Supplier Enforcement and the Opioid Crisis

By J. Travis Donahoe*

This paper examines a major way that policy has responded to the opioid crisis, which is by closing prescribers, dispensers, and distributors that inappropriately supplied prescription opioids. Theory is unclear about whether these enforcement actions will reduce harms from opioids or simply shift opioid users to other suppliers or more dangerous drugs. Exploiting differences in the timing and extent of enforcement across counties from 2006 to 2014, I find that enforcement actions caused large reductions in opioid supply and death rates. Enforcement was rare over this period; however, empirical evidence shows that increasing enforcement would have had considerable health benefits.

* University of Pittsburgh, A664, 130 De Soto St, Pittsburgh, PA 15261, tdonahoe@pitt.edu. I am grateful to my dissertation committee, David Cutler, Nicole Maestas, and Thomas McGuire, who have provided unrivaled guidance and support. I am also grateful to Marcella Alsan, Michael Barnett, Benjamin Barsky, David Bradford, Samantha Burn, Lucy Chen, Vilsa Curto, Richard Frank, Edward Glaeser, Laura Hatfield, Haiden Huskamp, Anupam Jena, Lawrence Katz, Edward Kong, Bruce Landon, Mary Beth Landrum, Timothy Layton, Sumedha Gupta, Ellen Meara, Ateev Mehrotra, Alice Ndikumana, Joseph Newhouse, Maximilian Pany, Eran Politzer, David Powell, Mark Shepard, Anthony Yu, José Zubizarreta, and numerous participants at Harvard's health policy, health economics, and labor and public finance seminars, whose comments and advice have greatly improved this paper. I am also grateful to Jonathan Novak for talking with me about Drug Enforcement Administration enforcement interventions.

Since 1990, drug poisoning death rates in the U.S. have risen more than 741 percent (mostly due to opioids) and taken the lives of 1,047,420 people.[1] This massive rise in preventable deaths is one of the worst public health crises in history. Yet, there is limited evidence about how to abate it or prevent future drug epidemics like it from occurring. One of the main ways policy has responded is through increased enforcement of the Controlled Substances Act, which requires prescribers, dispensers, and distributors of prescription opioids and other addictive prescription drugs to prevent drugs they sell from being diverted for non-medical uses. Enforcing Controlled Substances Act violations is costly, comprising $677 million of federal spending in 2022.[2] Meanwhile, evidence on the effects of shutting down suppliers that violate these obligations is limited, prompting debate over whether enforcement is a useful policy lever or if funds would be better spent elsewhere.

To contribute to this debate, this paper conducts the first systematic analysis of enforcement initiatives in the market for prescription opioids. I start by developing a theoretical model that captures key features of the prescription opioid industry and enforcement. I show that heterogeneity in physician altruism (i.e., how much physicians value profits relative to patient health) and in pharmacy and distributor perceptions about enforcement risks can drive a pooling of harmful opioid supply amongst the least altruistic physicians and most lenient pharmacies and distributors in a market. In this event, closing any one of the riskiest prescribers, pharmacies, or distributors will cause large and targeted reductions in aggregate opioid supply. However, without such heterogeneity, the effects of closing any single supplier will generally be undone by substitution to other suppliers in the same market. Furthermore, even if enforcement actions reduce prescription opioid supply, their effects on total social harms depends on whether there is substitution to other illicitly made drugs (such as heroin) which may be even more dangerous. To shed light on the quantitative importance of these different sources of substitution, I examine the effects of enforcement actions on opioid supply and mortality empirically.

To estimate the effects of enforcement actions on prescription opioid supply, I combine novel data on the timing of all 540 publicly reported DEA enforcement actions from 2006 to 2014 with detailed firm-level data on all opioid shipments in the U.S. over that time. I estimate an empirical model that relates pharmacy- and distributor-level opioid shipments over time to whether the pharmacy or distributor experienced an enforcement action that resulted in them being shut down, the total number of other pharmacies and distribution facilities that experienced an enforcement action in the same county (to estimate substitution and deterrence effects), and the total number of prescribers shut down in the county. I find that each type of enforcement action caused reductions in local opioid supply.

For pharmacies and distributors, the firm-level data allow me to estimate the pass-through of the enforcement actions—how much shutting down a pharmacy or distributor that would have supplied a given quantity of pills to a market reduced total supply. The average pharmacy enforcement action had more-than-complete (146 percent) pass-through

[1] Author's calculations using National Centers for Health Statistics vital records, 1990 to 2020.

[2] Fiscal Year 2023 Diversion Control Fee Account, available at: https://www.usaspending.gov/federal_account/015-5131.

into the affected county's aggregate opioid supply. In other words, there was no substitution on average following pharmacy enforcement actions and even some local deterrence effects (i.e., other pharmacies cutting back on supply in response to observing another pharmacy be shut down). Distributor enforcement actions had lower pass-through (38 percent). However, further analysis shows this is due to lower-risk pharmacies substituting to other distributors after their initial distributor was shut down. The highest-risk pharmacies (i.e., pharmacies with characteristics and opioid shipment patterns that most resembled the pharmacies that were shut down) were not able to substitute to other distributors and pass-through was nearly complete (95 percent). Overall, I estimate that close to half (47 percent) of the effects of distributor enforcement on supply came from reducing opioid supply to the 10 percent of pharmacies with the highest predicted diversion risk. This shows that distributor enforcement actions were well-targeted for reducing diversion and had small effects on the broader medical market.

Overall, I estimate the 540 enforcement actions that were taken over this period reduced total opioid supply in the U.S. by 973 million 50 morphine-milligram-equivalent doses of opioids from 2006 to 2014 (four percent). As the average individual action was highly effective and had substantial pass-through, this low estimate reflects how infrequently enforcement actions were deployed over this period, even as prescription opioid supply and diversion were at their highest.

Next, using my estimates of the effects of enforcement on local opioid supply, I examine effects on mortality. I construct a novel measure of each county's exposure to enforcement: the predicted cumulative number of doses of opioids disrupted by all enforcement activities in each county and time period. I then relate exposure to enforcement to drug poisoning mortality rates (separately for prescription opioids, heroin, unspecified drugs, and all drugs), controlling for county and state-by-time fixed effects. Causal identification relies on the plausible exogeneity of differences in the timing and extent of enforcement activities across areas, controlling for time-invariant characteristics and time-varying confounders at the state level (e.g., other opioid-related state policies). Consistent with this, I show the timing and intensity of enforcement was not related to pre-enforcement opioid death rates.

I find the enforcement actions caused substantial reductions in overall drug poisoning death rates. Every one percent of opioid supply that was disrupted by enforcement caused 0.27 percent fewer deaths from prescription opioids, 0.44 percent fewer deaths where no specific drug was mentioned, and 0.22 percent fewer total drug poisoning deaths. In total, I estimate that the 540 enforcement actions that occurred prevented 5,948 drug poisoning deaths. I also find that enforcement did not increase deaths from heroin, a potential substitute drug, as prior literature suggested it might (Alpert, Powell and Pacula, 2018; Evans, Lieber and Power, 2019). In particular, my estimates rule out (with 95 percent confidence) any increase in heroin deaths 54 percent as large as the reduction in prescription opioid deaths. I further support this conclusion with evidence from event studies that show that heroin mortality did not increase after the 100 largest supplier enforcement actions over this period. These interventions were followed by large and abrupt reductions in prescription opioid supply and prescription opioid deaths (29 and 20 percent, respectively).

However, they did not cause heroin mortality to increase at all for at least two years after the supply shocks occurred.

