Syringe Exchange Programs and Harm Reduction: New Evidence in the Wake of the Opioid Epidemic

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June 2021

Abstract

In light of the recent opioid crisis, many public health entities have called for an expansion in syringe exchange programs (SEPs), which provide access to sterile syringes and facilitate safe needle disposal for injection drug users. This paper uses a newly constructed administrative dataset to estimate the effects of recent SEP openings on HIV diagnoses and drug-related deaths. Estimates for HIV rates are relatively imprecise. However, I present new evidence that SEPs increase rates of opioid-related mortality, suggesting that needle exchanges alone may be less effective than other interventions at stimulating recovery, especially in areas with high barriers to substance abuse treatment.

JEL Classification: I10, I18, K42

Keywords: syringe exchange programs, opioid crisis, HIV

*Department of Economics, Vanderbilt University, Email: analisa.packham@vanderbilt.edu. I am especially grateful to Katherine Wells, who provided substantial data work and excellent research assistance. I am also grateful to Lisa Roberts for providing data and for many useful conversations about the interworkings of the Portsmouth syringe exchange program. I thank Felipe Barrera-Osorio, Lindsey Bullinger, Jeffrey DeSimone, Jennifer Doleac, Jevay Grooms, Erin Krupka, Ajin Lee, Mike Makowsky, Chuck Moul, Emily Owens, David Powell, Michelle Segovia, Nick Sanders, Rhet Smith, Sebastian Tello-Trillo, Barton Willage, seminar attendees at Cornell University, University of Memphis, and West Virginia University, and participants of the Southern Economics Association 2018 Meeting, Association for Public Policy Analysis & Management 2019 Meeting, and 2019 Texas Economics Crime Workshop for useful feedback on work in progress.

1 Introduction

The US is in the midst of an opioid crisis. In 2015 the US Drug Enforcement Agency stated that opioid misuse from prescription pain relievers, heroin, and fentanyl had reached “epidemic levels" (U.S. Department of Justice, 2015). The increase in opioid use involving syringes has not only led to large increases in overdose deaths, but has also led to greater risk of bloodborne illness due to needle sharing. In recent years, acute cases of hepatitis C infections increased by 150 percent, and HIV diagnoses for white males aged 25–34 increased in 2013, reversing a decades-long trend (Centers for Disease Control and Prevention, 2015).

In light of this public health emergency, many entities, including the CDC, US Department of Health and Human Services, and some state and local health departments, have called for an expansion in syringe exchange programs (SEPs), which provide access to sterile syringes and facilitate safe disposal of used needles for injection drug users (Centers for Disease Control and Prevention, 2016; Markell, 2016; Giroir, 2019). This new call for SEPs raises the question of the net effectiveness of SEPs on health. In this paper, I test the causal relationships between SEP openings and drug-related health outcomes. Since no official national directory of SEPs exists, I construct a nationwide county-level dataset on program locations and opening dates to identify areas exposed to SEPs in recent years. Using administrative health data from the CDC and state health agencies, I compare rates of HIV diagnoses and drug-related deaths in counties with SEP openings to other counties without SEPs before and after the initial year of implementation.

This new evaluation is critical in understanding the effects of a single-pronged harm reduction intervention on total social welfare and will shed new light on how policy can better address the ongoing epidemic. In theory, the impact of SEPs on total social harm is ambiguous and likely varies by substance and context. While standard rational addiction frameworks model total social harm as the number of users times the average harm associated with use, the number of users is also a function of the utility of consumption weighed against expectations of the costs of consumption, and these costs are correlated with the actual average harm. Because SEPs affect all of these parameters, it is unclear whether SEPs will lead to more or less drug use.

In other words, because the aim of SEPs is to prevent needle sharing, and not to provide substance abuse treatment, it is possible that even if SEPs reduce bloodborne illness, they will be ineffective at curbing drug usage. Three arguments support the notion that SEPs could promote continued or increased drug use, leading to more fatal overdoses. First, programs distribute free supplies, including needles, sharps containers, and personal hygiene items, which lowers the expected cost of using injection drugs. Second, SEPs provide a safe space to interact with other users, increasing networking opportunities and reducing stigma. Third, communities that build a SEP may attract nearby drug users and/or signal that they also support more police leniency for drug users, lowering the legal risk of using opioids. In turn, if SEP openings increase drug use, it is possible that bloodborne illness rates might also increase.

I find that SEPs do not increase new HIV diagnoses rates, and may decrease them up to 1.1 percentage points, although estimates from some models are imprecise. Estimates also indicate that SEP openings increase drug-related mortality. In particular, I find that SEPs increase opioid-related mortality rates between 2.0–3.5 percentage points, and lead to a higher rate of emergency room visits and in-patient stays for drug-related complications. Effects are largest in rural and high-poverty areas. Results are highly robust to differences in sample, the definition of control and treatment groups, and functional form. Overall, these estimates correspond to nearly 2 more opioid-related deaths per county each year, suggesting that the openings of SEPs across the US between 2009–2016 were responsible for 0.5 percent of the total increase in opioid-related deaths.

These new estimates fill an important gap in the literature, as previous research on SEPs is largely correlational, and focuses on syringe sharing during the AIDS crisis in the 1980s and 1990s. Notably, the recent opioid crisis differs from the AIDS crisis in many ways, not only in terms of geographic reach but also lethality, prompting a need for the reexamination of the effectiveness of SEPs. Existing studies generally find that the programs are associated with reductions in the spread of HIV and reduced syringe sharing behavior, and are not correlated with an increase in the amount of drugs used by current drug users or an increase in new drug users (General Accounting Office, 1993; World Health Organization, 2004; DeSimone, 2005). Other evidence documents that SEPs are largely ineffective at preventing the spread of more prevalent bloodborne illness, such as Hepatitis C (Pollack, 2001a).

Importantly, the data from the studies included in the aforementioned literature reviews (i.e. General Accounting Office (1993); World Health Organization (2004)) rely on small sample sizes and self-reported data regarding individuals' drug use, and do not typically consider attrition nor spillover effects on those not directly treated. Additionally, many studies use data from Canada, Sweden, or New Zealand to serve as a comparison group for drug rates in the US. Such methods are problematic for addressing causality, given that other developed countries have differing policies on the operations of SEPs and greater access to substance abuse treatment.[1] I overcome these existing limitations by creating a dataset that combines information on SEP opening dates with restricted administrative county-level data on HIV diagnoses. These data proxy for drug use without relying on self-reporting behavior, and are representative of counties across the US.

Lastly, although many studies attribute SEPs with reductions in bloodborne illness over time, since HIV rates have been falling nearly continuously during the last two decades, other factors likely also contributed to the decline in disease. The goal of this paper is to use newly constructed administrative data to separate out the effects of a SEP opening from the effects of these other factors to better measure the way in which SEPs can affect rates of disease and mortality. Using administrative and survey data from a select SEP, as well as data on drug-related hospitalizations, I additionally explore potential drivers of the reduced-form effects. In doing so, I posit that more recent SEP openings

[1]For example, New Zealand's syringe services are fee-based while Australia distributes syringes free-of-charge and supplies syringe vending machines that allow injection-drug users to obtain clean syringes at any time of the day (Sean Cahill and Nathan Schaefer, 2009). And many countries, including Canada, provide free substance abuse treatment to injection drug users.

occurring after the introduction of fentanyl led to less syringe sharing but an increase in drug use.

Overall, these findings shed new light on the effectiveness of SEPs alone in combating the ongoing opioid crisis and present the tradeoffs inherent in such public health interventions. This new evidence is crucial as state and local governments search for ways to reduce rising rates of opioid dependence, and, as state-level legal restrictions, including prescription limits, patient ID laws, prescription drug monitoring programs, doctor shopping restrictions, pain clinic regulations, and Naloxone laws have been shown to be ineffective at curbing opioid use (Meara, Horwitz, Powell, McClelland, Zhou, O'Malley, and Morden, 2016; Bao, Pan, Taylor, Radakrishnan, Luo, Pincus, and Schackman, 2016; Doleac and Mukherjee, 2018; Mallatt, 2017).

2 Background on Syringe Exchange Programs

SEPs, also known as syringe services programs, are community-based public health programs that provide harm reduction services and supplies such as sterile needles, syringes, and other injection and disposal equipment and safe needle disposal. Comprehensive programs also offer HIV counseling, testing, and education, as well as referrals to substance treatment facilities or other medical and mental health services. Because such harm reduction programs are not designed to treat addiction or other medical conditions, few SEPs provide medically assisted treatment or any type of in-patient care (Jarlais, Guardino, Nugent, and Solberg, 2014).

About 82 percent of SEP budgets are from public funding sources, through provisions from city, county, or state governments (Jarlais, Guardino, Nugent, and Solberg, 2014). While the federal government has the ability to prohibit federal funding to support SEPs, states have authority to determine regulations for the existence, operation, and local funding of SEPs. Currently, SEPs are legal in 26 states and the District of Columbia, permitted in 9 states, and illegal in 15 states (LawAtlas, 2017).[2]

Since the early 2000s, more communities have opened SEPs in an effort to curtail the spread of HIV and hepatitis C. In 1998 only 77 cities had a SEP, but by 2013, 116 did (Jarlais, Guardino, Nugent, and Solberg, 2014). That both the number of SEPs and syringes exchanged has increased dramatically over the course of the last twenty years has important implications for the effects on drug use and spread of bloodborne illness. Most obviously, one would expect that the exchanges reduce the proportion and/or number of used syringes improperly disposed. However, given that both the number of opioid-related deaths have been increasing steadily over time and that the number of new HIV cases has in recent years reversed a decades-long downwards trend for some groups, it is important to disentangle outside factors simultaneously contributing to these trends to determine how much these health outcomes would be affected in the *absence* of SEPs.

[2]States with permitted programs include those states where local units have interpreted state laws to allow syringe access services or where no law explicitly prohibits syringe exchange. States where SEPs remain illegal include Alabama, Arkansas, Florida, Georgia, Idaho, Iowa, Kansas, Missouri, Mississippi, Nebraska, Oklahoma, South Carolina, South Dakota, Texas, and Wyoming (LawAtlas, 2017).

3 Empirical Approach

3.1 Data

To analyze the effects of recent SEP openings on HIV rates and mortality rates, I use administrative data from several sources to construct a county-level panel spanning 2008–2016. Data on SEPs as of 2017 is from the North American Syringe Exchange Network (NASEN), a non-profit organization that previously maintained a directory of SEPs by state as a public health information resource. In particular, these data contain the name and address of the program, as well as contact information, when available.[3] To gather data on the timing of SEP openings, I used these listings to hand collect information on program dates by researching the history of individual programs online, contacting listed representatives for programs, and comparing yearly coverage maps of syringe service programs provided by the Foundation for AIDS Research (AMFAR). I then geocoded each clinic location to identify which counties were offering SEP programs before 2009, and those that experienced openings in the following 8 years, which serve as the treatment group for this analysis. In doing so, I identified 86 SEP openings in 79 counties between 2009–2016.[4,5]

To measure the effect of a SEP opening on county-level HIV diagnoses, I build on administrative data from the CDC Atlas, which is the only comprehensive source of annual, county-level sexually transmitted infection data to date. The data include annual counts of HIV diagnoses per county of residence starting in 2008.[6] One limitation of the CDC Atlas is that HIV data for counties with less than 5 HIV cases or populations less than 100 are censored to ensure confidentiality of personally identifiable information. Because HIV is a relatively rare event, this results in suppression for approximately 75 percent of county-year observations. To improve the quality of the data, I additionally include restricted administrative data from each state's HIV Surveillance Program separately. Of the 50 states in which I requested data, 34 states provided uncensored data.[7] In instances where a state did not provide data, and the observation is censored, I assign the number of new counts to be zero, although I note that the results are not sensitive to this choice.[8,9]

[3] NASEN does not release these data upon request. Therefore, only snapshots of directories are available, making it difficult to track clinics over time. I have additionally tried an approach scraping web data for news articles on openings, although this method is ad-hoc and did not alter my list of recent SEP openings in any way.

[4] Figure A1 depicts US counties identified as having, versus not having, SEPs by 2016 using this approach, while Figure A2 maps SEPs that opened between 2009–2016 and those that opened prior to 2009 to show the variation in recent SEP openings.

[5] One shortcoming of these data is that if a clinic opened and closed before 2017, *and* is not uniquely identifiable from the city-level AMFAR maps, I do not observe that location in the data. Using available data from AMFAR and an updated NASEN directory, I observe only two clinics closures pre-2016.

[6] The Atlas is available at `https://www.cdc.gov/nchhstp/atlas/index.htm`. The CDC did not require reporting or systematically collect information on HIV diagnoses before 2008. HIV cases are classified as those with confirmed diagnoses of infection or infection classified as stage 3 (AIDS) in a given year.

[7] These states include Alabama, Arizona, California, Colorado, Connecticut, Florida, Hawaii, Illinois, Iowa, Kansas, Louisiana, Maryland, Massachusetts, Michigan, Missouri, Montana, Minnesota, Mississippi, Nevada, New Hampshire, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Vermont, Virginia, Washington, and Wisconsin.

[8] Estimates for changes in HIV rates are statistically similar at the 1% level when dropping counties with fewer than 100 residents. Because South Dakota does not report HIV diagnoses to the CDC in any year, this state is dropped for all analysis of HIV rates.

[9] These data do not contain information on transmission at the county-level. According to CDC data, transmission via injection drug use comprises nearly 10 percent of total HIV cases, on average, although in areas where opioid use is high, this number can be much higher (Centers for Disease Control and Prevention, 2015).

