2020

Moral Hazards and Negative Externalities of Lifesaving Programs: How Naloxone Access Laws and Prescription Drug Monitoring Programs Affect HIV Transmission

Jeremy Horn

Claremont McKenna College

Moral Hazards and Negative Externalities of Lifesaving Programs: How Naloxone Access Laws and Prescription Drug Monitoring Programs Affect HIV Transmission

Submitted to

Professor Serkan Ozbeklik

by Jeremy Horn

for Senior Thesis

Spring 2020

1. Introduction

The opioid epidemic has become a public health crisis. Over 42,000 Americans died from opioid overdoses in 2016, which was over double the amount of deaths only six years prior.[1] Because of this, many different harm reduction practices have been adopted by various fire and health departments. Popular harm reduction practices include passing Nalaxone Access Laws (NALs) that remove legal liability and expand access to naloxone (a drug that prevents drug overdoses as they are happening) and Prescription Drug Monitoring Prongrams (PMDPs), which allow physicians to monitor the number of drug prescriptions individual users receive, thereby limiting the over prescription of opiates to drug-dependent users. As these policies have been implemented, it is imperative to study and understand the public health outcomes associated with these programs. While there has been great public and academic debate over whether or not PMDP's and NAL's are effective at stopping drug overdose deaths (scores of articles have been published in publications such as *The New York Times*[2] and *The Atlantic*[3]), there has been no research on how PMDPs and NALs affect the rate of HIV transmission among intravenous drug users. I suspect that NALs may encourage more drug use because they lower the risk associated with drug use, which could result in more drug-related HIV cases. PDMPs may also result in increased HIV transmission because when the supply of opiate prescriptions is decreased, the black-market price of prescription opiates increases, which could encourage drug users to switch to cheaper intravenous drug usage methods. With a lifetime public and private cost of over

[1] https://www.hhs.gov/opioids/about-the-epidemic/index.html
[2] https://www.nytimes.com/2016/07/28/us/naloxone-eases-pain-of-heroin-epidemic-but-not-without-consequences.html
[3] https://www.theatlantic.com/health/archive/2018/03/moral-hazard-opioid/555389/

$400,000[4] per new HIV diagnosis, it is imperative for policy makers to have an understanding on how these programs influence HIV rates among intravenous drug users.

The literature surrounding NAL is mixed. Local case studies and (Rees et al 2017) show that NALs are effective at limiting the number of overdose deaths by an estimated 9-11%. (Doleac and Mukherjee 2018), on the other hand, find the opposite showing that the implementation of NALs in the Midwest is correlated with a 14% increase in overdose deaths. Other regions had smaller differences.

The literature around PMDPs is also very mixed as well. While evidence shows that PMDPs are effective at limiting the number of prescription opiate prescriptions and "pill mills," it is unclear if this leads to less drug abuse. There is a great body of literature finding no evidence that PMDPs lead to fewer drug overdoses (Paulozzi, et al., 2011; Gugelmann et al., 2011; Li et al., 2014). One study shows that limiting the number of prescription opiates available for drug users encourages them to switch to heroin (Rudd et al., 2016). If this relationship is indeed true then PMDPs could lead to increased HIV transmission by increasing the number of intravenous drug users.

While studies do show that syringe exchange programs are effective at limiting the spread of infectious disease (Packham 2019), There are no current studies examining how other harm-reduction strategies effect HIV transmission. This is what I will look to examine in the text below. It is important for policy makers to understand the relationship between NALs, PMDPs and HIV transmission to reduce public cost and human suffering.

[4] https://www.cdc.gov/nchhstp/budget/infographics/HIV.html

The purpose of this thesis is to fill the aforementioned gap in the literature through my empirical model. Using CDC data and prior research by (Doleac and Mukherjee 2018), I regress the number of prescriptions and NAL's implementation on new HIV diagnoses. I then repeat the regression to see what if any effect NALs and PMDPs have on the number of overdose deaths.

