.5368*
Incarceration	-0.0100***	-0.0037	-	-
Adjusted Incareration	-	-	-0.5545***	0.0095
R-Sqaured	0.3506	0.8286	-0.3429	0.8279

*Note: ***, **, * are significant at 1%, 5%, 10% level respectively.*

Exhibit E:
Top 5 and Bottom 5 Coefficients in Fixed Effects

The tables show the states with the five highest and lowest coefficients from the fixed effects regression.

Five Highest Coefficients

	State
1.	West Virginia
2.	Nevada
3.	Oklahoma
4.	Kentucky
5.	Tennessee

Five Lowest Coefficients

	State
1.	North Dakota
2.	Hawaii
3.	Alaska
4.	California
5.	New York