Data on drug- and opioid-related fatal overdoses is from restricted-use CDC mortality files. These individual-level data contain information on county of residence, cause of death, as well as age, race, ethnicity, and gender. Drug-related deaths are defined and categorized by ICD-10 underlying cause of death codes X40-X44, X60-X64, X85, Y10-Y14 and Y352. To identify opioid- and other drug-related deaths, I use death certificate data on immediate or contributory causes of death, referred to as "T-codes". In particular, to measure effects of SEPs on opioid-related overdoses, I consider T-codes 40.0–40.4 and T40.6.[10] Because drug-related deaths are a relatively rare event in some areas, for my main analysis I omit counties that experience zero reported occurrences in any year during the sample period. As suggested by Kahn-Lang and Lang (2019), this sample restriction allows treatment and control groups to be more similar *ex ante*, which places less importance on functional form assumptions of the difference-in-differences model, although below I show that estimates are insensitive to this omission.[11]

Using data in conjunction with population counts from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER), I construct rates of HIV diagnoses and all drug-related outcome variables for my analysis, calculated as cases per 100,000 population. I additionally construct county-level measures of demographics, including the fraction of the county population that are black and the fraction Hispanic. To control for economic conditions over time, I use data from the Bureau of Labor Statistics (BLS) on county-level unemployment rates and poverty rates. Finally, I also construct several policy indicator variables using data from Meara, Horwitz, Powell, McClelland, Zhou, O'Malley, and Morden (2016) to help capture the broader policy environment surrounding opioid access in a given state and year. I also control for good Samaritan laws, which legally protect individuals while they are assisting others in danger and paraphernalia laws, in which a state bans drug paraphernalia with no exceptions related to syringes or SEPs, using data from the LawAtlas Policy Surveillance Program, as well as Naloxone Access Laws, using information on state policy changes from Doleac and Mukherjee (2018). As an alternative to using these state-level controls, in some specifications I additionally show estimates controlling for state-by-year fixed effects.

Summary statistics for variables used in the county-level analysis are shown in Table A1. In Column 1, I display means for counties that experienced SEP openings from 2009–2016 (i.e. treated counties), and in Column 2 I display means for counties without SEPs (i.e. comparison counties). Means for HIV diagnoses rates and opioid-related mortality rates are larger for the treatment counties, while comparison counties generally are more rural and experience lower poverty rates. In some analyses below, I will separately test for heterogeneous effects by these county characteristics in an attempt to more clearly compare my findings across county subgroups.

[10] I note that these categories (T40.0-40.4 and T40.6) are used in official CDC calculations of drug overdose deaths. See Slavova, O'Brien, Creppage, Dao, Fondario, Haile, Hume, Largo, Nguyen, Sabel, and Wright (2015) for an in-depth discussion on coding of drug-related deaths. Specifically, T40.0 includes opium, T40.1 includes heroin, T40.2 includes semisynthetic opioids, such as oxycodone and hydrocodone, T40.3 includes methadone, T40.4 includes synthetic opioids, such as fentanyl, a drug that is 80 to 100 times stronger than morphine and up to 50 times more potent than heroin (Waitemata District Health Board, 2014). T40.6 includes other and/or unspecified opioids. I refer to Ruhm (2017) on how to properly account for and impute drug-related mortality where at least one specific drug category is identified on a death certificate, although I note that the main results are not sensitive to these adjustments.

[11] These remaining counties (i.e. those with drug-related deaths during this time period) account for approximately half of all counties. For raw trends of HIV diagnoses and opioid-related deaths over time in counties with SEP openings and those without, see Figure A3.

3.2 Identification Strategies

My primary approach for estimating effects of SEPs is a dynamic difference-in-differences design that compares counties with a SEP opening from 2009–2016 to other US counties without a SEP, although below I provide evidence that my results are robust to other comparison groups. The identifying assumption underlying this approach is that changes in health and crime outcomes in the comparison counties provide a good counterfactual for the changes that would have been observed in the treated counties in the absence of the SEP. In other words, I exploit variation in the timing of recent SEP openings and test whether, conditional on a broad set of control variables, we would have expected rates of HIV diagnoses and drug-related deaths to trend similarly in counties that chose to open SEPs versus those that did not.

In particular, the main results are based on OLS models of the following form:

$$y_{ct} = \alpha_c + \alpha_t + \beta X_{ct} + \theta SEP_{ct} + s_{st} + C_c * t + u_{ct} \tag{1}$$

where y_{ct} is the HIV rate, drug- or opioid-related mortality rate in a county c in year t, SEP_{ct} is an indicator variable that takes a value of one for counties with a SEP opening from 2009–2016 during and after the first SEP opening and zero otherwise, α_c and α_t represent county and year fixed effects, respectively, and X_{ct} can include time-varying county-level economic variables, county-level demographic controls, and state-level policy controls.[12] Additionally, s_{st} represents state-by-year interaction terms to account for aggregate time-varying shocks, like changes in the national drug policy, as well as state-specific shocks, including state funding for drug-related initiatives, Medicaid generosity, or state-level strategies for law enforcement. To more directly account for the concern that differences in the pre-existing trends between counties with SEPs and those without SEPs might bias the estimations derived from the above equation, in some specifications I also include county-specific linear time trends, $C_c * t$. All county-level analyses allow errors to be correlated within counties over time when constructing standard-error estimates.

Similarly, to show how these estimates change over time, I present event-study figures, based on models of the following form:

$$y_{ct} = (\sum_{\substack{t=-3 \\ t\neq -1}}^{4} \theta SEP_{ct}) + \alpha_c + \alpha_t + \beta X_{ct} + s_{st} + C_c * t + u_{ct} \tag{2}$$

where $t = -3$ contains all years at least 3 years prior to a SEP opening, and $t = 4$ includes all years at least 4 years after opening. All other variables remain the same as described above.

Importantly, for my main analysis I include only counties that have an opening between 2009–2016 in the treatment

[12] Over 77 percent of treated counties contain no other existing SEP and only two counties experience more than one program opening during this sample period.

group, as a way to ensure that all treated counties contain at least one year of pre-period data to test for diverging pre-trends.[13] In some specifications, I additionally show results from OLS models that include indicator variables for treated counties prior to the SEP opening. I do so in an effort to verify that mortality rates and HIV rates did not deviate from expected levels relative to other US counties with SEPs in the years before the clinic opening, which would otherwise cast doubt on the notion that the latter provide a good comparison group.[14] Moreover, I show results from models that partial out pre-treatment trends from the full panel, in an effort to construct outcome variables that are robust to county-specific linear trends while avoiding weighting issues present in some dynamic difference-in-differences model (Borusyak and Jaravel, 2017).

4 Main Results

4.1 HIV Diagnoses

To show the effects of SEP openings on HIV rates, I first present graphical analyses that correspond to the preferred difference-in-differences identification strategy. The top panel of Figure 1 plots the event study coefficient estimates and their corresponding 95% confidence intervals from Equation 2. Since every treated county has at least one year of data before the SEP opening in my sample, I estimate effects relative to the year before treatment, $t = -1$. Notably, estimates to the left of the vertical line are statistically indistinguishable from zero, providing some evidence to support the notion that trends in HIV rates were not diverging in the years before treatment. The top panel of Figure 1 also provides initial evidence that the HIV rate in counties with SEP openings did not change relative to other counties following an opening, although lagged estimates from the preferred specification are fairly imprecise.[15]

In Table 1, I provide model-based estimates from Equation 1. Column 1 shows the estimated effects from a baseline model which controls for year and county fixed effects. Estimates indicate that the introduction of a SEP reduced HIV diagnoses rates by 11.8 percent, corresponding to approximately 1 fewer HIV case per county per year, on average.

In Column 2, I present estimates after adding demographic and economic controls. Estimates are statistically similar to the ones in Column 1. Column 3 addresses the fact that other state-level policies affecting access to opioid prescriptions and the legal climate of drug paraphernalia changed during the sample period, 2008–2016, which could bias the results. To account for these changes, I control for time-varying indicator variables for states with prescription

[13] I use these years for my main analysis to keep comparisons between the mortality and HIV data similar. Below I also show estimates using a longer panel spanning 2003–2016 to provide more pre-period data where available. Since a majority of programs started after 2011, and because HIV data is not available before 2008, these additional years of pre-period data are not used for the main analyses.

[14] Notably, defining the SEP opening variable as a binary outcome implies that the estimates will pick up effects on the extensive margin. It may be worth also considering the intensive margin, i.e. effects for counties with multiple programs. However, when estimating effects for counties with existing programs that experienced an opening from 2009–2016, estimates are statistically similar to the main results. Therefore, I focus on all counties with openings in the remaining analyses.

[15] For figure of difference-in-differences estimates using a longer panel of pre-period data, comparing counties with SEP openings from 2003–2016 to those without SEPs, see Figure A4. I note that since HIV data from the CDC and many state agencies is not available prior to 2008, any estimates on HIV diagnoses should be taken with caution.

limits, tamper resistant prescription forms, ID requirements, prescription drug monitoring programs, good Samaritan laws, paraphernalia laws, and other physician requirements, including required verification, and exams. These estimates are slightly smaller than those in Column 1, implying that states with higher HIV rates are more likely to implement opioid-related policies. Due to the fact that state-level initiatives appear relevant in this context, in Column 4 I include state-by-year fixed effects to control for shocks common to areas within a state. Estimates are similar to those reported in Columns 2–3 and indicate a statistically significant decrease of 15.4 percent.

Column 5 includes county-specific linear time trends that account for pre-existing trends in HIV rates. These trends may be especially important to account for, if, for example, treated counties have different outcomes levels pre-adoption and are following a different trajectory than comparison counties prior to SEP adoption. Estimates in Columns 5 are smaller in magnitude than those in Columns 1–4. Based on these estimates, I cannot rule out reductions in HIV rates smaller than 13.1 percent.

In Table A2 I also present estimates controlling for a one-year leading indicator variable to more formally address the idea that the trends in HIV rates in treated and comparison counties are not diverging in the year prior to the SEP opening. Indeed, the estimate for the lead is statistically insignificant, providing some additional support for the identification assumption. Overall, these estimates provide weak evidence that, at the very least, SEPs do not seem to result in additional HIV diagnoses and may reduce them.

4.2 Opioid-Related Mortality

The findings presented above suggest that SEPs do not facilitate, and could reduce, the spread of HIV. If SEPs provide also drug counseling and resources for injection drug users to seek treatment, such programs could also discourage drug use and facilitate recovery. However, if SEPs lower the costs of using opioids, we would expect opioid use and–potentially–opioid-related mortality to increase. Below, I test to what extent opening a SEP affects drug- and opioid-related mortality.

I first present a graphical analysis of the effects of SEPs on opioid-related mortality over time. Figure 1 plots the difference-in-differences coefficient estimates from Equation 2, comparing changes in mortality in counties with a SEP opening to changes in mortality in counties without a SEP. Prior to the introduction of a SEP, estimates are all statistically similar to zero, indicating that opioid-related mortality trends in each group were not diverging prior to the program opening. In the first three years of the SEP, effects are positive and increase over time, indicating that deaths due to SEPs relative to other areas continue to trend even further upward during the height of the opioid crisis.

In Table 1, I expand on this analysis and display point estimates from Equation 1 for drug-related mortality, opioid-related mortality, and illicit opioid-related mortality, which specifically includes heroin- and synthetic opioid-related deaths. Notably, drug-related mortality includes all types of drug-related deaths, although opioid-related deaths

account for over 60 percent of this category.

Across Columns 1–5, estimates are consistent and indicate that SEPs increase drug-related mortality by 11.7–14.6 percent, corresponding to approximately 3 more drug-related deaths per county per year, on average. These effects are largely a result of increases in opioid-related, and, specifically, illicit opioid-related mortality. In particular, I find that SEPs increase opioid-related mortality by 23.2 percent, or about 3 more cases per county per year. Estimates for illicit opioid-related mortality are even larger, and indicate an increase of 37.4 percent, driven by fentanyl-related deaths.[16] In Figure A5 I further explore effects of SEPs on other drug-related mortality rates. Deaths due to methadone, a pain reliever and drug commonly used to treat opioid dependence, are relatively unresponsive to SEP openings, and may even fall slightly. However, I find that SEPs lead to large and increasing mortality rates for fentanyl. This drug is often laced with cocaine, which also experiences a similar, albeit smaller, increase.

For all outcomes, mortality rates in comparison counties appear to be tracking those in counties with SEP openings in the year prior to the opening (e.g. Table A2).[17,18]

These effects correspond to nearly 2.5 additional fentanyl-related deaths per county over the 0–7 years following a SEP opening, providing support for a stark conclusion: SEPs lead to greater risk of fatal opioid overdoses. Below, I additionally use other administrative datasets to fully explore potential mechanisms, including enrollments to substance abuse treatment facilities, migration, changes in drug potency over time, and non-fatal opioid-related hospitalizations that could provide further insight for these results.

In Table 2 and Figure A6, I present mortality estimates analogous to Table 1 Column 5 for county subgroups. Estimates are largest for rural counties and counties with relatively high poverty rates, suggesting that individuals with higher financial and transportation barriers are most affected by new SEP openings. In Figure A7, I present estimates by county population size, reinforcing the idea that opioid-related mortality is more responsive to SEP openings in low-population areas. I additionally present WLS estimates weighted by county population in Figure A8. These findings also support the notion that successfully providing harm reduction services in a rural area, where there is less access to substance abuse treatment and more stigma and networking barriers, may require additional resources to stymie opioid abuse.