I find that enacting a NAL is correlated with a statistically significant 23% decrease in new HIV cases. Every additional opioid prescription per 100,000 people is associated with a one percent decrease in HIV infections. Translating that to percentages, a 10% percent decrease in the number of opioid prescriptions is correlated with a 7% increase in the number of HIV infections. Furthermore, I find that NALs are found to be in my model to be correlated with a 14% increase in overdose deaths. Opioid prescriptions are found to have a similar effect on overdoses as they had with new HIV infections: there is a 7% increase of overdoses for a 10% decrease in opioid prescriptions.

Accordingly, Section Two of this thesis will provide background information about the opioid epidemic, and NALs and PDMPs as responses to the epidemic. In Section Three, I will go into further depth about the data. In section Four, I will then explain the empirical methods that I use in order to obtain the results seen above. The final section concludes.

2. Background

The opioid epidemic claims nearly 115 lives a day (CDC 2018). This addiction is usually caused by people being prescribed opiates from a doctor and becoming addicted. As many as four out of five heroin users begin with prescription opiates (Muhuri et al., 2013). Drug overdoses is a major reason why the all-cause mortality of 45-54 white males has increased 0.5% per year between 1999 and 2013 (Case and Deaton 2015). This has led to lawmakers to think of ways to mitigate the devastating impact and to prevent new drug users and new overdose deaths.

Policy makers have recently been pushing to make Naloxone legal to use in the treatment of drug users. Naloxone is an opioid that can effectively reverse overdose symptoms when properly used (CDC). US surgeon general, Dr. Jerome Adams, has issued an advisory encouraging everyone to have naloxone in their medicine cabinet[5] .

Previously, obtaining Naloxone required a prescription from a doctor. Due to the liability associated with prescribing and administrating naloxone it was rarely administered as a lifesaving drug. However, NALs have increased the reach of which these drugs can be used. In some states Naloxone is available to purchase without a prescription in a pharmacy. Other states passed laws offering immunity civil liability when dispensing naloxone (NM stats 30-31-27). Recently, NALs have received bipartisan support in an effort to curve the opiate epidemic (Ollove 2014). These laws allow pharmacists to provide prescriptions for naloxone. This is effective because untrained people can successfully administer naloxone (Doe-Simkins et al 2014). In fact, 83% of drug overdose reversals are performed by drug users (Wheeler et al 2015). One possible benefit of these programs is that NALs can lower the number of 911 calls local fire and police departments receive Seal et Al (2003). However, there is no data about the amount of naloxone dispensed in the United States.

There have been multiple case studies showing the effects of Naloxone access on the opioid death rate in the local context. (Albert et.al 2011) and (Walley et al. 2013) find that Naloxone access when coupled with other harm reduction programs seems to lower the opiate death rate. (Rees et. al 2017) look at this issue on a state by state basis. They look at when (NAL's) were enacted and find a 9-11% decrease in opiate related fatalities attributed to NAL

[5] https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html

implementation. (Deiana and Guia 2018) find no correlation between NAL's and overdose deaths.

(Doleac and Mukherjee 2019) also look at NAL implementation and find the exact opposite effects of (Rees. et al 2017). (Doleac and Mukherjee 2019) found that Naloxone access laws had significant effect on opiate mortality rates in the South, Northeast and West and a 14% increase in opiate related deaths in the Midwest. They also find NALs to be associated with increased crime, which suggests that these laws potentially create a moral hazard because drug users may inject heroin laced with dangerous additives such as Fentanyl. This theory builds off a larger body of literature that drug and alcohol dependent people are still rational and sensitive to prices (Becker and Murphy 1988), (Grossman and Chaloupka 1998). While NALs are able to prevent deadly overdoses, there is evidence to suggest that these programs might lead to more harm then they negative consequences they intend to prevent.