I also examine whether the effects of enforcement on mortality were different or similar in Florida compared to other areas of the U.S. Florida is the state that was targeted by the largest and most supplier enforcement actions during this time. Past work suggested that increased enforcement in Florida starting around 2010 caused large reductions in state-level opioid supply and mortality (Kennedy-Hendricks et al., 2016; Meinhofer, 2016). I provide new evidence that the relationship between enforcement activity intensity and mortality was the same in Florida as it was in other areas. The average area outside of Florida experienced significantly less enforcement compared to Florida; thus, a disproportionate share of deaths that were prevented by enforcement (30 percent) were in Florida. However, had other areas experienced as much enforcement as Florida did, results suggest that mortality effects would have been similar. Furthermore, the large amounts of enforcement activities that took place in Florida (and limited amounts in other areas that had as much opioid supply and diversion) shows that large increases in enforcement in other areas of the country were possible over this period and would have had beneficial mortality effects.

Overall, this paper demonstrates a significantly larger role for enforcement and other supply-side interventions in markets for prescription opioids and other addictive prescription drugs compared to prior research. Previous work on prescription opioid supply-side interventions examined national and state policy changes (e.g., *OxyContin* reformulation, implementation of Prescription Drug Monitoring Programs, and pain clinic legislation) that were implemented around the same time as the enforcement actions in this study and found these interventions caused increased deaths from heroin (a pharmacologically similar drug to prescription opioids) that offset the benefits from reducing prescription opioid deaths (Alpert, Powell and Pacula, 2018; Evans, Lieber and Power, 2019; Powell and Pacula, 2021; Balestra et al., 2021; Kim, 2021; Mallatt, 2022). I find enforcement did not have this effect.[3] Understanding why is an important area for future research. On one hand, enforcement may have different effects compared to other interventions. In particular, the presence of enforcement activities in an area may have broader deterrence effects in illicit opioid markets that inhibit the types of substitution found in other work. On the other hand, isolating the effects of local supply shocks is also a significant advance relative to past literature which examined more aggregate interventions and may be confounded by changes in illicit opioid markets that occurred around the same time.[4] More work is needed to disentangle which of these theories is correct.

This paper also establishes that extremely limited oversight of prescription opioid supply chain entities and their obligations was a significant contributor to the opioid crisis. Past

[3] Using a different identification strategy, Soliman (2022) shows that DEA crackdowns on prescribers that were triggered by audits also reduced net mortality rates but caused some increase in heroin deaths.

[4] The DEA's 2011 National Drug Threat Assessment (p. 3) notes that increased heroin production in Mexico was causing increased availability of heroin throughout the U.S. over this period, including in markets where heroin was previously unavailable (available at https://www.justice.gov/archive/ndic/pubs44/44849/44849p.pdf). It is difficult for research that leverages the timing of aggregate interventions to account for this kind of shock. The distinctly local nature of the enforcement-driven supply shocks allows me to include rich controls (e.g., state-by-time fixed effects) and provide evidence that the results are not being driven by the national or regional evolution of heroin markets.

literature has shown that marketing of *OxyContin* caused large increases in prescription opioid use, addiction, and mortality in the U.S. starting in the mid-1990s (Alpert et al., 2021; Arteaga and Barone, 2021). I show that as the problem grew and reached its zenith, the government agency responsible for overseeing the sale and distribution of prescription opioids took extremely limited steps to curtail inappropriate supply—closing just 540 of the thousands of suppliers in operation. I also show enforcement activities were extremely limited in many areas of the U.S. with the most prescription opioid shipments, suspicious pharmacies, and deaths, such as the rural Appalachian areas of West Virginia, Kentucky, and Tennessee, due to the DEA pooling staff in large urban areas. Results imply that late and limited enforcement overall, and in areas where prescription opioid problems were the worst, directly contributed to increased deaths and the development of the opioid crisis.

Lastly, the results also have important implications for preventing future crises like the opioid epidemic from occurring. Following the enforcement actions in this study, several companies that were affected spent millions lobbying Congress on legislation to limit the DEA's authority in pharmaceutical markets. This was ultimately successful. In 2015, Congress passed the "Ensuring Patient Access and Effective Drug Enforcement Act," which raised the standard of proof that is required before the DEA can shut down pharmaceutical distributors for supplying suspicious pharmacies.[5] In 2022, the U.S. Supreme Court also raised legal standards required to prosecute prescribers for prescribing opioids and other addictive drugs in a harmful manner. Both these facts suggest that constraints on the legal supply of dangerous and addictive prescription drugs have weakened, rather than tightened, in the wake of the opioid epidemic. Results imply this will limit the ability to respond effectively to future crises involving the diversion of harmful prescription drugs.

The remainder of the paper proceeds as follows. Section I provides context about the prescription opioid industry and enforcement, and develops a model to frame the empirical results. Section II introduces the data. In section III, I present a case study of enforcement in Mingo County, W.Va., which highlights key empirical challenges and previews the main results. Section IV discusses the empirical strategy. Section V presents the effects of enforcement actions on opioid supply. Section VI presents impacts on mortality. Section VII examines the robustness of the results. Lastly, section VIII concludes.

I. Background on Prescription Opioid Supply and Enforcement

A. Prescription opioid suppliers

The sale and distribution of prescription opioids involves five types of entities, depicted in **Appendix Figure A1**: (i) manufacturers, who produce and market drugs; (ii) distributors, who acquire drugs from manufacturers and deliver them to pharmacies, (iii) prescribers, who write prescriptions for drugs to be used medically, (iv) pharmacies (dispensers), who ultimately fill prescriptions, and (v) the end consumers. Some pharmacies also handle their own distribution. In some areas where it is legal, practitioners also

[5]See S. Higham and L. Bernstein, "The Drug Industry's Triumph over the DEA," 2017, available at https://www.washingtonpost.com/graphics/2017/investigations/dea-drug-industry-congress/.

dispense drugs to the patients they prescribe to. Under the Controlled Substances Act of 1970, all suppliers that handle opioids and other drugs with dangerous and addictive potential (called "controlled substances") have federal obligations to prevent the sale of the drugs for nonmedical use. These obligations include registering with the U.S. Drug Enforcement Administration (DEA; part of the Department of Justice) as well as specific security, record-keeping, monitoring, and reporting obligations which vary according to the supplier's role in the supply chain.

The obligations of each type of supplier are presented in **Appendix Table A1**. I focus on distributors, pharmacies, and practitioners as there was no manufacturer enforcement over the period of my study. Distributors must submit detailed data on opioid sales through the DEA's Automation of Reports and Consolidated Orders System (ARCOS). They must also design and operate systems to prevent sales to customers placing suspicious orders and report suspicious customers to the DEA. Specific characteristics that distributors are obligated to screen for, such as orders that are of unusual size or deviate from a normal pattern, are listed in **Appendix Table A1**. Pharmacies are obligated to screen patients for red flags and to not dispense opioids to customers that they suspect will misuse prescriptions. Red flags that pharmacies must look for include many customers receiving the same combination and types of prescriptions from the same prescriber, as well as other red flags listed in **Appendix Table A1**. Lastly, prescribers must examine patients for medical need and prescribe consistently with medical practice norms. They must not prescribe prescription opioids for recreational use or maintenance of addiction.