These findings may be unsurprising, as a recent literature has documented that rural areas have prescription rates per capita that are double those of urban areas, have a higher rate of both mortality and opioid use disorder, and are associated with higher amounts of prescribed opioids (Guy Jr., Zhang, Bohm, Losby, Lewis, Young, Murphy, and Dowell, 2017; Goetz and Davlasheridze, 2017; Barocas, White, Wang, Walley, LaRochelle, Bernson, Land, Morgan,

[16] Heroin-related deaths are responsible for approximately 20 percent of the effect shown for illicit opioid-related mortality.

[17] Notably, estimates for natural opioids (T40.2), which are less likely to be injected than heroin or unnatural opioids, are positive but statistically insignificant at the 10 percent level. This suggests that injection opioids are driving the main findings.

[18] Given that drug-related deaths were increasing at an increasing rate after 2013, I have also considered specifications controlling for quadratic time trends. Estimates are similar to those in Column 5, and indicate a statistically insignificant decline in HIV rates of 2 percent and a statistically insignificant increase in opioid-related mortality rates of 13 percent ($p = 0.14$).

Samet, and Linas, 2018; Lund, Ohl, Hadlandsmyth, and Mosher, 2019; Blanco, Ali, Beswick, Drexler, Hoffman, Jones, Wiley, and Coukell, 2020), while maintaining limited access to medication-assisted treatment facilities and alternative therapies (Kvamme, Catlin, Banta-Green, Roll, and Rosenblatt, 2013; Andrilla, Moore, Patterson, and Larson, 2018). These existing disparities suggest that rural areas may be most in need of drug-related treatment services, and that SEPs may exacerbate drug use in areas with substantial barriers to substance use treatment and appropriate medical care.

5 Robustness Checks

To test the sensitivity of the main results, in Figure 2 I present estimates–ordered by magnitude–from over 100 empirical approaches that consider different samples, control and treatment groups, and functional form. Estimates for opioid-related mortality rates are always positive; they are statistically significant at the five-percent level in 76 of 105 specifications, and they are statistically significant at the ten-percent level in 86 specifications. When analyzing HIV rates, all but 10 of these 105 estimates are negative, and 24 are statistically significant at the ten-percent level, suggesting that my main HIV estimates are relatively conservative. (Notably, one reason estimates are relatively noisy for this measure may be because HIV diagnoses are a relatively rare event.)[19]

I also conduct permutation inference using placebo difference-in-differences estimates to provide more evidence that the observed effects are a result of the SEP opening and not an existing artifact of the data. To conduct the analysis, I randomly select a county from the main sample from 2008–2016, and assign it as a treated county with a randomly assigned treatment year, without replacement.[20] I then generate distributions of coefficients and their corresponding standard errors based on these difference-in-differences estimates, using the preferred specification associated with Column 5 Table 1, and present these distributions of beta coefficients in Figure A11. Only 1.1 percent of placebo coefficients are greater than the reported estimates for opioid-related mortality rates, which provides additional support for the idea that the SEP opening is driving these reported results.[21]

Moreover, because the effects for opioid-related mortality could be a result of population composition changes due to a SEP opening, in Figure A12 I investigate whether the treatment counties simultaneously experience increases

[19] For the event studies spanning 2003–2016, see Figure A4. For a graphical representation of estimates without county-specific trends, see Figure A9. For event-study graphs of the preferred specification using these alternative comparison groups, see Figure A10. In Table A3 I present estimates from the preferred specification using even more alternative comparison groups, including counties with existing SEPs (Column 3) and counties only in states that allow SEPs (Column 4), to provide comparison groups that may be more similar to treatment counties prior to adoption. In Columns 5 I also estimates from an approach comparing treatment counties to their border counties to account for the fact that migration of users to SEP locations is a potential threat to identification. All estimates for opioid-related mortality range from 14–23 percent. When including a leading indicator variable, estimates are statistically similar at the 5 percent level. For more information on how county-level observables affect the likelihood of a SEP opening, see Table A4. All estimates are statistically insignificant. Table A5 shows that the estimates are insensitive to the omission of counties with zero drug-related deaths.

[20] When randomly selecting a treatment county, I drop observations that would be included as a treatment county in my main analysis.

[21] Results are similar when requiring the distribution of placebo opening dates to be identical to the actual opening dates, and are even stronger when omitting county-specific linear trends. When accounting for pre-trends, the main estimate for HIV rates is smaller than 93.3 percent of all placebo coefficients.

in mortality rates from other causes, including vehicle-related and/or alcohol-related mortality, or total mortality. I find no statistically significant effects of SEP openings on any of these other mortality rates, implying that SEPs more directly affect outcomes related to drug use.[22]

Ideally, this analysis would also be able to speak to how SEPs affect rates of hepatitis C, another bloodborne illness that can be contracted through needle sharing. However, county-level data for hepatitis C are unavailable. When I estimate how SEPs affect state-level diagnoses of hepatitis C, estimates on the effects of SEPs on hepatitis C rates are small and close to zero, and I can rule out reductions greater than 0.03 percent. This is consistent with previous work suggesting that SEPs mostly address the spread of disease through the channel of reducing HIV and are ineffective at reducing hepatitis C (Pollack, 2001a,b).[23]

Finally, I consider the extent to which the dynamic two-way fixed-effects linear regression model leads to bias in this context. One way to do so, as suggested by Callaway and Sant'Anna (2020), is to compute the average treatment effect for each group, and then average across groups.[24] Estimates from this doubly robust procedure indicate a 17.8 percent increase in the opioid-related mortality rate. The effect size is statistically significant at the 1% level and statistically similar to the main results. Estimates by treatment year suggest that effects are largest for later adopters, which I investigate in further detail below.

In Table 3, I also show estimates from a model analogous to Equation 1 that partials out pre-treatment trends, as suggested by Goodman-Bacon (2018). To do so, I calculate residuals from a regression of demeaned variables for all counties and all years and then estimate Equation 1 using these residualized variables to avoid any bias resulting from estimating group specific trends off the full set of data. Estimates for HIV rates are similar across all columns and indicate statistically significant reductions ranging from 17.3–19.3 percent. These estimate magnitudes are in line with those from Columns 1–4 in Table 1, but are more precise. Mortality estimates are similar to the main results, and indicate a 20.5 percent increase in opioid-related mortality.

6 Potential Mechanisms

As noted above, the primary reason to believe that SEPs can reduce bloodborne illness while increasing drug-related mortality is through reduced social barriers or networking costs, costs of obtaining clean needles, and costs of finding more potent injection drugs. Although it is infeasible in this context to analyze drug use and drug networks directly, below I present evidence to address these possible contributing factors. On their own, each piece is insufficient to

[22] In Table A6 I additionally analyze whether SEPs affect other sexually transmitted infections (STIs) that is not contracted through needle sharing: chlamydia. I find no evidence that rates of chlamydia decrease after the introduction of a SEP. I similarly find no effects on gonorrhea.

[23] I additionally estimate no statistically significant effects of SEP openings on county-level HIV prevalence, indicating that any reduction in bloodborne illness by SEPs yields small aggregate effects.

[24] This sort of procedure provides an average treatment effect parameter with a very similar interpretation to the Average Treatment Effect on the Treated (ATT) in the two period and two group case.

tell the full story of why SEPs could have increased opioid-related mortality in recent years. However, together, they provide a collage of additional support to explain the main findings.

6.1 Substance Abuse Treatment Referrals

Because there is no national reporting system for SEPs or their clients, I cannot track how a SEP opening affects the number or composition of patients at each center. Nonetheless, in an attempt to speak to the daily activities of SEPs and visitor characteristics, in Table A7, I present 2018 visit-level data on client attributes and equipment and services received for a rural, Midwest SEP located in Portsmouth, Ohio. I note that these data are not representative of the entire US, but may shed light on program-level operations in an area of the country that has been largely affected by the opioid epidemic.

According to self-reported survey data, most users inject heroin, although those reporting having injected fentanyl has increased over time, which reflect trends in the general US population. Of those visiting the SEP, one-fifth have been diagnosed with hepatitis C, and 1 percent have been diagnosed with HIV. Despite the fact that SEPs offer drug counseling and referrals to substance treatment facilities, only 1 percent of clients in Portsmouth accepted a referral during the sample period. Therefore, clients are either not interested in treating their addiction, have little resources to afford medical care, and/or are not able to access facilities due to capacity constraints.[25] Data on client zip codes also shows that a majority of clients live in Portsmouth or West Portsmouth, traveling an average of 14 miles to access the SEP. This, paired with population data discussed earlier, indicates that SEP openings likely do not induce substantial migration across county lines.

6.2 Effects on Drug Potency

If SEP openings induce heroin users to increase their injection frequency, it is also possible that SEP visitors switch to more potent drugs, which may become available via new social networks. I analyze this possibility in light of the introduction of fentanyl to the US in 2013.

Above, I provide evidence that SEP openings have larger effects on fentanyl-related deaths compared to all opioid-related deaths (37 percent versus 23 percent). However, since fentanyl has only been available in the US since 2013 and because different types of counties may have adopted SEPs at different times, I additionally test the extent to which mortality rates for earlier adopters differ from later adopters and present these estimates in Table A9. Column 1 displays the baseline results, while Columns 2 and 3 separately show effects for counties with SEP openings between 2009–2012 and 2013–2016 separately. Splitting the sample yields less precise estimates; however, for both HIV rates

[25] This conclusion holds in urban areas as well. In Table A8 I analyze data from the Treatment Episode Data Set and present effects of a SEP opening in an urban area on admission rates to SAT facilities. I find no evidence that the presence of a SEP increases the likelihood of an individual entering treatment, likely due to excess demand and existing capacity constraints.

and opioid-related mortality rates, effects are driven by the later adopters. This suggests that counties that opened SEPs at the height of the opioid crisis during the availability of fentanyl may have had either more clients and/or clients using injection drugs at higher frequencies or more fatal doses.[26]

6.3 Effects on Opioid-Related Hospitalizations as a Proxy for Drug Use

Despite the fact that mortality data is able to capture one measure of opioid misuse, the above effects may not be picking up drug *usage* if users are injecting more frequently but not at fatal doses. To explore the more comprehensive effects of SEPs on drug use, I use data on drug-related emergency room visits and in-patient stays from the Healthcare Cost and Utilization Program (HCUP) State Emergency Department Databases (SEDD) and State Inpatient Databases (SID). One limitation of these publicly available data are that they are at the state level, which does not allow for a county-level analysis.[27,28]

In Figure A14 and Table A10, I provide state-level difference-in-differences estimates showing the effects of the opening of a SEP in a state on the rate of opioid-related emergency department (ED) admissions and in-patient stays. Effects are positive and grow over time. Given that 12.1 percent of ED admits die before or while receiving treatment, these estimates imply an additional 3.6 drug-related deaths per county, on average, which is similar to the magnitudes reported above. Moreover, when allowing for treatment to account for the number of SEPs in a given state over time, estimates are similarly positive and indicate a 4.0 percent increase in emergency room admissions.

In other words, these findings suggest that SEPs increase emergency visits at ten times the rate that they increase opioid-related mortality. To the extent that SEPs connect users to life-saving technology, such as naloxone, or introduce ways to recognize overdose and encourage calling for help, then any increase in emergency room visits may represent a reduction in opioid-related deaths that would have occurred otherwise. Therefore, my results provide some evidence that SEPs help the marginal client from fatal overdose, but are unable to reverse addiction.[29]

Taken together, the findings suggest that while SEPs may lead to a reduction in diseases spread by needle sharing, lowering the cost of obtaining clean needles and other supplies unintentionally encourages more drug use, leading to more opioid-related overdoses. While many of these overdoses can be reversed in the ED, SEPs do little to prevent mortality rates from rising in subsequent years. These effects become more pronounced over time, indicating that any future cost-benefit analyses of SEPs should consider effects at least 2–4 years after the introduction of the program.

[26] This is consistent with the Callaway and Sant'Anna estimates discussed earlier, which show positive treatment effects for later treatment groups (e.g. post-2010).

[27] HCUP does not contain data on every state. In particular, I drop Colorado, Louisiana, Michigan, New Mexico, Oregon, Pennsylvania, Texas, Washington, and West Virginia for this analysis.

[28] I have also considered analyzing opioid-related crimes, which also serves as a proxy for drug use. Using FBI Uniform Crime Report arrest data, I find that opioid-related possession arrests increase by 12.7–28.0 percent after the opening of a SEP. See Figure A13.

[29] Indeed, estimates by hospital condition, shown in Figure A15 are consistent with this notion. At-home drug-related mortality rates and mortality rates for those reaching the ER did not experience a large increase after a SEP opening.

7 Conclusion

In this paper, I document the effects of expanding access to clean needles and opioid-related counseling through syringe exchange programs. Using a newly compiled dataset on HIV cases and drug-related mortality, I compare health outcomes in counties that experienced a SEP opening from 2009–2016 to counties without a SEP. Consistent with the existing literature, I find that SEPs do not increase HIV cases, and could reduce HIV diagnoses by up to 18.2 percent. However, I present new evidence that a SEP opening corresponds to an average increase in drug-related mortality by 11.7 percent and opioid-related mortality by 23.2 percent, and that these effects are driven by increases in injection drugs, like heroin and fentanyl. Moreover, I provide some evidence that opioid-related emergency room visits increase after the opening of a SEP.

Overall, these estimates correspond to almost 4 more drug-related deaths per county each year, or over 6,000 drug-related deaths across the US. Effects are concentrated in rural and high-poverty areas, suggesting that low-income individuals living in areas with fewer health care resources may face larger hurdles in obtaining drug counseling and/or substance abuse treatment.