Another harm reduction strategy that has been implemented is prescription drug monitoring programs (PDMPs) which track patients' opioid prescriptions and give that information to doctors. This prevents doctors from over prescribing opiates and provides them with a better understanding about which patients may have a drug dependency problem. This policy is also effective at shutting down "pill mills." These programs have led to a great decrease in prescription opiates across the board (Rutkow et al 2015). However, it is unclear if decreasing the supply of opiates leads to less opioid abuse overall.

PMDPs have come under major criticism about whether they are actually effective at preventing drug overdoses (Paulozzi, et al., 2011; Gugelmann et al., 2011; Li et al., 2014). The concern is that some users have substituted prescription opiates for heroin after PMDPs have been enacted. This is believed to have led to a more than tripling of the number of heroin-related

deaths (Rudd et al., 2016). However, different studies show that PDMP's are reasonably effective at preventing overdose deaths and increasing drug treatment admissions (Haegerich et al. 2014 Bao er al. 2016). A larger meta-analysis found no clear relationship between PMDP's and drug overdose deaths (Pardo et al, 2018).

Most studies of infectious disease prevention measures for opiates are based on the proliferation of Syringe Exchange Programs (SEP's). (Packham 2019) looks at the syringe exchange programs in the context of the opioid epidemic. She finds that access to SEPs results in reducing new HIV diagnoses up to 18.2%. However, she also finds that SEPs are correlated with higher opiate mortality rates and higher rates of hospitalization. [6]

This is the only study looking at the effects of NAL and PMDPs on the HIV rate. I believe that this connection should not be overlooked and should be studied further. If NALs encourage more drug use and if PMDPs lead drug users to switch to intravenous methods, then these programs can result in a large public cost due to an increased numbers of HIV cases. There is also no clear consensus in the literature on If NAL or PMDPs increase or decrease drug overdose deaths.

3. Data:

I use data from a number of different sources. Specifically, I obtain state-by-state HIV infection data from the Center of Disease Control Prevention's National center for HIV/AIDS, Viral Hepatitis, STD and TB prevention (NCHHHSTP) Atlas. This is the only complete source of annual state-level sexually transmitted disease data that is currently up to date. This data

[6] For previous case studies about the effectiveness of SEP's at preventing HIV transmission look at the literature review in Packham (2019).

separates HIV infections based on cause. It allows me access information to look at new and existing diagnoses. This is especially useful because I am only interested in HIV infections due to intravenous drug use. However, this might be a reason for underestimating the true number of HIV infections prevented because if HIV spreads through intravenous drug use, then this will also put the sexual partners of drug users at risk as well. State level data is preferable because all county-level data is blocked if the number of infections is less than five. This prevents access to 75 percent of the county level data[7]. State-level data includes panel data from 2008- 2018 including all 50 States and the District of Columbia. This means that there is a total of 561 observations in my sample.

To isolate the effect of naloxone access laws on HIV transmission I also wanted to control for the effects of syringe exchange programs. Syringe Exchange programs are proven to be effective on stopping the spread of HIV among people who inject drugs. To do this, I made an index of the estimated percentage of people who live in a county in which there is a syringe exchange program in a given state. To create this index, I used the NASEN (North American Syringe Exchange Network) index of operational needle exchange programs to calculate the percent of the state that resides in a county with an operational SEP in 2018. NASEN never accepted my requests to provide historical data on syringe exchange openings. Because of this, I had to extrapolate using the 2018 data. For earlier years, I made estimations of the number of needle exchange programs from the AMFAR Syringe exchange coverage maps from 2013 and 2014. I recalculated the index from those years and used the 2013 figure as an estimation for 2008- 2013. I also looked for any relevant laws or new articles from 2008- 2018 about when

[7] This is to protect the privacy of individuals who have contracted HIV. HIV due to drug transmission is a relatively rare event. Due to time constraints while writing this thesis I was unable to get permission from each state's HIV surveillance program

syringe exchange programs were authorized in the states. However, in many states needle exchange programs operated without being authorized. This makes it difficult to look at a single law to provide information about when syringe exchange programs were operational. To deal with problems with this figure I separated the syringe exchange index into four different binary variables, using only three in the regression to limit collinearity.