B. Compliance and enforcement

The DEA is the primary agency responsible for monitoring and enforcing compliance with suppliers' obligations to prevent diversion. To do so, it performs inspections of suppliers and investigates them following complaints and as part of regulatory and criminal investigations. If suppliers are found to be neglecting their obligations or actively participating in criminal diversion schemes, the DEA may pursue administrative, civil, or criminal enforcement actions. Administrative enforcement actions include letters of admonition that advise suppliers of violations, "orders to show cause" that initiate proceedings to revoke a supplier's license to handle controlled substances, "immediate suspension orders" that temporarily suspend a supplier's license, and license revocations. Civil enforcement actions involve fines for violations of obligations. Lastly, criminal enforcement actions involve indictment and criminal prosecution of particular individuals (e.g., a physician, pharmacist, pharmacy owner, or executive at a distribution facility). Industry documents show that it is common for different types of actions to be pursued together (e.g., for a prescriber to first lose their license and then later be indicted) and for investigations and prosecution to take multiple years to complete.

In response to concerns about rising prescription opioid diversion and mortality in the mid-2000s, the DEA undertook several initiatives to increase enforcement and compliance in the industry. The first is that it significantly expanded its Tactical Diversion Squad program in 2009, increasing the number of squads located throughout the U.S. from just 5 in 2009 to 40 in 2011.[6] The number of Tactical Diversion Squad personnel increased from 44 to 476. The program has also continued to be expanded over time, with an additional 29 squads being established throughout the US since the initial expansion. According to a 2011 Government Accountability Office report on the DEA's activities over this period, these squads were predominantly established in major cities where the DEA had available staff and office space (i.e., not areas that had the greatest diversion or need). Tactical Diversion Squads are personnel that support local law enforcement agencies in diversion-related investigations, providing them with additional authority (e.g., the ability to revoke controlled substances licenses), personnel to undertake undercover investigations, and resources (e.g., the ability to review data on opioid dispensing). This expansion enabled the DEA to increase criminal investigations. In **Appendix Table A2**, I show the timing and extent of enforcement activities over this period were strongly related to proximity to cities where the DEA's Tactical Diversion Squad offices were located.

Second, the DEA increased compliance and enforcement efforts targeting pharmaceutical distributors. This entailed increasing regulatory inspections of distribution facilities, educating distributors about their obligations, and shutting down and sanctioning distributors that shipped opioids to suspicious pharmacies and clinics and did not report them to the DEA.[7] Industry documents suggest that because distributors handled significantly larger volumes of opioids compared to pharmacies and prescribers, and there were fewer of them, the DEA believed targeting distributors could be a more effective way of intervening in the market.

Using data that I describe in the next section, **Figure 1** shows the locations of prescribers, pharmacies, and pharmaceutical distribution facilities that were shut down by an enforcement action between 2006 and 2014. The figure shows that enforcement actions were highly clustered in particular areas. There are two fundamental reasons for this. First, interventions were clustered near major cities where the DEA located its offices and had staff to conduct investigations. Second, the investigations that unfolded often led to information that was then used to prosecute other suppliers in the same networks and areas. For example, following the prosecution of a physician, it was common for the pharmacy that filled the physician's scripts to face enforcement later on, and ultimately for the distributor that supplied the pharmacy to be shut down as well. I illustrate this phenomenon in a case study in section III.

A disproportionate share of the enforcement activities were also undertaken in Florida. There are several reasons for the concentration of enforcement there. First, around 2010, Florida was an epicenter for prescription opioid diversion.[8] Second, discussions with in-

[6]See United States Government Accountability Office (GAO), "Prescription Drug Control: DEA Has Enhanced Efforts to Combat Diversion, but Could Better Assess and Report Program Results," August 2011, available at: https://www.gao.gov/products/gao-11-744

[7]See Rannazzisi, "Responding to the Prescription Drug Abuse Epidemic," 2012, available at: https://www.justice.gov/sites/default/files/testimonies/witnesses/attachments/07/18/12//07-18-12-dea-rannazzisi.pdf.

[8]The DEA has traced prescription opioid supply from Florida to essentially all U.S. states. Prescription opioid trafficking from Florida was particularly extensive into Appalachian areas in Tennessee, Kentucky, Ohio, and West Virginia that were served by Interstate-75, earning the highway the moniker the "Oxy Ex-

dustry personnel suggest that several successful investigations in Florida (and the learning that occurred there) had a snowball effect that led to further DEA resources being pooled in Florida and further investigations and enforcement there. Importantly, Florida also implemented a number of state-level policies in tandem with the enforcement such as a pill mill tip line, more stringent pain clinic legislation, and a Prescription Drug Monitoring Program.[9] The DEA also initiated on-site investigations against all pharmacies seeking to open in the state. Past work has attributed these activities collectively, as well as the increased enforcement, as the cause of large declines in opioid supply and mortality in Florida after 2010 (Kennedy-Hendricks et al., 2016; Meinhofer, 2016).

Table 1 provides further details about the 15 distribution facility enforcement actions that took place over the study period. The first actions took place in 2006 and 2007 and targeted facilities located all over the US, including an AmerisourceBergen Drug facility in Florida, three Cardinal Health facilities (Florida, New Jersey, and Washington), and single-site California (Southwood Pharmaceuticals), Kentucky (Richie Pharmacal), and New York (Bellco Drug Corporation) distribution facilities. The actions against the facilities owned by AmerisourceBergen Drug and Cardinal Health were settled (in 2007 and 2008 respectively) and the facilities were permitted to reopen. The majority of distributor enforcement post-2010 was targeted at facilities located in Florida or that supplied very large quantities of opioids to pharmacies and clinics there. The first action was coordinated against four distributors (Anda, Inc., Harvard Drug Group, Paragon Enterprises, Inc., and Sunrise Wholesale, Inc.) for distributing unusual quantities of opioids to Florida pain clinics. These actions took place in June 2010 and were followed by further actions against other distributors in 2011. Lastly, there were two enforcement actions targeting specific distribution facilities owned by Cardinal Health and Walgreens in 2012.[10]

C. Theory: possible effects of enforcement on opioid supply and health

The effects of shutting down a particular supplier on non-medical prescription opioid supply and the harms that result are ambiguous and depend on a number of market forces, which I describe in this section. Non-medical prescription opioid use (i.e., diversion) requires a matching between four actors: (i) a consumer demanding opioids for non-medical use, (ii) a prescriber willing to write them a prescription, (iii) a pharmacy willing to fill the prescription, and (iv) a distributor willing to supply the pharmacy (see section I.A). Each of these different suppliers faces different incentives. Thus, targeting them with enforcement involves different mechanisms and may have different effects. I start by examining the

press." See, e.g., Drug Enforcement Administration, "National Drug Threat Assessment," 2010, available at: https://www.justice.gov/archive/ndic/pubs38/38661/38661p.pdf and Beal, P., "How Florida spread oxy across America," 2018, The Palm Beach Post, available at: https://heroin.palmbeachpost.com/how-florida-spread-oxycodone-across-america/?ref=leftnav.

[9] Baltimore Sun, "DEA launches pill mill tip line," 2011, available at: https://www.baltimoresun.com/os-pill-mill-tip-line-20110228-story.html; Senate Bill 2722, available at: https://www.flsenate.gov/Session/Bill/2010/2722; Florida House Bill 7095, available at: http://www.flsenate.gov/Session/Bill/2011/7095; and Florida House Bill 1167, available at: https://www.myfloridahouse.gov/Sections/Bills/billsdetail.aspx?BillId=48411.

[10] At this time, Walgreens had its own distribution facilities. The one that was shut down was located in Jupiter, Florida, and supplied its pharmacies there and in other southern US states.

situation for prescribers, who are most commonly physicians.