Importantly, the primary goal of SEPs is to provide clean supplies to injection drug users in a safe environment with the intent of reducing needle sharing, while drug counseling and treatment referral are secondary services. Given the aims of harm reduction services, it is perhaps unsurprising that SEPs are more effective at preventing the spread of bloodborne illness than reducing opioid dependence. Given the well-documented benefits of substance abuse treatment facilities and medication-assisted treatment clinics (Swensen, 2015; Bondurant, Lindo, and Swensen, 2018), my findings suggest that providing funding for and increasing access for other types of directed medical care may be a more fruitful avenue for reducing drug-related mortality.

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Table 1: The Effect of a Syringe Exchange Program on HIV Diagnoses Rates and Drug-Related Mortality Rates, Difference-in-Differences Estimates Using Counties Without a SEP for Comparison

	(1)	(2)	(3)	(4)	(5)
HIV Diagnoses					
Average Effect of SEP	-0.736*	-0.641	-0.508	-0.958**	0.020
	(0.430)	(0.424)	(0.440)	(0.407)	(0.420)
Mean	6.24	6.24	6.24	6.24	6.24
Observations	14094	14094	14094	14094	14094
Drug-Related Mortality (X40–44)					
Average Effect of SEP	2.373**	2.442**	2.128*	1.946**	1.958*
	(1.133)	(1.123)	(1.111)	(0.971)	(1.030)
Mean	16.68	16.68	16.68	16.68	16.68
Observations	14121	14121	14121	14121	14121
Opioid-Related Mortality (T40.0–40.4 and T40.6)					
Average Effect of SEP	2.623**	2.739**	2.335**	2.116**	2.267**
	(1.084)	(1.083)	(1.062)	(0.915)	(0.959)
Mean	9.78	9.78	9.78	9.78	9.78
Observations	14121	14121	14121	14121	14121
Illicit Opioid-Related Mortality (T40.1 and T40.4)					
Average Effect of SEP	3.458***	3.495***	2.957***	2.512***	1.390**
	(1.033)	(1.030)	(0.999)	(0.809)	(0.666)
Mean	3.72	3.72	3.72	3.72	3.72
Observations	14121	14121	14121	14121	14121
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Demographic and Economic Controls	No	Yes	Yes	Yes	Yes
State-Level Policy Controls	No	No	Yes	No	No
State-by-Year Fixed Effects	No	No	No	Yes	Yes
County-Specific Linear Time Trends	No	No	No	No	Yes

Notes: Estimates are based CDC and state agency data on HIV diagnoses counts by county for the entire United States from 2008–2016 and NCHS restricted mortality files by county for the entire United States from 2008–2016. Rates are calculated as cases per 100,000 individuals. South Dakota does not report HIV diagnoses to the CDC in any year and is dropped for the HIV analysis. Economic control variables include the county-level poverty rate and unemployment rate, demographic controls include percent Hispanic and percent black, and state-level policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the county level.
*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table 2: The Effect of a Syringe Exchange Program on HIV Diagnoses Rates and Opioid-Related Mortality Rates by Subgroup

	Counties W/Out SEPs	**Urban Counties**	**Rural Counties**	**Low Pov. Counties**	**High Pov. Counties**
	(1)	(2)	(3)	(4)	(5)
HIV Rate					
Average Effect of SEP	-0.001	0.535	-0.799*	-0.548	0.709
	(0.420)	(0.643)	(0.477)	(0.483)	(.)
Mean	6.23	9.08	4.32	5.05	7.81
Observations	14094	5643	8451	8073	6021
Opioid-Related Mortality Rate					
Average Effect of SEP	2.267**	1.210	3.012**	1.055	3.475***
	(0.959)	(1.189)	(1.479)	(0.983)	(0.000)
Mean	9.78	9.46	9.99	8.98	10.85
Observations	14121	5643	8478	8100	6021
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Demographic and Economic Controls	Yes	Yes	Yes	Yes	Yes
State-by-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
County-Specific Linear Time Trends	Yes	Yes	Yes	Yes	Yes

Notes: See Table 1. Data on urbanicity is from the USDA. “Counties W/Out SEPs" represents the baseline sample, comparing counties with SEP openings to counties without SEPs. “Urban" counties include metropolitan areas, while “Rural" counties include micropolitan areas, small towns, and rural areas. “High Pov." counties are defined as counties with average poverty rates above their state median poverty rate. “Low Pov." counties are those with average poverty rates at or below this median. All specifications limit the sample to include counties with new SEPs or counties without SEPs.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

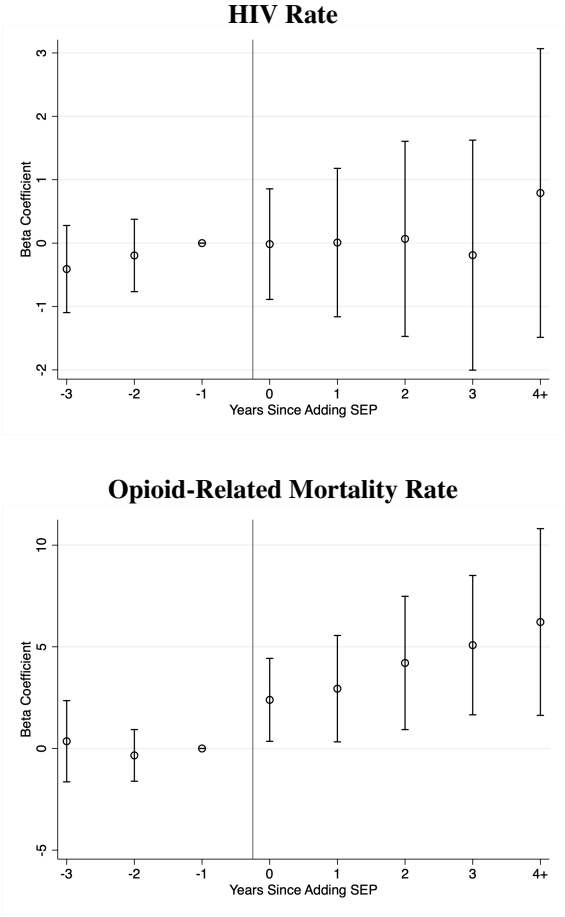
Table 3: The Effect of a Syringe Exchange Program on HIV Diagnoses Rates and Opioid-Related Mortality Rates, Accounting for Pre-Trends

	(1)	(2)	(3)	(4)	(5)
HIV Rate					
Average Effect of SEP	-1.188***	-1.127***	-1.074***	-1.071***	-1.060**
	(0.405)	(0.390)	(0.392)	(0.392)	(0.429)
One-Year Lead					0.041
					(0.392)
Mean	6.14	6.14	6.14	6.14	6.14
Observations	14085	14085	14085	14085	14085
Opioid-Related Mortality Rate					
Average Effect of SEP	1.873**	1.920**	1.981**	2.010**	2.145**
	(0.914)	(0.911)	(0.911)	(0.913)	(1.023)
One-Year Lead					0.513
					(0.804)
Mean	9.79	9.79	9.79	9.79	9.79
Observations	14085	14085	14085	14085	14085
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Demographic and Economic Controls	No	Yes	Yes	Yes	Yes
State-by-Year Fixed Effects	No	No	No	Yes	Yes

Notes: See Table 1. Estimates are from a model analogous to Equation 1 that partials out pre-treatment trends.

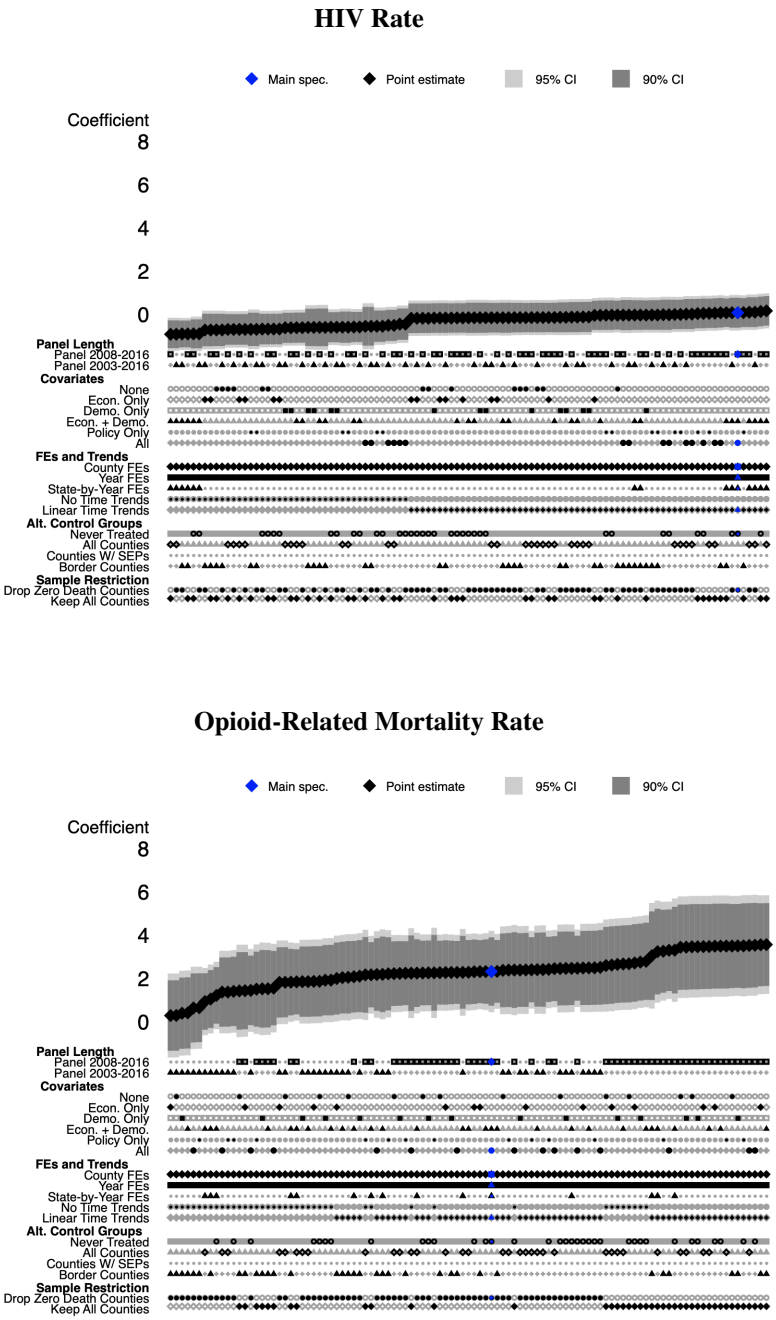
*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Figure 1: Event Study Estimates of the Effect of Opening a
Syringe Exchange Program on HIV Diagnoses Rates and Opioid-Related Mortality Rates



Notes: Each figure displays the coefficients and their respective 95% confidence intervals for the leading indicators and lagged treatment effects from OLS regressions, as specified in Equation 2, and include economic and demographic controls, county and year fixed effects, state-by-year fixed effects, and county-specific linear time trends. The vertical line represents the first year during the sample period that a county experienced a syringe exchange program opening. Estimates are based on restricted mortality files by county for the entire United States from 2008–2016 and HIV diagnoses rates from the Center for Disease Control and Prevention's NCHHSTP Atlas and 34 state agencies. Economic control variables include the county-level poverty rate and unemployment rate, and demographic controls include percent Hispanic and percent black. Standard errors are clustered at the county level.

Figure 2: Specification Chart, Effects of SEP Openings on Opioid-Related Mortality and HIV Diagnoses Rates



Notes: Each figure displays the coefficients and their respective 95% confidence intervals for the leading indicators and lagged treatment effects from OLS regressions, based on variations of Equation 1, using the denoted panel years, covariates, fixed effects, trends, and comparison groups. Estimates are based on restricted mortality files by county for the entire United States from 2008–2016 and HIV diagnoses rates from the Center for Disease Control and Prevention's NCHHSTP Atlas and 34 state agencies. Economic control variables include the county-level poverty rate and unemployment rate, demographic controls include percent Hispanic and percent black, and state-level policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the county level.

Appendix A. Additional Tables and Figures

Table A1: Summary Statistics

	Treated Counties *(N=79)*	**Comparison Counties** *(N=1,491)*
County-Level Variables		
HIV and Mortality Rates		
HIV Diagnoses	10.78	5.82
Drug-Related Mortality	18.85	16.57
Opioid-Related Mortality	12.34	9.85
Illicit Opioid-Related Mortality	5.35	3.53
County Characteristics		
Population	552762	137196
Rural	0.35	0.60
Percent Poverty Rate	17.21	15.96
Unemployment Rate	7.59	8.10
Percent Hispanic	0.12	0.07
Percent Black	0.12	0.09
State-Level Variables		
Opioid-Related Hospitalization Rates		
Emergency Department Admissions	172.61	146.59
In-Patient Hospital Visits	250.40	219.14
Policy Indicators		
Prescription Limits	0.97	0.98
Tamper-Resistant Prescription	0.67	0.50
ID Requirement	0.37	0.45
Doctor Shopping Restrictions	0.29	0.31
Physician Exam Requirements	0.70	0.77
Pain Clinic Regulations	0.56	0.15
Pharmacist Verification	0.30	0.45
Paraphernalia Laws	0.25	0.39
Good Samaritan Laws	0.40	0.27
Prescription Drug Monitoring Program	0.83	0.79
Naloxone Laws	0.30	0.25

Notes: Data for all outcome and control variables span 2008–2016. Data on HIV diagnoses is from the CDC NCHHSTP Atlas and 34 state agencies. Drug-related deaths are based on the National Center for Health Statistics (NCHS), Division of Vital Statistics Mortality Files. Unemployment rates are from the BLS. State-by-year opioid-related hopsitalizations data are from the Healthcare Cost Utilization Project (HCUP). Information on state-level policy changes is from Meara, Horwitz, Powell, McClelland, Zhou, O'Malley, and Morden (2016), Doleac and Mukherjee (2018), and the LawAtlas Policy Surveillance Program. Column 1 shows the means for treated counties in the sample, i.e., counties with a syringe exchange program opening from 2009–2016. Column 2 displays the means for the comparison counties, i.e., other US counties without a syringe exchange program. Rates are calculated as cases per 100,000 individuals.