In addition to controlling for the effects of syringe exchange programs, also controlled for the following variables. First, I controlled for the opioid prescription rate per 100,000 people. For this, I used the CDC U.S. prescribing rate maps that are available online from 2006 to 2018. These maps are a good indicator to see how bad the opioid epidemic has hit certain states. I also controlled for the number of overdoses due as well. I obtained this information from the Center of Disease Control National Wonder multiple cause of death database, which provides information about different causes of death including the number of drug overdose deaths per year per state. Over 70% of drug overdoses deaths comes from opioid use. This means that total drug overdose death should be highly correlated with the amount of intravenous drug use. The information about the pass date of naloxone access laws was passed based on prior research of Doleac and Mukherjee (2018). In addition, I controlled for state and year fixed effects. I also added socioeconomic and racial controls such as percent of population food insecure, percent of population in poverty, unemployment rate and percent of the population that identifies as African American. Table 1 presents summary statistics [8].

4. Empirical Strategy and Results

[8] For Hivd100k I divided the number of new hiv cases by 100,000. Scripts is the number of prescription opiates per 100,000 people. NAL is whther the state has inacted a Naloxone access law. Oddpop is (Overdoses / population) *100000

In order to study the effects of NALs on the HIV rate I estimate an ordinary least squares method (OLS) model of the following seen below.

$$Y_1 = B_0 + B_1 NAL_1 + B_2 SEP_2 + B_3 OPR_3 + B_4 OD_4 + B_5 E_5 + t_i + s_i + \varepsilon$$

where Y is the HIV rate per 100,000, and NAL is an indicator variable equal to 1 if the state has an NAL enacted and 0 if the state has not. X is a vector for the indicator variables for the SEP index (seplow, sepmid, sephigh). OPR is the number of opiate prescriptions. OD is the overdose rate. E is a vector for socioeconomic controls such as poverty, unemployment and percent of the population which is food insecure . t_i is year fixed effects and s_i is state fixed effects.

In order to study the effects of NALs on the number of overdose deaths rate I estimate an ordinary least squares (OLS) model of the following seen below.

$$OD = B_0 + B_1 NAL_1 + B_2 SEP_2 + B_3 OPR_3 + B_4 HIV_4 + B_5 E_5 + t_i + s_i + \varepsilon$$

In the first regression (results located on table 2), I found that NALs implementation is associated with a 23% decrease in the number of new intravenous drug related HIV infections. I also found that every additional opiate prescription per 100,000 is associated with a one percent increase in HIV rates. This means that if a PMDP was to decrease the number of opiate prescriptions by 10% this would be correlated with a 7% increase in the number of HIV diagnoses. I found NALs to also increase the number of drug overdose deaths by 14%. I also found that decreasing opiate prescriptions by 10% is associated with an increase in overdose deaths of 7%. Surprisingly, I also found that syringe exchange access is correlated with increased HIV transmission.

The results that I have obtained are surprising on multiple levels. Before running this regression, I did not expect NALs to have a negative rate on HIV rates. I expected NALs to raise HIV rates because of the fact that I would expect NALs to encourage more drug use, which

would increase the transmission of HIV. NALs may encourage riskier drug use (such as using cheaper additives like fentanyl) but the data suggests that they may not necessarily encourage more drug use among drug users. That being said, the intuition about NALs decreasing HIV transmission rates is unclear.

Another surprising result is the strong effect that NALs had on the HIV rate and the overdose rate. Casual empiricism would suggest that expanding access of naloxone alone would not lower HIV transmission among drug users by 23%. This is a strong effect while not having a strong intuitive explanation. In regard to the relation between to NAL's I find results relatively consistent with (Doleac and Mukherjee 2018). I find that NAL implementation results in an 14% increase in the number of overdose deaths. However, (Doleac and Mukherjee 2018) only found the 14% percent increase in the Midwestern region of the United States. This indicates that my result is more general than theirs.