I assume there is excess demand for prescription opioids $x(p_x)$ for non-medical use at price p_x (exogenously set by insurance agencies) and that non-medical opioid use is harmful to health (which I denote $V_x < 0$). I also assume there is no resale of prescription opioids from medical users to individuals seeking to use them non-medically.[11] Following the standard approach in health economics, I assume that prescribers $i \in 1, ..., I$ experience utility from improving patient health and profits: i.e., $u_i = \alpha_i V_x + (1 - \alpha_i)\pi_x$ (McGuire, 2000). π_x denotes the prescriber's net financial gain from writing an opioid prescription (exogenously set) and α_i is a parameter for prescriber "altruism" (i.e. how much the prescriber values patient health relative to profits). The problem for consumers, then, is to find a prescriber who values profits from prescribing non-medically greater than the negative health impacts it causes: i.e., for whom

$$(1 - \alpha_i)\pi_x > -\alpha_i V_x. \tag{1}$$

In a market with many prescribers who are equally altruistic or profit-motivated (i.e., $\alpha_i = \bar{\alpha}$ for all i), shutting down a single prescriber would be expected to have no effect on aggregate supply. Shutting down a prescriber will clearly reduce the amount of prescriptions that the prescriber who is shut down writes. However, consumers can substitute to other prescribers with the same propensity to prescribe to them, causing prescriptions by other prescribers to increase and there to be no aggregate effects of the intervention. Substitution may be limited in the short term (e.g., if search is costly or if other prescribers are capacity-constrained); however, incentives for entry and business expansion should lead to offsetting substitution in the long run.

Imagine an alternative market, however, where most prescribers have strong professional norms that discourage non-medical prescribing (i.e., $(1 - \alpha_i)\pi_x < -\alpha_i V_x$) and there is a single "bad actor" j who prefers profits (i.e., $(1 - \alpha_j)\pi_x > -\alpha_j V_x$). In such a market, all the consumers who demand opioids for non-medical use will be forced to try and obtain prescriptions from the bad actor and the bad actor will face tremendous demand. The bad actor, in turn, will prescribe to as many patients as they profit from, leading to a high concentration of prescribing in the industry.[12] Furthermore, shutting down the bad actor will reduce aggregate supply. If some of the bad actor's customers are legitimate, they may substitute; however, none of the consumers who misuse opioids will be able to substitute (since other prescribers will turn them away), leading aggregate supply to fall. Without the entry of further bad actors, the action will cause long-term reductions in non-medical prescription opioid use.

Next, consider the case of enforcement targeting pharmacies. Let pharmacies have

[11] Empirically, many people obtain opioids from family and friends. This seems, however, to be an issue about extra and unused pills. I do not consider this in my framework but refer readers to Schnell (2022) for an analysis of the resale market for prescription opioids.

[12] Several studies show that opioid prescribing was very highly concentrated during the peak years of the opioid crisis. Cutler and Glaeser (2021) show the top 5 percent of prescribers wrote prescriptions for 38 percent of all opioids in Massachusetts, 40 percent in California, and 58 percent in Kentucky.

marginal dispensing costs c_x and a dispensing fee p_d that is exogenously set by their consumers' insurers. In view of section I.A, suppose that pharmacies observe an *ex-ante* signal $s \sim F_s$ about how likely each script is illegitimate (i.e., written by one of the bad type prescribers described above). *Ex-post*, an enforcement agency observes whether a given pharmacy filled scripts written by bad type prescribers, with some probability that depends on government spending on prescription opioid enforcement e_x. If the agency identifies a pharmacy that filled illegitimate scripts, it sanctions the pharmacy. Reimbursement is the same for all scripts filled (i.e., pharmacies cannot set prescription-specific prices), however, pharmacies need not fill every prescription. Pharmacies' decisions about filling a particular prescription are driven by whether the revenue from filling the prescription exceeds their cost, including expected enforcement costs (denote $c_{e,j}(e_x, s)$). Maximizing of profits leads pharmacies to adopt threshold policies τ_j^* that equate marginal revenues from more lenient dispensing with marginal expected enforcement costs, i.e.,

$$(p_d - c_x)\frac{dQ}{d\tau_j^*} = \frac{dc_{e,j}}{d\tau_j^*}. \tag{2}$$

The pharmacy j then fills all scripts with $s \leq \tau_j^*$ and refuses all those with $s > \tau_j^*$. The problem for consumers with script s, then, is to find a pharmacy with $\tau_j^* \geq s$.

Similarly to the example for prescribers, if all pharmacies have the same profit conditions in equation 2, shutting down a single pharmacy would not affect aggregate non-medical opioid supply. Consumers would simply substitute from pharmacies that are shut down to pharmacies that are not shut down and have the same threshold policies. However, suppose that there is also heterogeneity in this industry and that there are some "bad type" pharmacies that are more willing to run the risks of enforcement. This could be because some pharmacies do not value the damage enforcement would do to their reputation (part of the costs of enforcement) as much as others in the industry or because some believe they will not be caught or could avoid prosecution if caught. In this case, customers with the highest risk prescriptions will pool with the most lenient pharmacies.[13] Furthermore, shutting down the most lenient pharmacy (i.e., that has the highest threshold, τ_1^*) eliminates prescriptions with risk above the second-most lenient pharmacy's threshold τ_2^*, causing aggregate supply to fall. Because pharmacies decide whether or not to fill prescriptions based on their risk: the scripts that are no longer filled are also disproportionately likely to be illegitimate, a desirable targeting property.

The situation for distributors is identical to that of pharmacies, just at a higher level of the supply chain. Distributors observe signals about how risky the pharmacies they supply are and make decisions about sales that weigh marginal profits against marginal expected costs of enforcement. Heterogeneity in expected enforcement costs may lead to the pooling of bad-type pharmacies with the most lenient distributors, causing interventions that shut down the most lenient distributors to reduce aggregate supply. One key

[13]Industry documents suggest that it was very common for excessive prescribers to only be able to have their prescriptions filled at certain pharmacies and actively direct their patients to those pharmacies.

difference in distribution, however, is the distribution of prescription opioids is far more concentrated amongst a few firms compared to prescribing or dispensing. While there were more than 84,684 pharmacies that dispensed opioids in the US in 2014, there were only 374 distributors.[14] Thus, targeting enforcement at the relatively smaller number of distributors and forcing them to adopt strict thresholds and monitoring of the pharmacies they supply has the potential to have greater impacts on supply relative to targeting downstream prescribers or pharmacies themselves. A key concern, however, is that shutting distributors down may have unintended effects on other legitimate pharmacies they serve and reduce access to medical opioid supply. I study whether distributor enforcement actions had this effect in section V.B.

One final way that enforcement at any level of the supply chain can have an effect is if the enforcement action causes general deterrence effects: i.e., causes all other suppliers in the market (or even outside it) to perceive a higher risk of enforcement. This would cause other non-targeted suppliers to cut back on supply after a targeted supplier is shut down, something I test for in section V.A.

Importantly, the effects of enforcement on prescription opioid supply are not the only important effect to consider for social harms. Another possible effect is that consumers who lose access to prescription opioids might substitute to illicitly made opioids (such as heroin) that are unregulated and potentially more dangerous. The extent of this will depend on how closely consumers view illicit opioids as substitutes for non-medical prescription opioids.[15] In section VI, I study the effects of enforcement on mortality involving illicitly made substitutes as well as prescription opioids and any drug.