Table A2: Testing the Divergence of Trends in the Year Prior to an Opening

	HIV Rate	**Drug-Related Mortality Rate**	**Opioid-Related Mortality Rate**	**Illicit Opioid-Related Mortality Rate**
	(1)	(2)	(3)	(4)
Average Effect of SEP	0.338	3.130**	2.698**	1.516*
	(0.471)	(1.514)	(1.332)	(0.844)
One-Year Lead	0.470	1.729	0.636	0.185
	(0.373)	(1.254)	(1.028)	(0.624)
Mean	6.24	16.68	9.78	3.72
Observations	14094	14121	14121	14121
County and Year Fixed Effects	Yes	Yes	Yes	Yes
State-by-Year Fixed Effects	Yes	Yes	Yes	Yes
County-Specific Linear Time Trends	Yes	Yes	Yes	Yes

Notes: See Table 1. “One-year lead" represents an indicator variable equal to one in the year prior to an SEP opening and zero otherwise.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table A3: The Effect of a Syringe Exchange Program on HIV Diagnoses Rates and Opioid-Related Mortality Rates Using Various Comparison Groups

	Counties W/Out SEPs	**All Counties**	**Counties W/ SEPs**	**Counties in SEP States**	**Border Counties**
	(1)	(2)	(3)	(4)	(5)
HIV Rate					
Average Effect of SEP	0.020	0.045	-0.020	0.056	-0.088
	(0.420)	(0.418)	(0.454)	(0.416)	(0.415)
Mean	6.24	6.34	8.03	5.51	6.47
Observations	14094	14922	3186	10917	4248
Opioid-Related Mortality Rate					
Average Effect of SEP	2.267**	2.195**	1.750*	2.203**	2.027**
	(0.959)	(0.949)	(0.954)	(0.946)	(1.001)
Mean	9.78	9.85	12.47	10.68	8.96
Observations	14121	14949	3186	10917	4248
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Demographic and Economic Controls	Yes	Yes	Yes	Yes	Yes
State-Level Policy Controls	Yes	Yes	Yes	Yes	Yes
State-by-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
County-Specific Linear Time Trends	Yes	Yes	Yes	Yes	Yes

Notes: See Table 1. “Counties W/Out SEPs" represent the baseline results comparing counties with SEP openings to those without SEPs, “All Counties" represents a full sample of US counties comparing counties with recent SEP openings to all other US counties, “Counties W/ SEPs" compares counties with recent SEPs openings to counties in the US with an existing SEP, “Counties in SEP States" represents a subsample of all counties in US states with legal access to SEPs, and “Border Counties" shows estimates from a model comparing counties with SEP openings to their respective bordering counties.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table A4: Testing the Likelihood of A County Opening a SEP, Based on Economic and Demographic Characteristics

	Poverty Rate	**Unemployment Rate**	**Percent Hispanic**	**Percent Black**
	(1)	(2)	(3)	(4)
Average Effect of SEP	0.083	0.106	-0.000	-0.000
	(0.239)	(0.085)	(0.000)	(0.000)
Mean	16.10	7.61	0.08	0.10
Observations	14130	14130	14121	14121
County and Year Fixed Effects	Yes	Yes	Yes	Yes
State-by-Year Fixed Effects	Yes	Yes	Yes	Yes
County-Specific Linear Time Trends	Yes	Yes	Yes	Yes

Notes: See Table 1. Outcome variables include each of the demographic and economic controls included in the main analysis and are listed at the top of each column. Standard errors are clustered at the county level.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table A5: The Effect of a Syringe Exchange Program on HIV and Drug-Related Mortality Rates, Difference-in-Differences Estimates Using Counties Without a SEP for Comparison, Including Counties with No Opioid-Related Deaths

	(1)	(2)	(3)	(4)	(5)
HIV Rate					
Average Effect of SEP	-0.866**	-0.823**	-0.730*	-0.712*	-0.124
	(0.410)	(0.398)	(0.406)	(0.409)	(0.400)
Mean	5.03	5.03	5.03	5.03	5.03
Observations	26721	26721	26721	26721	26721
Opioid-Related Mortality					
Average Effect of SEP	4.281***	4.290***	3.651***	3.729***	3.549***
	(1.203)	(1.201)	(1.183)	(1.179)	(1.192)
Mean	7.15	7.15	7.15	7.15	7.15
Observations	27306	27306	27306	27306	27306
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Demographic and Economic Controls	No	Yes	Yes	Yes	Yes
State-Level Policy Controls	No	No	Yes	No	No
State-by-Year Fixed Effects	No	No	No	Yes	Yes
County-Specific Linear Time Trends	No	No	No	No	Yes

Notes: Estimates are based on NCHS restricted mortality files by county for the entire United States from 2008–2016. Rates are calculated as cases per 100,000 individuals. Economic control variables include the county-level poverty rate and unemployment rate, demographic controls include percent Hispanic and percent black, and state-level policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the county level.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table A6: The Effect of a Syringe Exchange Program on Chlamydia Rates, Difference-in-Differences Estimates using Counties Without SEPs for Comparison

	(1)	(2)	(3)	(4)	(5)
Average Effect of SEP	-9.821	-7.589	-6.811	-6.517	-6.902
	(11.028)	(11.039)	(10.989)	(10.952)	(10.110)
Mean	351.17	351.17	351.17	351.17	351.17
Observations	14948	14948	14948	14948	14948
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Demographic and Economic Controls	No	Yes	Yes	Yes	Yes
State-Level Policy Controls	No	No	Yes	No	No
State-by-Year Fixed Effects	No	No	No	Yes	Yes
County-Specific Linear Time Trends	No	No	No	No	Yes

Notes: Estimates are based on CDC NCHHSTP Atlas data on county-level rates of chlamydia for the entire United States from 2008–2016. Economic control variables include the county-level poverty rate and unemployment rate, demographic controls include percent Hispanic and percent black, and state-level policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the county level.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table A7: Summary Statistics for a Rural Midwest Syringe Exchange Program

Client Characteristics	**Mean**	**St.Dev.**
Number of Clients Per Week	144.59	30.27
Age	37.84	10.13
Percent White	0.97	0.18
Percent Male	0.59	0.49
First Injection Age	27.14	10.25
Previously Sought Addiction Treatment	0.22	0.41
Percent Ever Overdosed	0.32	0.47
Number of Times Overdosed	3.42	4.83
Proportion Injected Heroin at First Use	0.49	0.50
Proportion Injected Opioid Pills at First Use	0.29	0.46
Proportion Prescribed Opioid Pain Pills	0.26	0.44
Proportion Carry Naloxone	0.67	0.47
Visit Characteristics		
First Exchange	0.22	0.42
Number of Syringes Exchanged	30.15	11.49
Proportion Inject Heroin	0.80	0.40
Proportion Inject Fentanyl	0.16	0.37
Proportion Inject Opioid Pills	0.02	0.15
Proportion Diagnosed with HIV	0.01	0.07
Proportion Diagnosed with Hepatitis C	0.21	0.41
Proportion Given a Referral	0.01	0.07
Proportion Given Naloxone	0.14	0.34
Proportion Received HIV Education	0.14	0.35
Distance Traveled, in Miles	14.52	40.37

Notes: Data is from the Portsmouth syringe exchange program from 2018.

Table A8: The Effect of a Syringe Exchange Program on Admission Rates to Substance Abuse Treatment Facilities

	Total	**Opioids**	**Heroin**	**Painkillers**
	(1)	(2)	(3)	(4)
Average Effect of SEP	-264.140	-70.927	-56.799	46.761
	(282.963)	(94.827)	(69.840)	(44.210)
Mean	1120.53	345.10	196.79	359.95
Observations	4680	4680	4680	2273
County and Year Fixed Effects	Yes	Yes	Yes	Yes
Demographic and Economic Controls	Yes	Yes	Yes	Yes
State-by-Year Fixed Effects	Yes	Yes	Yes	Yes
County-Specific Linear Time Trends	Yes	Yes	Yes	Yes

Notes: See Table 1. Estimates are from Equation 1, using substance abuse treatment facility admissions rates for each of the listed outcomes. Data is from the Treatment Episode Data Set from 2008-2016 for urban core-based statistical areas (matched to counties). Standard errors are clustered at the county level.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Table A9: The Effect of a Syringe Exchange Program on HIV Diagnoses Rates and Opioid-Related Mortality Rates, by Treatment Year

Treated Year (# Treated Counties)	**2009–2016** ($n = 79$)	**2009–2012** ($n = 24$)	**2013–2016** ($n = 55$)
	(1)	(2)	(3)
HIV Rate			
Average Effect of SEP	-0.046	0.057	-0.074
	(0.422)	(0.785)	(0.503)
Mean	6.20	6.35	5.80
Observations	14094	13599	13878
Opioid-Related Mortality Rate			
Average Effect of SEP	2.419***	0.137	3.349***
	(0.911)	(1.012)	(1.191)
Mean	9.78	8.40	11.37
Observations	14121	13626	13905
County and Year Fixed Effects	Yes	Yes	Yes
Demographic and Economic Controls	Yes	Yes	Yes
State-Level Policy Controls	Yes	Yes	Yes

Notes: See Table 1. "Treated Year" represents the first year a county experiences a SEP opening. Column 1 displays the main estimates for counties with an opening between 2009–2016, while Column 2 displays estimates comparing counties with an opening between 2009–2012 to counties without a SEP and Column 3 displays estimates comparing counties with an opening between 2013–2016 to counties without a SEP.

*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

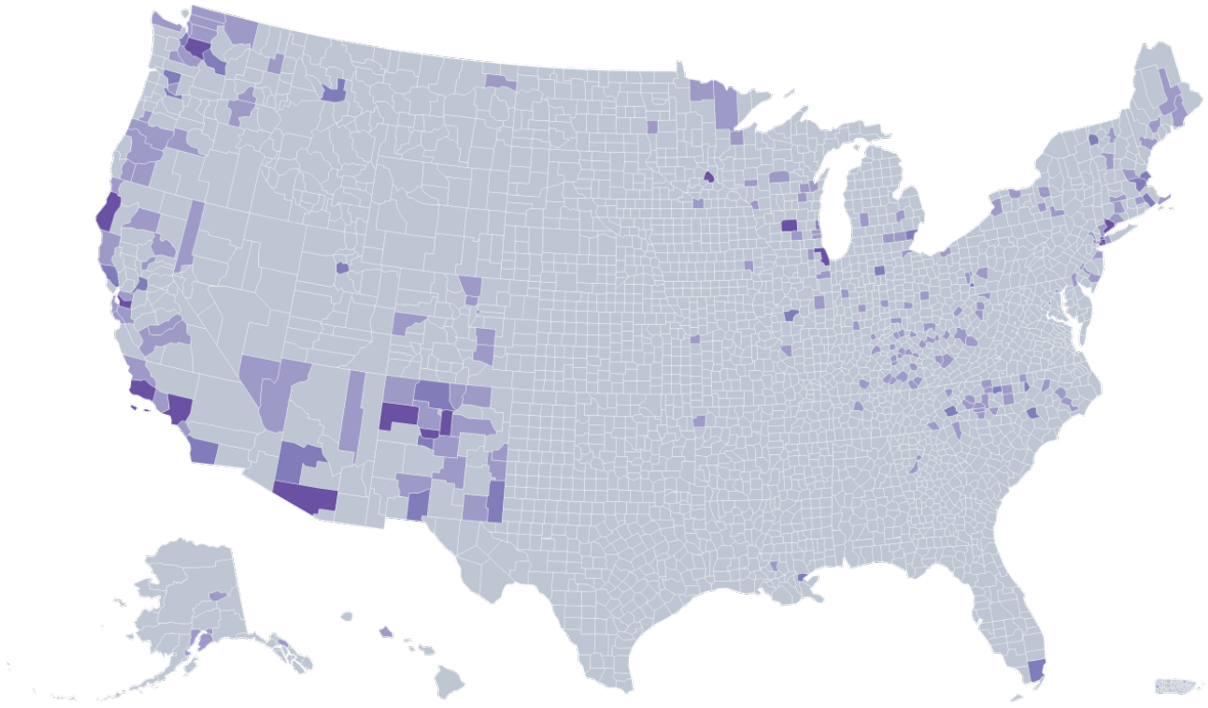
Table A10: The Effect of a Syringe Exchange Program on Opioid-Related Hospital Visits, Difference-in-Differences Estimates using States Without SEPs for Comparison

	(1)	(2)	(3)
Emergency Room Admission Rate			
Average Effect of SEP* Number of SEPs	8.117***	8.207***	6.479***
	(2.285)	(2.252)	(1.943)
Mean	150.75	150.75	150.75
Observations	258	258	258
In-Patient Stay Rate			
Average Effect of SEP* Number of SEPs	4.797***	4.801***	3.420**
	(1.341)	(1.277)	(1.374)
Mean	209.26	209.26	209.26
Observations	375	375	375
County and Year Fixed Effects	Yes	Yes	Yes
Demographic and Economic Controls	No	Yes	Yes
State-Level Policy Controls	No	No	Yes

Notes: Estimates are based on state-level opioid-related emergency room visits from the Healthcare Cost Utilization Project for 2008–2016. Rates are calculated as cases per 100,000 individuals. The treatment variable indicates the number of SEP openings in a given state. Economic control variables include the state-level poverty rate and unemployment rate, demographic controls include percent Hispanic and percent black, and policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the state level.