Another surprising result is that my results show that syringe exchange programs result in higher rates of HIV rates among intravenous drug users. This goes against (Packham 2019) and all of the prevailing academic literature on the subject. The idea that giving clean needles to intravenous drug users would raise HIV rates also goes against casual empiricism. I believe that this positive effect of syringe exchange programs has to do with either an error in my data set. As mentioned above, I had to use estimation strategies while creating my syringe exchange index due to information and time restrictions. This could have led to an upward bias in my model.

My results also show that lowering the number of prescription opiates results in higher rates of HIV transmission and more overdose deaths. A plausible explanation for this could be that when the supply of oral opioids is limited then the price of illicit prescription opiates rises. With rising prices, opioid-dependent users are incentivized to move to cheaper intravenous

alternatives such as heroin. Heroin has a much higher rate of overdose and is a way for infectious diseases such as HIV to spread. (MM Ali et al 2017) and (Fink et al 2018) have shown that reducing the supply of opiates can result in drug users moving to using heroin.

5. Conclusion

The opioid epidemic continues to destroy communities and families. To combat this, NALs and PDMPs have been proliferating across the United States to lessen the negative impact of the opioid epidemic. However, the effects of these programs have not been properly studied and recently the effectiveness of these programs has been called into question. One major externality of these programs that has not been studied is how these programs affect HIV rates. Intravenous drug use is associated with spreading HIV, which bears a lifetime private and public cost of over $400,000 per individual case. To prevent suffering and to save taxpayer dollars it is imperative for policy makers to consider how policies such as NALs and PMDPs effect HIV transmission.

NALs are laws that remove legal liability and improve access to naloxone, a drug that prevents drug overdoses from turning deadly. This has led to increased access to naloxone in much of the United States. The results are mixed on whether or not this is actually effective at preventing drug overdoses. (Rees et. al 2017) finds that NALs save lives and lower the amount of drug overdoses by approximately 10%. (Doleac and Mukherjee 2018) find the opposite, they find that NALs incentivizes intravenous drug users to inject more potent cheaper substitutes like fentanyl resulting in a 5-14% (depending on region) increase in the number of drug overdose deaths.

PDMPs are programs that provide records of how many opiate prescriptions each individual has received. These programs have been effective at limiting the number of opiate

prescriptions that are available. The literature on these studies has been mixed, with (MM Ali et al 2017) and (Fink et al 2018) show that PDMP's can lead to opiate users using intravenous methods such a heroin. The wider body of research of (McDonald, Carlson, and Izrael, 2012; Reifler et al., 2012; Jena et al. 2014; Haegerich et al. 2014) show very small positive or no effects of PMDP's on drug misuse.

This paper addresses multiple gaps in the literature. While there have been studies of the NALs and their effect on overdose deaths, there have been no studies on how NALs effect HIV transmission. There is also no study on the effects of decreasing opioid prescriptions on the overdose rate. This a gap in the literature that I am looking to solve through my empirical methods. To solve this issue, I used data from the Center of Disease control and the University of Kentucky poverty research center. In my model, I run an ordinary least squares regression with different variables such as HIV infection rate, opioid prescription rate, overdose rate and syringe exchange proliferation.

I find that Naloxone access laws are negatively correlated with HIV rates. Adding a NAL has leads to an estimated 22% decrease in HIV rates. I also find, based on my results, NAL implementation is correlated with a 14% increase in overdoses. In regard to PDMP's I find that there is a 7% increase in HIV infections for every 10% decrease in opioid prescriptions. I also find decreasing opioid prescriptions to be correlated with increase overdose rates. For every 10% decrease in opioid prescriptions there is an estimated 7% increase in drug overdose deaths.