II. Sources of Data

A. *Data on controlled substances enforcement*

To study the effects of enforcement, I compiled data on all publicly reported federal enforcement interventions against opioid suppliers from 2006 to 2014. This includes all interventions that are listed in the DEA's archive of criminal cases against doctors, register of administrative enforcement actions, and archive of press releases over this time. For each intervention, I searched local press releases and public records to obtain information about the nature of the interventions and when they began. Occasionally, I identified additional enforcement interventions through these searches and added them to the data as well. I focus on interventions that resulted in temporary or permanent loss of the ability of a supplier to handle opioids (e.g., a license suspension or arrest) and that were related to widespread misconduct (i.e., not just theft or prescribing to one's family and friends). I also

[14] Author's analysis of ARCOS data described in section II.B.

[15] While prescription opioids and heroin are pharmacologically very similar, there are important differences. Prescription opioids are sold on a legal and regulated market with quality certification. In contrast, heroin has no quality certification and may place consumers at greater risk. Heroin and other illicitly made opioids are also typically used differently. While prescription opioids are typically taken orally, heroin is typically injected. Lastly, illicit opioid use may also be more stigmatized relative to prescription opioid use.

exclude interventions that targeted physicians and pharmacies facilitating illegal internet pharmacy schemes, as it is unclear whether these would have had any local effects.

In total, my sample includes enforcement actions that shut down 540 suppliers (shown in **Figure 1**). These include 401 prescribers (almost all physician prescribers, also includes practitioners that dispensed opioids), 125 pharmacists and/or pharmacies, and 14 distribution facilities (including one which was shut down twice; see **Table 1**). As described in the background section, the periods when suppliers were ultimately shut down were often preceded by a series of events that included undercover investigations, inspections and interviews, and administration of search warrants. For each intervention, I identify the initial intervention that a supplier would have known about in the chain of events preceding the supplier being shut down. This was typically a search warrant, though it also included other types of events such as raids of businesses, interviews of people involved, subpoenas of records, filing of complaints by state boards, and other similar types of actions.[16] Using data on supplier-level opioid shipments that I describe next, **Figure 2** plots trends in opioid supply around these initial interventions. As shown, suppliers sharply reduced opioid supply after these initial intervention dates, even though many were not formally shut down until sometime later.[17]

B. Data on prescription opioid supply and mortality

Data on opioid supply comes from the Drug Enforcement Administration's Automation of Reports and Consolidated Orders System (ARCOS). These are data on all prescription opioid transactions that distributors must submit to the DEA annually under the Controlled Substances Act, described in section I.A. I use a unique extract that contains information on the names, addresses, and DEA registration numbers of distributors, pharmacies, and clinics involved in each oxycodone and hydrocodone shipment.[18] The data also contain information on the drug manufacturer, type, potency, and quantity of each opioid shipment. These data covering the years from 2006 to 2014 were made public following a lawsuit by The Washington Post and HD Media against the pharmaceutical industry.[19] I drop opioid shipments to hospitals and mail-order pharmacies using additional data provided by The Washington Post (as these prescriptions would not have been consumed locally).[20]

I link the ARCOS data with suppliers that experienced enforcement actions using the suppliers' names, DEA registration numbers, professional degrees (for prescribers), and ad-

[16] I do not include dates of undercover interventions and assume these would not have had an effect on supplier operations.

[17] Pharmacies and distribution facilities were shut down at different lengths from the initial event. Some were not shut down until years later. Furthermore, some distributors were permitted to re-open after being shut down after settling with the DEA. This is why shipments from the average pharmacy/distributor that was shut down in **Figure 2** never reach zero. The time series for each individual supplier does.

[18] These were the two most common prescription opioids, accounting for 64 percent of all prescription opioid shipments, and were the drugs primarily targeted by DEA enforcement interventions.

[19] See The Washington Post, "Drilling into the DEA's pain pills database," 2020, available at https://www.washingtonpost.com/graphics/2019/investigations/dea-pain-pill-database/.

[20] See: https://github.com/wpinvestigative/arcos-api.

dresses. I construct a firm-level dataset on opioid supply and timing of enforcement. Each row in the data identifies the total amount of opioids supplied by a pharmacy-distributor pair in a given calendar quarter. To standardize shipments by potency, I convert shipments to doses of 50 morphine milligram equivalents (MMEs; 50 MME is considered a high daily dose of opioids and places users at considerable risk of overdose). I also construct a county and quarterly data set of opioid shipments, which I denominate on a per capita basis using population counts from the Survey of Epidemiology and End Results.

Data on opioid poisoning mortality comes from restricted all-county cause-of-death data from the National Center for Health Statistics (NCHS) National Vital Statistics System (NVSS). I follow coding conventions used in previous literature to identify drug poisoning deaths by cause, including prescription opioids, heroin, deaths where a specific drug was not mentioned, and any drug.[21] I construct rates of poisoning deaths for each cause in each county and calendar quarter per 100,000 population. I also age- and sex-adjust poisoning death rates to the U.S. 2010 population.

III. Case Study of Enforcement in Mingo County, W.Va.

To motivate my empirical approach and findings, I start with a case study that shows how enforcement played out in Mingo County, a county bordering Kentucky and Virginia in southwest West Virginia. Mingo County has received national attention over the extreme volumes of prescription opioids that were supplied to it, as well as the harms that followed. Between 2006 and 2014, more than 43 million prescription opioid pills were shipped to Mingo County despite just 26,839 people living there.[22] Over that time, Mingo County had the fourth-highest prescription opioid poisoning death rate in the U.S.[23] For this case study, I draw material on the timing of specific interventions and networks of actors from a 2018 House Committee Report.[24] In the ARCOS data, I also observe data on all opioid shipments involving the specific pharmacies and distribution facilities cited in the report, but not the specific physicians.

Three pharmacies and three medical clinics played outsized roles in supplying so many opioids in the county. These were the Sav-Rite Pharmacies #1 and #2 (both owned by the same pharmacist), Tug Valley Pharmacy, Justice Medical Complex (a clinic in neighboring Wayne County), Mountain Medical Care Center clinic, and an orthopedic physician's clinic. Before a wave of enforcement that eventually shut down each of the suppliers, Sav-Rite Pharmacy #1 and Tug Valley Pharmacy dispensed the sixth and eighth most oxycodone and hydrocodone pills of any pharmacy in the U.S. According to the 2018 House Report, the

[21] Drug deaths were identified based on the International Classification of Diseases (ICD), 10th edition underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Cause-specific opioid poisoning deaths were identified using multiple-cause-of-death codes T40.1 (heroin) and T40.2 (prescription opioids).

[22] The extraordinary amount of prescription opioids shipped into Mingo County were first reported on by Eric Eyre in a series of articles in the Charleston Gazette-Mail in 2016 titled "Drug firms fueled 'pill mills' in rural W.Va.," "780M pills, 1,728 deaths," and "Pill rules not enforced." A description of this work and the original articles are available here: https://www.pulitzer.org/winners/eric-eyre.

[23] Author's calculations using NCHS vital statistics data.

[24] See "Red Flags and Warning Signs Ignored: Opioid Distribution and Enforcement Concerns in West Virginia," available at https://www.ruralhealthinfo.org/assets/2616-9819/Opioid-Distribution-Report-FinalREV.pdf.

pills these pharmacies dispensed were primarily for prescriptions written by the physicians at the three aforementioned clinics.