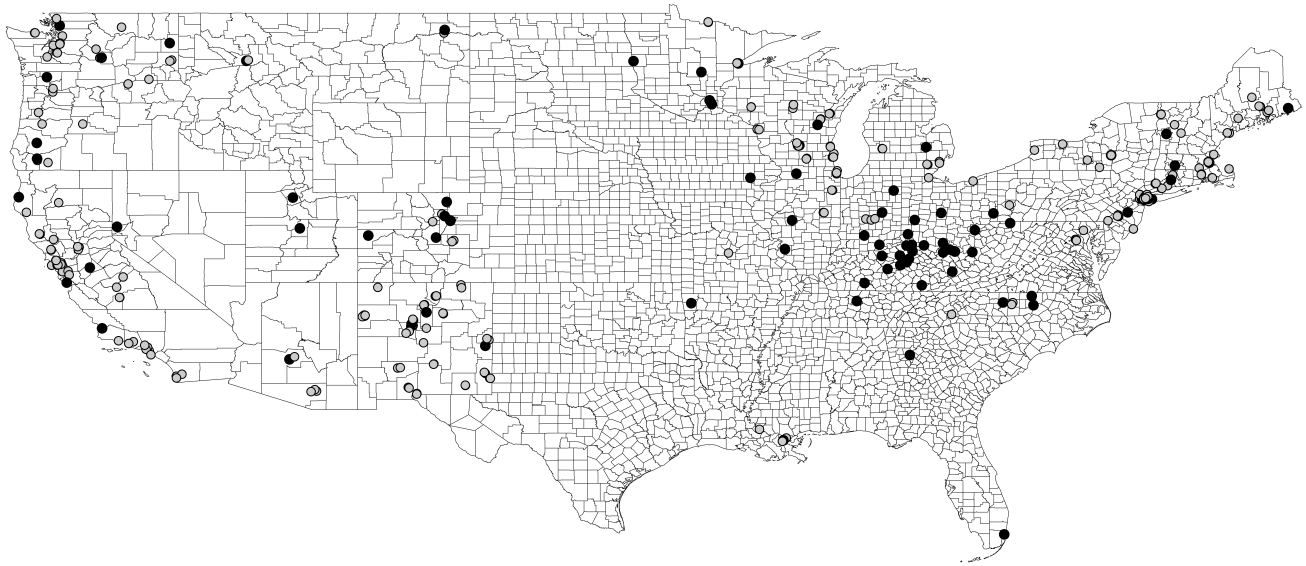
*, **, and *** indicate statistical significance at the ten, five, and one percent levels, respectively.

Figure A1: County-Level Locations of SEPs



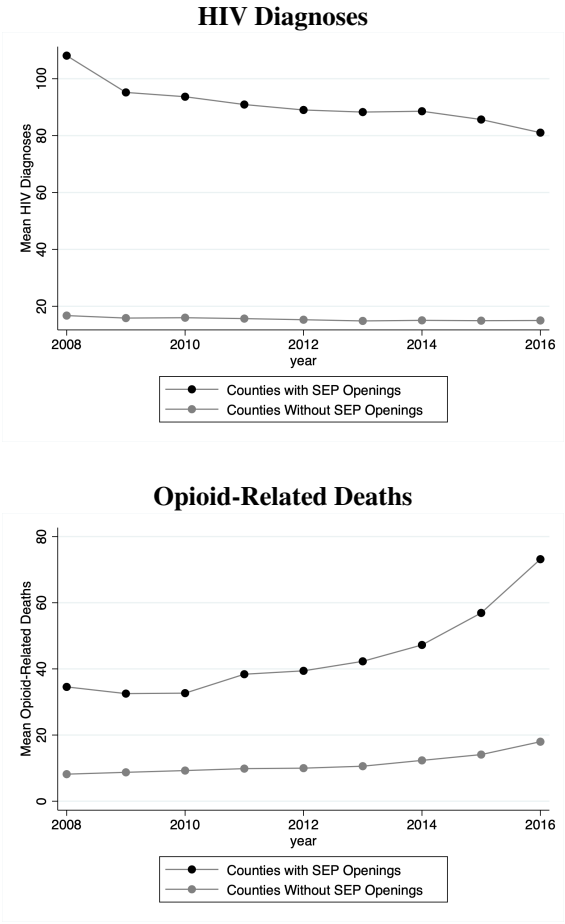
Notes: Geocoded data on SEP location by county is from NASEN. Shaded counties represent those with SEPs as of 2016.

Figure A2: Locations of Existing SEPs and Recent SEP Openings



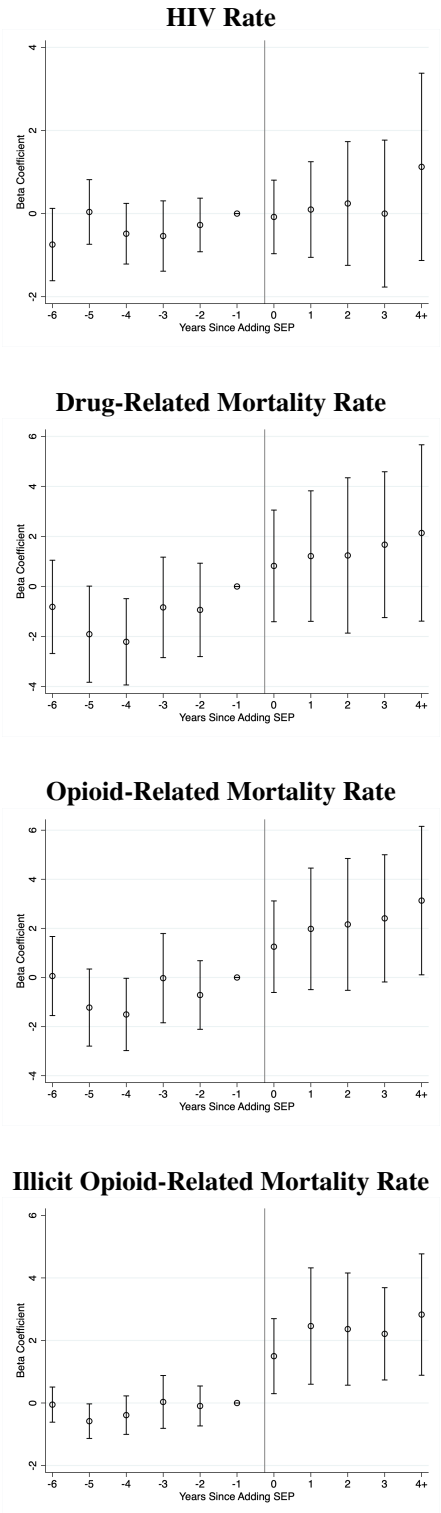
Notes: Geocoded data on SEP location is from the NASEN directory. Darker shaded circles represent SEPs opened between 2009–2016. Lighter shaded circles represent SEPs opened prior to 2009.

Figure A3: Trends in HIV Diagnoses and Opioid-Related Deaths in Counties with SEP Openings and Counties Without SEPs



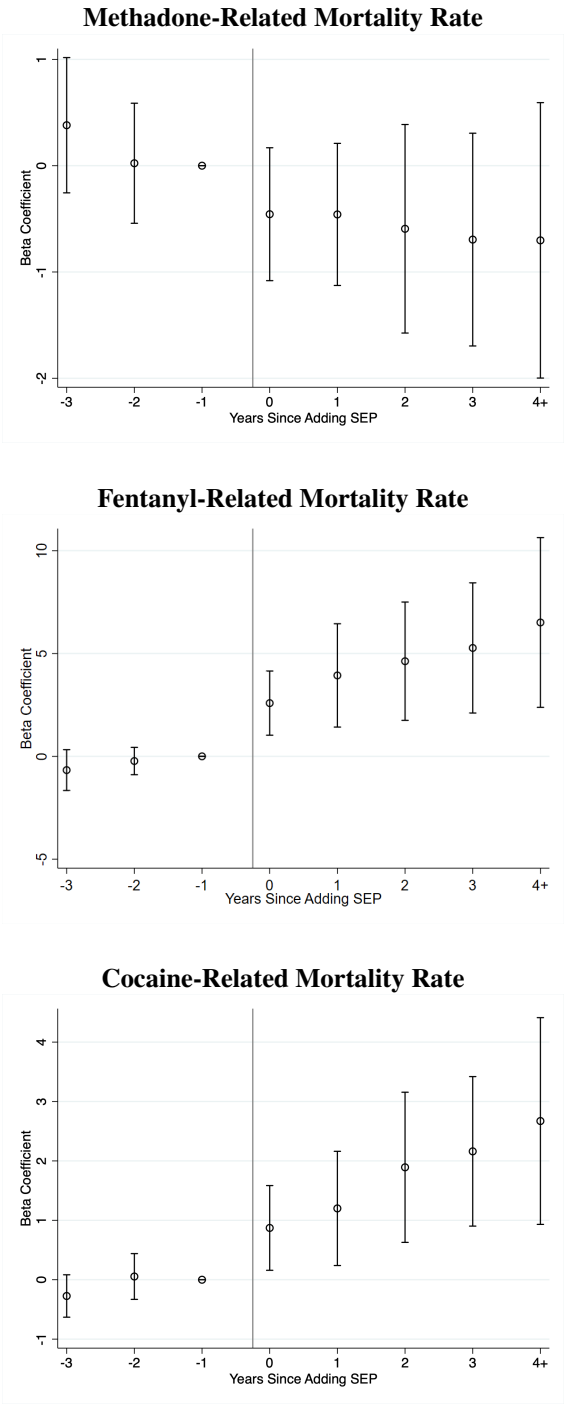
Notes: Each point displays the county-level means of the listed outcome variable in each year. The black line represents means for counties with SEP openings between 2008–2016, while the gray line represents means for counties that never experienced a SEP opening. Estimates are based on restricted mortality files by county for the entire United States from 2008–2016 and HIV diagnoses from the Center for Disease Control and Prevention's NCHHSTP Atlas and 34 state agencies.

Figure A4: Event Study Estimates of the Effect of Opening a Syringe Exchange Program, Using Data from 2003–2016



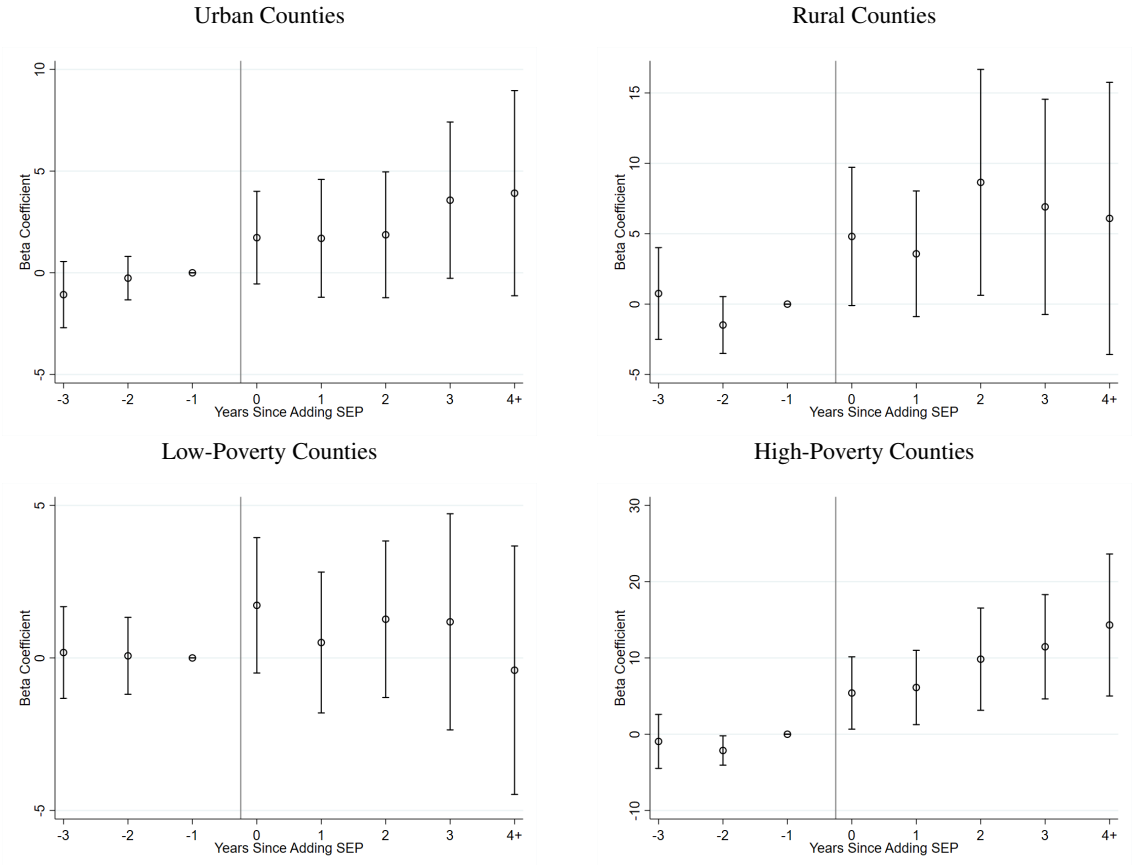
Notes: See Figure 1. Estimates are based on restricted mortality files for the entire United States from 2003–2016.