One limitation of this paper is that it is unclear why NALs have such a large positive effect on HIV rates. While I would have expected NALs to either have no effect or increase transmission I did not expect NALs to lower HIV transmission rates. The mechanism by which NALs would lower HIV infections is unclear.

Consistent with (Doleac and Mukherjee 2018), I find that NALs do in fact lead to an increased number of drug overdose deaths. However, my nationwide result of 14% increase is higher than (Doleac and Mukherjee 2018) 14-5% increase. My model may have overestimated the effects of these programs. Nevertheless, based on the effects that I have found, I would encourage local and state governments to consider the moral hazards that may result from implementing NALs. NALs have the possibility of lowering the "cost" of a drug overdose, by lowering the risk of death. This would incentivize drug users to use cheaper more dangerous alternatives like fentanyl, increasing the incidence of overdose despite naloxone's lifesaving properties,

I also find that decreasing opioid prescriptions is correlated with statistically significant increase in HIV rates. For every ten percent increase, there is in seven percent increase in the number of new HIV infections associated with drug use. There is a similar effect of prescription drugs on overdoses with a 7% increase in drug overdose deaths for every 10% decrease in opioid prescriptions. This is because when the supply of opiates is decreased then the price of illegal prescription opiates increases. This incentivizes drug users switch to more dangerous alternatives like fentanyl.

There are major shortcomings associated with my model. For one, syringe exchange programs are correlated with more HIV cases. This goes against the empirical literature and is much more likely due to some sort of flaw in how I constructed the syringe exchange index due to a lack of available information. Another problem is how the effect of NALs on seems to be the opposite of what I expected and there is unclear intuition on why that might be.

The reduction of prescription opiates seems to result in a 7% increase in overdose deaths and HIV diagnoses for every 10% decrease in prescription opiates. The mechanism in which this

happens is due to the fact that drug users when prescription opiates become less available switch to less expensive more intravenous options such as heroin. This speaks to the difficulty in implementing harm reduction strategies.

A major takeaway from this paper is that when policy makers make laws to curb the spread of drug use, they should consider possible unintended consequences of these policies. With a lifetime cost of over 400,000 dollars per new HIV diagnosis it is imperative for local policy makers to consider how NAL's and PMDP's affect HIV and other infectious disease transmissions.

Table 1

Variable	Observations	Mean	Std. Dev	Min	Max
Hivd100k	561	.83	1.43	0	22.23
scripts	561	77.37	23.92	25	146.9
NAL	561	.3529	.4783	0	1
Oddpop	561	14.25	7.59	1.16	54.68
Serplow	561	.196	.397	0	1
Sepmid	561	.2121	.409	0	1
sephi	561	.215	.4116647	0	1
Pctblack	561	11.33	10.847	.67	50.06
Poverty	561	13.2608	3.34543	6.1	23.1
Unemploy	561	6.219	2.24	2.4	13.7
Foodi	561	14.39	3.42	6.11	25.22

Table 2

Variables	(1) Hivd100k	(2) Oddpop
NAl	-.188***	1.91***
	(.065	(.0653)
scripts	-.0087***	-.1216***
	(.00322)	(.0032)
oddpop	-.076*	-------
	(-.009)	
Hivd100k	------	-1.02918***
seplow	.047	-1.55*
	(.235)	(.8805)
Sepmid	.433***	4.37***
	(.319)	(1.16)
sephi	.529***	4.48***
	(.429)	(1.569)
pctblack	-.007	-.03777
	(.0114)	(.1135)
unemploy	-.0652***	-.0901
	(.022)	(.2145)
Foodi	.01243	.1677**
	(.0084)	(.0799)
State Fixed effects	Yes	Yes
Year fixed effects	Yes	Yes
R^2	0.7186	0.8352

Standard error in parentheses * significant at 10% level ** significant at 5% level *** significant at 1% level

References

Rudd RA, Seth P, David F, Scholl L. Increases in Drug and Opioid-Involved Overdose Deaths — United States, 2010–2015. MMWR Morb Mortal Wkly Rep 2016;65:1445–1452. DOI: http://dx.doi.org/10.15585/mmwr.mm655051e1

Becker, Gary S., and Kevin M. Murphy. "The Family and the State." The Journal of Law and Economics, vol. 31, no. 1, 1988, pp. 1–18., doi:10.1086/467147.