Trends in opioid shipments to Mingo County between 2006 and 2014 are shown in **Figure 3**, overall and for some specific pharmacies. These include Sav-Rite Pharmacies #1 and #2, Tug Valley Pharmacy, and fourteen other pharmacies and physician clinics operating in Mingo County over the time period. The DEA launched an investigation into several of the suppliers in the area in March 2008. One year later in 2009, the DEA raided the Justice Medical Complex and Sav-Rite Pharmacy #2, forcing the businesses to close. Two physicians who had been working at Justice Medical Complex were indicted and sentenced to one year in prison within the following year. Notably, Sav-Rite Pharmacy #1 (owned by the same pharmacist as Sav-Rite #2) remained open. However, opioid shipments to both Sav-Rite pharmacies and the county overall plummeted, falling by 28 percent from the first to the last quarter of 2009. In the first quarter of 2010, the DEA took additional action in the county and raided the Mountain Medical Care Center. Two physicians affiliated with the clinic were indicted and sentenced to six months in prison. Another fled the U.S. According to the 2018 House Report, Tug Valley Pharmacy had been filling large quantities of prescriptions for the physicians who were indicted and whose practices were closed. When the practice was closed, Tug Valley's opioid shipments sharply decreased. All told, this initial phase of investigations and enforcement actions took more than two years and reduced opioid shipments to the county by 73 percent.

Additional enforcement followed in subsequent years. The pharmacist and owner of the Sav-Rite pharmacies was arrested in the first quarter of 2012. The pharmacist and owner of Tug Valley Pharmacy was indicted in 2019. The enforcement was also not just limited to those who prescribed and dispensed the opioids in the county. Several distributors that supplied the pharmacies were later shut down or prosecuted. Three distributors supplied most of Sav-Rite and Tug Valley pharmacies' drugs—H.D. Smith, McKesson Corporation, and Miami-Luken. The DEA suspended shipments from several of McKesson Corporation's distribution facilities in 2017 (including one in Ohio that supplied the Sav-Rite pharmacies) and fined McKesson $150 million. A second distributor that supplied both pharmacies, Miami-Luken, was indicted on criminal charges by a federal grand jury in 2019. In **Appendix Figure A2**, I plot trends in distributor shipments to the Sav-Rite and Tug Valley Pharmacies by these distributors. Of these three distributors, only H.D. Smith ever reported the pharmacies as suspicious to the DEA.[25]

The case study highlights two key points. First, the enforcement interventions take a long time to play out and involve multiple steps against multiple different supply chain entities. In the typical area, it is difficult to study the effects of any single enforcement action because each action is systematically correlated with other actions targeting other suppliers. The interventions must be evaluated collectively. Second, after the physicians and pharmacies were shut down, supply fell sharply and was not replaced—seemingly at all—by other suppliers in the market. This previews my overall findings regarding the effects of enforcement on local opioid supply.

[25]See the 2018 House Committee Report.

IV. Econometric Framework

A. Estimating direct and indirect effects on local opioid supply

As described in section I.C, each enforcement action may have a number of effects on opioid supply. First, there is the direct effect of closing the targeted supplier (whether it be a pharmacy or distribution facility). Second, there is potential offsetting substitution to other firms in the same market as well as general deterrence effects. The extent of substitution or deterrence may also vary depending on the type of supplier targeted. I quantify each of these effects by estimating firm-level regressions of the following form,

$$S_{i,j,c,s,t} = \underbrace{\alpha_1 e_{i,t} + \alpha_2 e_{j,t}}_{\text{Direct effects}} + \underbrace{\gamma_1 \tilde{N}^{pharm}_{c,t} + \gamma_2 \tilde{N}^{dist}_{c,t}}_{\text{Substitution / deterrence}} + \rho N^{doc}_{c,t} + \delta_{i,j} + \tau_{s,t} + \epsilon_{i,j,c,s,t}. \tag{3}$$

S denotes 50 MME doses of opioids, with subscripts as follows: i denotes dispensers (pharmacies and health care clinics), j denotes distribution facilities, c denotes counties, s denotes states, and t denotes time (calendar quarter).

$e_{i,t}$ is a binary variable that turns on after pharmacy i experiences an initial enforcement action that ultimately leads to it being shut down (e.g., a search warrant; see section II.A). $e_{j,t}$ is a binary variable that turns on during quarters after distribution facility j experiences an enforcement action, but that also turns back off if the facility is permitted to re-open following a settlement (see section II.A). The terms that accompany these variables, α_1 and α_2, estimate the direct effects of enforcement actions on the targeted suppliers (i.e., how much local supply fell specifically from targeted suppliers).

The next two terms estimate within-county substitution and deterrence effects. $\tilde{N}^{pharm}_{c,t}$ is the number of pharmacy-distribution facility pairs where the pharmacy was shut down in county c at time t, normalized by the total number of pharmacy-distribution facility pairs where the pharmacy was not shut down at that time.[26] $\tilde{N}^{dist}_{c,t}$ is the number of pharmacy-distribution facility pairs where the distribution facility was shut down in the county, normalized by the total number where the distribution facility was not shut down. Thus, γ_1 and γ_2 estimate the total within-county substitution and deterrence effects for the average enforcement action. If substitution fully offsets the direct effects of shutting down a pharmacy (i.e., if $\hat{\alpha}_1 = -\hat{\gamma}_1$), there is no net effect of enforcement actions on aggregate opioid supply. If there is no substitution (i.e. if $\hat{\gamma}_1 = 0$) enforcement actions pass through fully into aggregate county opioid supply. Lastly, if there are deterrence effects (i.e., if $\hat{\gamma}_1 < 0$), enforcement actions reduce aggregate supply by even more than through closing targeted firms. I estimate the pass-through of each type of enforcement action (pharmacy and distributor) as $\hat{\theta}_1 = \frac{\hat{\alpha}_1 + \hat{\gamma}_1}{\hat{\alpha}_1} \times 100\%$ and $\hat{\theta}_2 = \frac{\hat{\alpha}_2 + \hat{\gamma}_2}{\hat{\alpha}_2} \times 100\%$.

[26] Specifically, let N_c denote the total number of pharmacy-distribution facility pairs ever operating in county c. $\tilde{N}^{pharm}_{c,t} = \frac{\sum_i \sum_j e_{i,j,c,t}}{N_c - \sum_i \sum_j e_{i,j,c,t}}$.

$N_{c,t}^{doc}$ denotes the number of prescribers shut down in county c up to time t. I use the number of prescribers in the affected county because I do not observe prescriptions in the ARCOS data. Thus, the term ρ shows how much losing a doctor in the county affected the average pharmacy and distribution facility pair's opioid shipments. Lastly, $\delta_{i,j}$ and $\tau_{s,t}$ are pharmacy-by-distribution facility and state-by-time fixed effects. The $\delta_{i,j}$ control for time-invariant pharmacy-distributor pair characteristics, and the $\tau_{s,t}$ control for time-varying factors at the state level (e.g., state policies that affect opioid supply).

I also present results without state-by-time fixed effects (only pharmacy-distributor pair and time fixed effects) and which control for policy variables (state prescription drug monitoring programs [PDMPs], state pain clinic laws, and *OxyContin* reformulation).[27] I cluster standard errors at the pharmacy-distribution facility pair level, the level of treatment variation. I construct confidence intervals on the pass-through estimates (non-linear transformations of the parameters of equation 3) using the Delta method.