Figure A5: Event Study Estimates of the Effect of Opening a Syringe Exchange Program on Other Drug-Related Mortality Rates



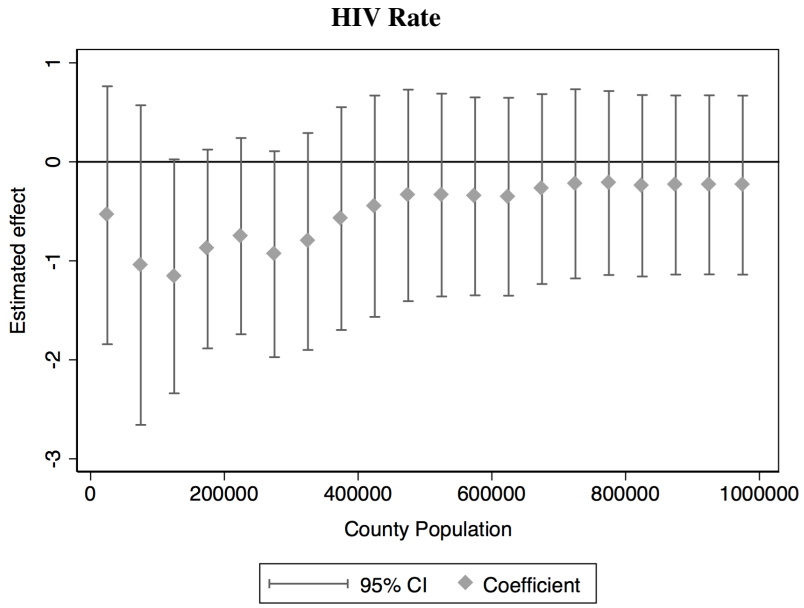
Notes: See Figure 1. Each mortality rate includes multiple cause of death diagnoses (e.g. cocaine-related deaths may also be categorized as opioid-related deaths, if both drugs were present during the toxicology screening). Cocaine is recorded in over 55 percent of fentanyl deaths.

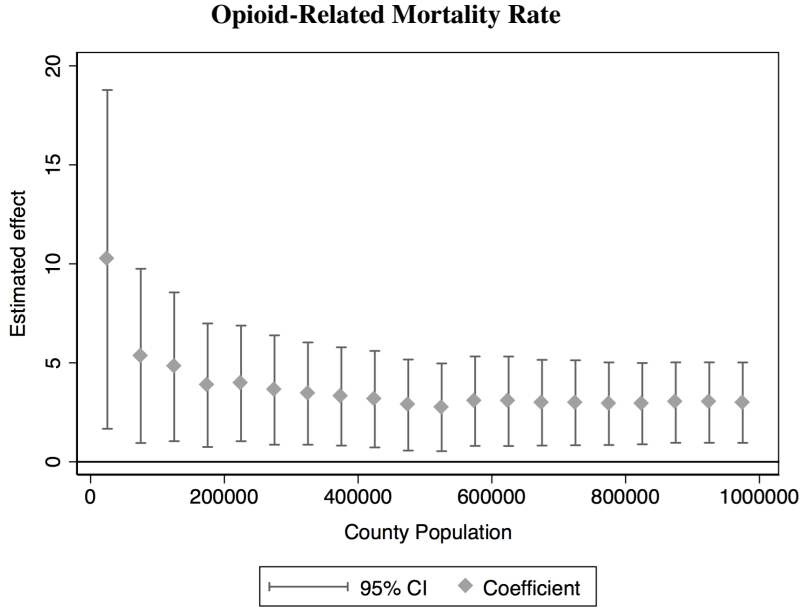
Figure A6: Event Study Estimates of the Effect of Opening a
Syringe Exchange Program on Opioid-Related Mortality Rates, by County Subgroup



Notes: See Figure 1. Data on urbanicity is from the USDA. “Urban" counties include metropolitan areas, while “Rural" counties include micropolitan areas, small towns, and rural areas. “High-Poverty" counties are defined as counties with average poverty rates above their state 2016 median poverty rate. “Low-Poverty" counties are those with average poverty rates at or below this median.

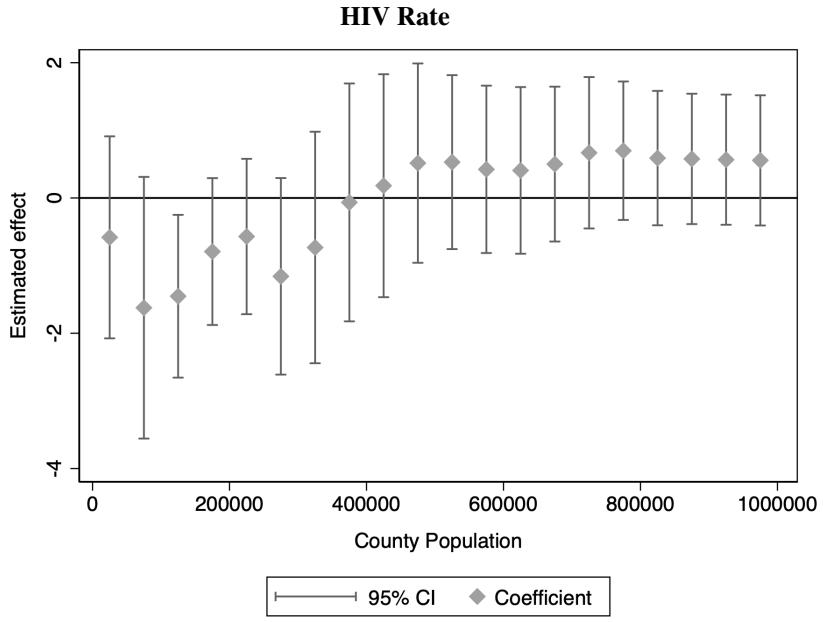
Figure A7: Difference-in-Differences Estimates for HIV Rates and Opioid-Related Mortality Rates by County Population Size

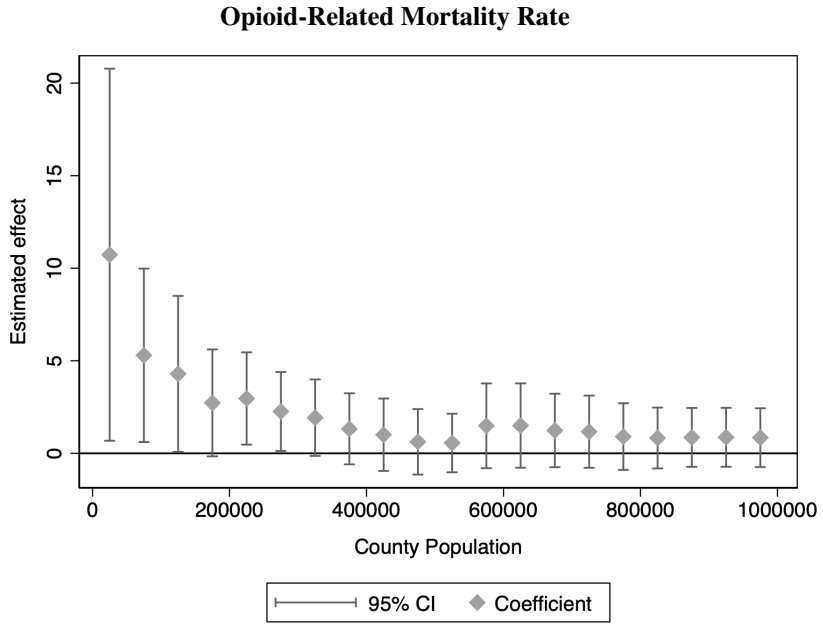




Notes: Each figure displays the coefficients and their respective 95% confidence intervals for the effects from OLS regressions, as specified in Equation 2, by population size. A x-axis value of "i" where $i = 25,000, 75,000, 125,000, ...1,000,000$ indicates an estimate from a difference-in-differences analysis comparing health outcomes in treated and comparison counties with less than i individuals. Estimates are based on restricted mortality files and CDC HIV diagnoses counts by county for the entire United States from 2008–2016. HIV diagnoses rates are from the Center for Disease Control and Prevention's NCHHSTP Atlas and 34 state agencies. Economic control variables include the county-level poverty rate and unemployment rate and demographic controls include percent Hispanic and percent black. Standard errors are clustered at the county level.

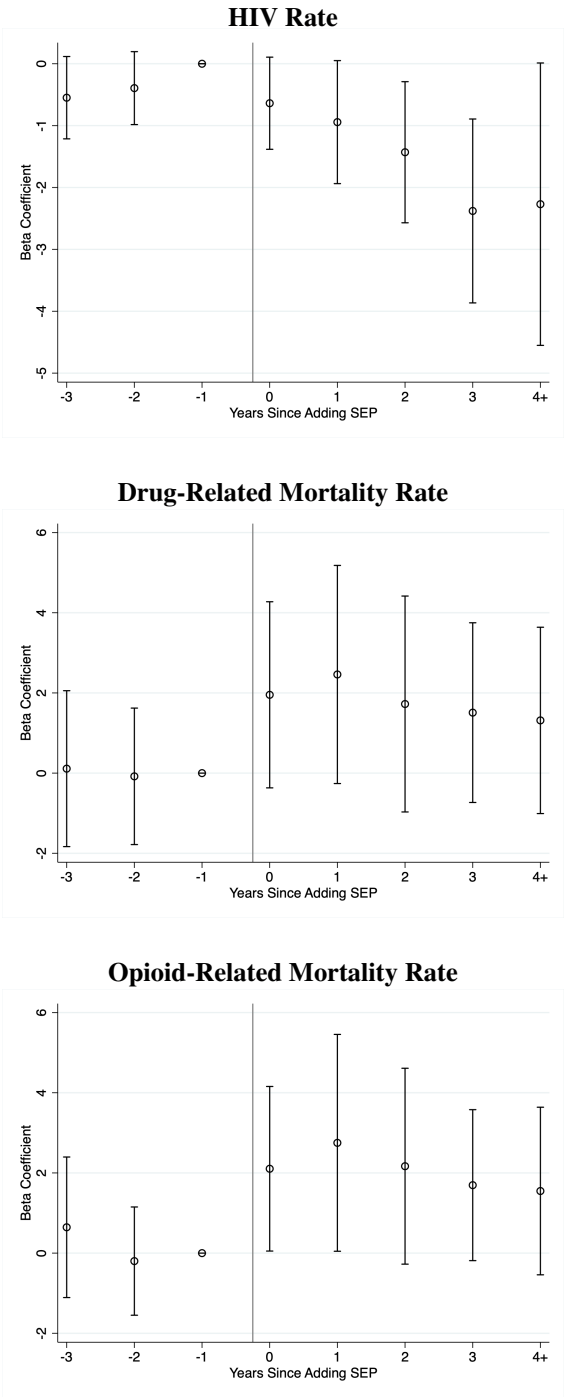
Figure A8: Difference-in-Differences Estimates for HIV Rates and Opioid-Related Mortality Rates by County Population Size (WLS)





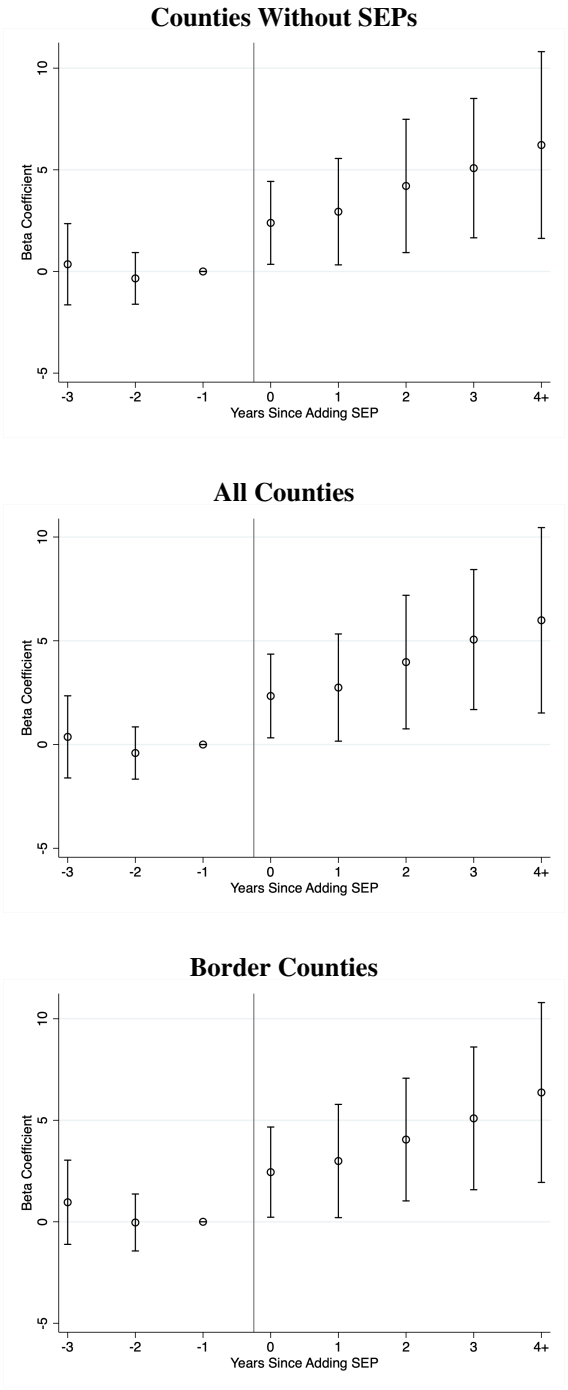
Notes: Each figure displays the coefficients and their respective 95% confidence intervals for the effects from WLS regressions analogous to Equation 1, weighted by county population size. A x-axis value of "i" where $i = 25,000, 75,000, 125,000, ...1,000,000$ indicates an estimate from a difference-in-differences analysis comparing health outcomes in treated and comparison counties with less than i individuals. Estimates are based on restricted mortality files and CDC HIV diagnoses counts by county for the entire United States from 2008–2016. HIV diagnoses rates are from the Center for Disease Control and Prevention's NCHHSTP Atlas and 34 state agencies. Economic control variables include the county-level poverty rate and unemployment rate, demographic controls include percent Hispanic and percent black, and state-level policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the county level.