Case, Anne, and Angus Deaton. "Suicide, Age, and Wellbeing: an Empirical Investigation." 2015, doi:10.3386/w21279.

Chaloupka, Frank, et al. "The Demand for Cocaine and Marijuana by Youth." 1998, doi:10.3386/w6411.

Doe-Simkins, Maya, et al. "Overdose Rescues by Trained and Untrained Participants and Change in Opioid Use among Substance-Using Participants in Overdose Education and Naloxone Distribution Programs: a Retrospective Cohort Study." BMC Public Health, vol. 14, no. 1, Jan. 2014, doi:10.1186/1471-2458-14-297.

Doleac, Jennifer L., and Anita Mukherjee. "The Moral Hazard of Lifesaving Innovations: Naloxone Access, Opioid Abuse, and Crime." SSRN Electronic Journal, 2018, doi:10.2139/ssrn.3135264.

Paulozzi, Leonard J., et al. "A National Epidemic of Unintentional Prescription Opioid Overdose Deaths: How Physicians Can Help Control It." The Journal of Clinical Psychiatry, vol. 72, no. 05, 2011, pp. 589–592., doi:10.4088/jcp.10com06560.

Rees, Daniel, et al. "With a Little Help from My Friends: The Effects of Naloxone Access and Good Samaritan Laws on Opioid-Related Deaths." 2017, doi:10.3386/w23171.

Rutkow, Lainie, et al. "Effect of Florida's Prescription Drug Monitoring Program and Pill Mill Laws on Opioid Prescribing and Use." JAMA Internal Medicine, vol. 175, no. 10, Jan. 2015, p. 1642., doi:10.1001/jamainternmed.2015.3931.

Walley, A. Y., et al. "Opioid Overdose Rates and Implementation of Overdose Education and Nasal Naloxone Distribution in Massachusetts: Interrupted Time Series Analysis." Bmj, vol. 346, no. jan30 5, 2013, doi:10.1136/bmj.f174.

Sgc, Servicio Geológico Colombiano. "Guía Metodológica Para El Mejoramiento Productivo Del Beneficio De Oro Sin El Uso De Mercurio. Andes Antioquia. Versión Año 2018. Guía." Jan. 2018, doi:10.32685/46.114.2018.786.

Public Affairs. "What Is the U.S. Opioid Epidemic?" HHS.gov, Https://Plus.google.com/ HHS, www.hhs.gov/opioids/about-the-epidemic/index.html.

Paulozzi, Leonard J., et al. “A National Epidemic of Unintentional Prescription Opioid Overdose Deaths: How Physicians Can Help Control It.” The Journal of Clinical Psychiatry, vol. 72, no. 05, 2011, pp. 589–592., doi:10.4088/jcp.10com06560.

Khazan, Olga. “Why a Study on Opioids Ignited a Twitter Firestorm.” The Atlantic, Atlantic Media Company, 14 Mar. 2018, www.theatlantic.com/health/archive/2018/03/moral-hazard-opioid/555389/.

“CDC's HIV Work Saves Lives and Money Infographics.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 6 Feb. 2020, www.cdc.gov/nchhstp/budget/infographics/HIV.html.

Seelye, Katharine Q. “Naloxone Saves Lives, but Is No Cure in Heroin Epidemic.” The New York Times, The New York Times, 27 July 2016, www.nytimes.com/2016/07/28/us/naloxone-eases-pain-of-heroin-epidemic-but-not-without-consequences.html.