B. *Examining the targeting of distributor enforcement actions*

In addition to examining the overall effects of distributor enforcement actions, I also examine how well distributor enforcement was targeted. A potential benefit of distributor enforcement is that each distribution facility supplies many different pharmacies and clinics. Thus, targeting distributors has the potential to reduce harmful supply by more than closing any single prescriber or pharmacy alone. However, a concern is that because they serve so many different customers, shutting down distribution facilities may disrupt opioid supply to legitimate pharmacies and clinics (see section I.C). To study this, I estimate a variant of equation 3 that allows for heterogeneous substitution to pharmacies with different proxies R_i for how risky the pharmacy is. To proxy risk, I use a least absolute shrinkage and selection operator (LASSO) regression analysis to select characteristics that best predict whether a pharmacy was shut down by a DEA enforcement action (indicating diversion at that pharmacy). Results from the LASSO selected model are reported in **Appendix Table A2**. Using the model, I predict the risk of enforcement for each pharmacy in the data. Results are illustrated in **Appendix Figure A3**, which shows the cumulative share of pharmacies that were targeted by enforcement actions at different percentiles of the risk distribution. Most pharmacies that were targeted had high predicted risk. In particular, 65 percent of pharmacies that were shut down by the DEA were in the top decile of the predicted risk distribution.

Using predictions from the model, I estimate heterogeneous substitution to pharmacies at different percentiles of the risk distribution as follows:

$$S_{i,j,c,s,t} = \alpha_1 e_{i,t} + \psi_r e_{j,t} R_i + \gamma_1 \tilde{N}_{c,t}^{pharm} + \chi_r \tilde{N}_{i,t}^{dist} R_i + \rho N_{c,t}^{doc} + \delta_{i,j} + \tau_{s,t} + \omega_{R_i,t} + \epsilon_{i,j,c,s,t}. \quad (4)$$

I interact each pharmacy's risk group R_i (decile of predicted risk from the LASSO model) with the variable indicating distributor enforcement, $e_{j,t}$, and $\tilde{N}_{i,t}^{dist}$, the number of times

[27] I control for *OxyContin* reformulation using the state's 2004-2009 rate of *OxyContin* misuse (Alpert, Powell and Pacula, 2018), interacted with a variable for post-reformulation (2010Q3).

a distributor was shut down that supplied each pharmacy.[28] I also add risk-group-by-time fixed effects $\omega_{R_i,t}$. With this equation, ψ_r estimates the direct effects of distributor closures on opioid shipments to affected pharmacies in risk group r. χ_r estimates within-pharmacy substitution and deterrence effects. Importantly, this does not estimate impacts on total supply (as unaffected may pharmacies may substitute for affected ones); however, I estimate impacts on total supply using equation 3. Here, I focus on the impacts of distributor enforcement actions on specific pharmacies. I define the pass-through of distributor enforcement actions to pharmacies in each risk group r as $\hat{\theta}_r = \frac{\hat{\psi}_r + \hat{\chi}_r}{\hat{\psi}_r} \times 100\%$.

C. Estimating effects on local mortality rates

To estimate the effects of enforcement on mortality, I exploit variation in the timing and extent of enforcement activities across areas. Areas that experienced a single pharmacy being shut down experienced a lower-intensity treatment than areas that experienced multiple prescriber, pharmacy, and distribution facility enforcement actions over many years. I take advantage of this and develop a novel measure of the extent of enforcement activity in an area: the predicted quantity of opioids that enforcement disrupted in an area up to time t. Using the parameters of equation 3, I construct this metric as

$$\hat{\mathbf{E}}_{\mathbf{c},\mathbf{t}} = -1 \times \frac{1}{Pop_{c,t}} \sum_{i,j} \left(\hat{\alpha_1} e_{i,c,t} + \hat{\alpha_2} e_{j,c,t} + \hat{\rho} N^{doc}_{c,t} \right). \tag{5}$$

$Pop_{c,t}$ is the county's population at t. $\hat{\mathbf{E}}_{\mathbf{c},\mathbf{t}}$ estimates the stock of enforcement activity in county c at time t, denominated on a per capita doses of opioids basis. Specifically, it denotes the predicted quantity of opioids per capita that have been disrupted by enforcement interventions in each county and time period. Note that in equation 5, I only use the direct effects in equation 3 and the effects of prescriber enforcement so the measure represents the effects of a specific policy: shutting down suppliers that would have otherwise supplied a specific quantity of opioids. I do not instrument for opioid supply using equation 3 because I seek to estimate the causal effects of enforcement activity on mortality—not the causal effects of opioid supply on mortality.[29]

I estimate the causal effects of enforcement on mortality using the following regression,

$$Y_{c,s,t} = \beta \hat{\mathbf{E}}_{\mathbf{c},\mathbf{t}} + \xi_c + \upsilon_{s,t} + \nu_{c,s,t}. \tag{6}$$

$Y_{c,s,t}$ denotes the rate of drug poisoning deaths (separately for prescription opioids, illicit opioids, unidentified drugs, and all drugs) per 100,000 people in county c, state s, and

[28] $\tilde{N}^{dist}_{i,t} = \frac{\sum_j e_{i,j,t}}{N_i - \sum_j e_{i,j,t}}$.

[29] Instrumenting for opioid supply with enforcement and estimating the causal effects of opioid supply on mortality assumes an exclusion restriction: that enforcement only affects mortality through its effects on total opioid supply. The targeting of enforcement (see section I.C) implies that enforcement affects the types of customers that are supplied opioids in addition to the total quantity, violating the exclusion restriction. Reducing diverted prescription opioid supply would be expected to have different effects on mortality compared to reducing medical supply.

time t. ξ_c are county fixed effects, $\upsilon_{s,t}$ are state-by-time fixed effects, and $\nu_{c,s,t}$ is the error term. As the variables in equation 6 are rates, I weight by county population. To account for estimation error in the first stage, I use a county-level block bootstrap for inference on the parameters of equation 6. Specifically, I randomly draw 3,000 counties with replacement and repeat estimation of equations 3, 5, and 6 1,000 times. I construct 95 percent confidence interval sets as the range between the 2.5$^{\text{th}}$ and 97.5$^{\text{th}}$ percentiles of the boostrap distribution of $\hat{\beta}$.

Identification of equation 6 relies on the plausible exogeneity of the timing and extent of enforcement with respect to overdose deaths, controlling for time-invariant characteristics and time-varying confounders at the state level. Consistent with this, in **Appendix Table A3**, I show the strongest predictors of enforcement-driven supply shocks are time-invariant characteristics (enforcement was more common in urban areas that were near the DEA's Tactical Diversion Squad office locations, see section II.B) and lagged enforcement (see sections II.B and III). I also show enforcement was somewhat correlated with other state policies targeting opioids, which I account for with state-by-time fixed effects. Enforcement was only weakly related to levels of pre-enforcement opioid shipments, consistent with where diversion personnel were physically present being more important. Lastly, and most importantly from a causal identification standpoint, the timing and extent of enforcement were not related to county pre-enforcement prescription opioid or heroin death rates.

V. Effects on prescription opioid supply

In this section, I present estimates of the effects of supplier enforcement on local opioid supply. I have two main findings. The first is that all types of enforcement actions reduced local opioid supply. Second, I find that distributor enforcement actions had the largest effects on pharmacies and clinics that had the highest ex-ante risk of diversion. Other seemingly legitimate pharmacies were able to substitute to other distributors and were mostly unaffected. These results are consistent with there being heterogeneity in risk in the pharmacy industry (see section I.C) and a relatively small number of distributors that are willing to supply the riskiest pharmacies. Overall, results demonstrate a large role for enforcement to affect aggregate supply and diversion in prescription drug markets.

A. Aggregate impacts

I start by discussing the signs of the coefficients in equation 3 and implied pass-through rates. Because equation 3 is estimated at the firm (pharmacy-distribution facility pair level), the estimates are most informative about net effects: whether the average intervention was offset by substitution, passed through to aggregate supply, or led to deterrence effects that caused reductions beyond the firms targeted. After discussing net effects, I aggregate the parameter estimates and their implied effects across counties to provide additional context about how large and quantitatively important they are.