Figure A9: Event Study Estimates of the Effect of Opening a Syringe Exchange Program on Drug-Related Mortality Rates, Without County-Specific Linear Trends



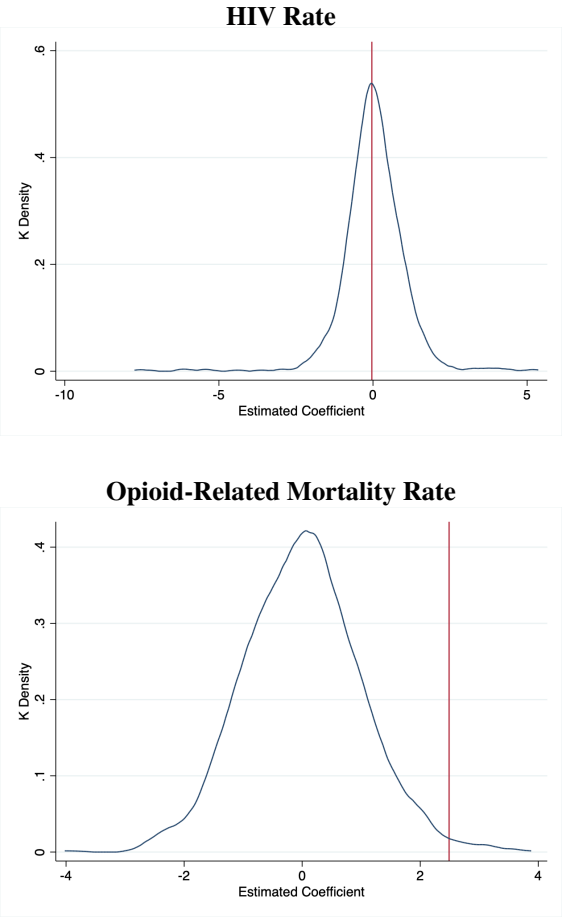
Notes: See Figure 1. Each figure displays the coefficients and their respective 95% confidence intervals for the leading indicators and lagged treatment effects from OLS regressions, as specified in Equation 2, omitting controls for county-specific linear time trends.

Figure A10: Event Study Estimates of the Effect of Opening a Syringe Exchange Program on Opioid-Related Mortality Rates, by Various Comparison Groups



Notes: See Figure 1. The top panel displays coefficients and their 95% confidence intervals from a model specified by Equation 2, comparing counties with SEP openings to those without SEPs. The middle panel displays coefficients and their 95% confidence intervals from a model specified by Equation 2 comparing counties with SEP openings to all other US counties. The bottom panel displays coefficients and their 95% confidence intervals from a model specified by Equation 2 comparing counties with SEP openings to those with existing SEPs.

Figure A11: Empirical Distribution of Placebo Difference-in-Differences Estimates

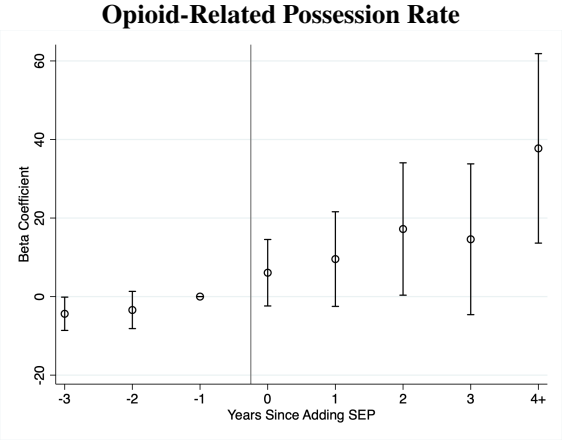


Notes: Each figure plots the distribution of 1,000 difference-in-differences coefficients from placebo regressions of the preferred specification (Equation 1) using randomly drawn treatment counties and treated years and health and mortality data from 2008-2016. The vertical line displays the main estimate, for comparison. For HIV rates and opioid-related mortality rates, 47.3 percent and 1.1 percent of placebo coefficients (in absolute value) are larger than those reported in Table 1. Estimates are based on HIV diagnoses counts by county and restricted county-level mortality files for the entire United States from 2008–2016. HIV diagnoses rates are from the Center for Disease Control and Prevention's NCHHSTP Atlas and 34 state agencies. Economic control variables include the county-level poverty rate and unemployment rate, and demographic controls include percent Hispanic and percent black.

Figure A12: Event Study Estimates of the Effect of Opening a
Syringe Exchange Program on Alcohol-Related Mortality, Traffic-Related Mortality, and Total Mortality Rates

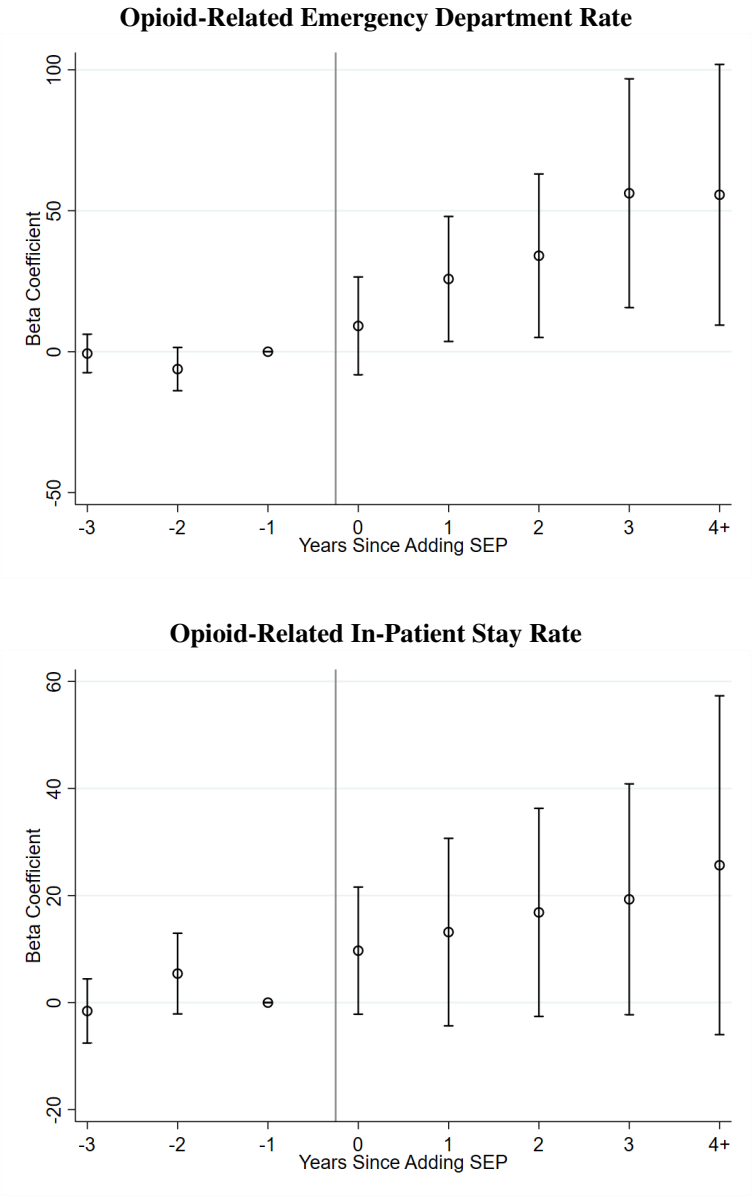
Notes: See Figure 1. Estimates are based on restricted mortality files by county for the entire United States from 2008–2016.

Figure A13: Event Study Estimates of the Effect of Opening a Syringe Exchange Program on Drug-Related Crime Rates



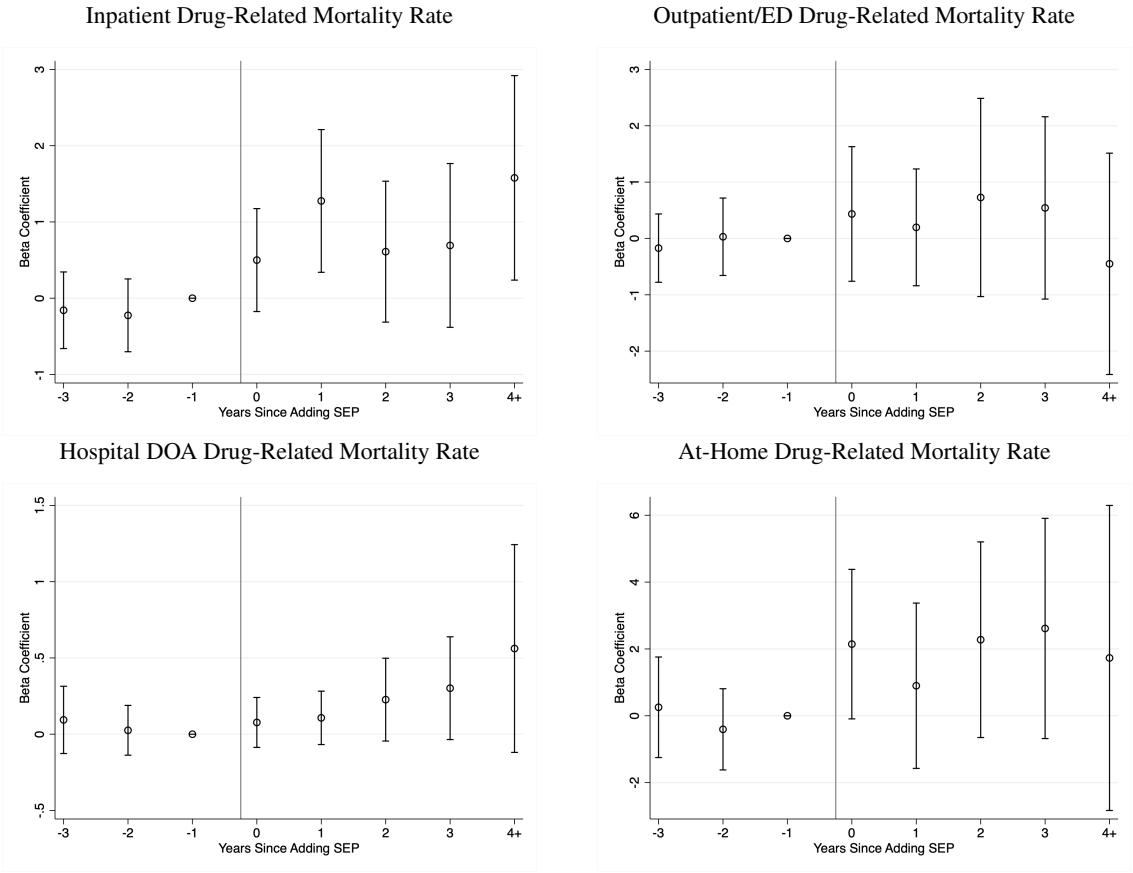
Notes: Each figure displays the coefficients and their respective 95% confidence intervals for the leading indicators and lagged treatment effects from OLS regressions, as specified in Equation 2. The vertical line represents the first year during the sample period that a county experienced a syringe exchange program opening. County-level arrest data from 2008–2016 is from the FBI Uniform Crime Reports. Economic control variables include the county-level poverty rate and unemployment rate, and demographic controls include percent Hispanic and percent black. Standard errors are clustered at the county level.

Figure A14: Event Study Estimates of the Effect of Opening a
Syringe Exchange Program on Opioid-Related Hospital Visits (State-Level)



Notes: Each figure displays the coefficients and their respective 95% confidence intervals for the leading indicators and lagged treatment effects from OLS regressions. The vertical line represents the first year during the sample period that a state experienced a syringe exchange program opening. Estimates are based on state-level data on emergency department (ED) visits and in-patient (IP) hospital stays from 2008–2016 from the Healthcare Cost and Utilization Project (HCUP). Economic control variables include poverty rate, unemployment rate, demographic controls include percent Hispanic and percent black, and state-level policy controls include whether a state imposes quantitative prescription limit, tamper-resistant prescription forms, pain clinic regulations, patient identification requirements, doctor shopping restrictions, requirements with respect to physician examination or pharmacist verification, prescription drug monitoring programs, paraphernalia laws, and good Samaritan laws. Standard errors are clustered at the state level.

Figure A15: Event Study Estimates of the Effect of Opening a Syringe Exchange Program on Drug-Related Mortality Rates, by Hospital Condition



Notes: See Figure 1. Information on hospital condition are included in the CDC mortality files. "Hospital DOA" represents patients receiving medical care but arriving to an in-patient facility deceased. "At-home" mortality includes patients that experienced a fatal overdose outside of emergency care or hospital care.