Results from estimating equation 3 are presented in **Table 2**. Starting with model 1, which does not include time-varying state controls or state-by-time fixed effects, the direct effects of enforcement are negative. Unsurprisingly, closing pharmacies and distribution facilities reduces the amount of opioids they supply to the market. The net effect of shutting down additional prescribers is also negative, implying the average prescriber closure caused lower overall opioid shipments to pharmacies in the same county (i.e., actions were not offset by substitution to other prescribers). Results are highly stable across model specifications.

Next, I examine substitution and deterrence. In model 1, the effects of pharmacy and distribution facility enforcement on non-targeted suppliers is also negative—implying potential deterrence effects. However, the effects of enforcement on non-targeted suppliers are more sensitive to model specification. In model 2 which includes time-varying state controls, the deterrence effects on non-targeted distribution facilities flips signs—implying some substitution. In the model with state-by-time fixed effects, the deterrence effects on non-targeted pharmacies also attenuate and results imply significantly more substitution following distributor enforcement actions. This suggests that part of the reductions among non-targeted firms in models 1 and 2 may be driven by other time-varying state factors that are correlated with the enforcement (e.g., states implementing policies at the same time as some enforcement actions were being undertaken, see section I.B and **Appendix Table A2**). Thus, I consider model 3 my preferred specification.

Importantly, across all specifications, there is substantial pass-through of each type of enforcement action into aggregate opioid supply. Pass-through is the highest for pharmacy enforcement actions (ranging from 146 percent in the model with state-by-time fixed effects to 185 percent in the model without state-by-time fixed effects or the policy variables). The pass-through estimate exceeding 100 percent is due to the pharmacy interventions having some local deterrence effects. Pass-through for distributor enforcement actions was lower, ranging from 38 percent in the model with state-by-time fixed effects to 117 percent in the model without state-by-time fixed effects or the policy variables. These all imply enforcement actions reduced aggregate supply.

Using my preferred specification with state-by-time fixed effects, **Table 3** demonstrates the quantitative importance of enforcement-driven supply reductions nationally. The first column shows the implied reduction in millions of 50 MME doses of opioids caused by each type of enforcement activity from 2006 to 2014. Pharmacy enforcement reduced aggregate prescription opioid supply by 102 million doses. Distributor enforcement reduced it by another 271 million doses. Prescriber enforcement (the most common type of intervention) had the largest effect, reducing supply by 600 million doses. Overall, I estimate that total U.S. opioid supply would have been 973 million doses (four percent) higher from 2006 to 2014 if there had not been any enforcement.

The intensity of enforcement and its impacts was heterogeneous across areas and over time. **Appendix Figure A4** shows trends in opioid supply and how much enforcement activities reduced opioid supply over time. There was little enforcement activity prior to 2010; thus, enforcement caused minimal reductions in overall opioid supply. Enforcement increased markedly after 2010, as several large distribution facilities were shut down (see **Table 1**), leading to much larger reductions in opioid supply attributable to enforcement from 2010 to 2014. Enforcement activity was also highly skewed across areas and was concentrated in a fairly small number of counties. **Appendix Figure A5** shows a map of the predicted doses of opioids disrupted per capita in each county of the U.S. by 2014 (from equation 5). Disruptions were most concentrated in Florida, consistent with section I.C, and affected other areas scattered throughout the country. Almost half of counties (46 percent) were not affected by any enforcement action over this period, reflecting the scarcity with which enforcement was used over this period which was characterized by high levels of prescription diversion. I exploit the variation in enforcement activity intensity across time and counties to study enforcement's effects on mortality in section VI.

B. Targeting of distributor enforcement

Next, I examine how well distributor enforcement actions were targeted toward disrupting diversion. As described in section I.C, a major policy concern about distributor enforcement actions is that they may disrupt opioid supply to legitimate businesses and patients. I examine whether this is true using equation 4, which allows for heterogeneous substitution for pharmacies and clinics with different risk profiles following distributor enforcement. Results are illustrated in **Figure 4**. The x-axis shows the pharmacies' predicted diversion risk decile (from the LASSO model presented in section IV.B). Pharmacies further to the right have higher ex-ante risk and features (such as historical opioid shipment patterns) that look more like pharmacies that were shut down by the DEA for diversion. The y-axis shows the change in opioid shipments due to distributor enforcement for pharmacies in each risk decile.

The figure shows three effects. First, the direct effects of the distributor enforcement actions (i.e., how much opioid supply fell from distributors that were shut down, ψ_r from equation 4) are shown in the red line with vertical hashes. Mechanically, these are negative throughout the distribution. They are also generally larger for higher-risk pharmacies (as higher-risk pharmacies ordered higher amounts of opioids, see **Appendix Table A2**). Next, the green line marked with triangles shows how much opioid shipments from non-targeted distributors increased to affected pharmacies in response (i.e., how much substitution there was). Lastly, the total effect (the sum of the direct effects and substitution) is shown in the black line with a shaded 95 percent confidence interval.

For most pharmacies (those below the 70^{th} percentile of the risk distribution), substitution to other distributors almost completely offset the effects of losing a distributor. Pass-through for these pharmacies ranged from 24 percent for the lowest risk pharmacies to 43 percent for the pharmacies between the 61^{st} and 70^{th} percentile (see the numerical values in **Appendix Table A4**). However, for the highest-risk pharmacies, there was limited substitution. For the 10 percent of pharmacies with the highest predicted risk, there was effectively no substitution and pass-through was complete (95 percent) (see **Appendix Table A4**). Thus, the distributor enforcement actions were well-targeted at disrupting opioid shipments to the riskiest pharmacies and had small effects on the broader market. In **Appendix Figure A6**, I show the cumulative distribution of distributor enforcement's overall effects on supply that come from pharmacies in each risk decile. The vast majority of effects (84 percent) come from reducing opioid supply to above-median-risk pharmacies.

Nearly half of the effects (47 percent) come from reducing supply to the 10 percent of pharmacies with the highest risk alone.

VI. Effects on mortality

In this section, I present estimates of the effects of enforcement-driven opioid supply shocks on mortality. I find that exposure to greater amounts of enforcement activity caused significant reductions in mortality from prescription opioids. Furthermore, I find that reductions in prescription opioid supply and mortality did not cause substitution to heroin or other potential substitute drugs. Results show that enforcement actions were effective at reducing overall drug poisoning mortality in targeted areas.

A. Overall impacts

Results from estimating equation 6, which relates the extent of enforcement across counties and over time to mortality rates, are presented in **Table 4**. All results control for state-by-year fixed effects to adjust for any policies or other factors that are unfolding at the state level in areas that were affected by the enforcement actions. The first column shows results for prescription opioid deaths. Each additional dose of prescription opioids that was disrupted per capita caused 0.13 fewer prescription opioid deaths per 100,000 people. To illustrate the magnitude of this effect, I also translate the estimate into an implied elasticity of the effectiveness of enforcement: the percent change in deaths from disrupting one percent of a county's opioid supply.[30] The results imply that disrupting prescription opioid supply by one percent caused 0.27 percent fewer prescription opioid poisoning deaths.

The next column shows that these enforcement actions did not cause increased heroin deaths. The point estimate is negative and the 95 percent confidence interval excludes any increase in heroin deaths greater than 54 percent as large as the reduction in prescription opioid deaths. The third column shows enforcement also caused reductions in drug poisoning deaths where the specific underlying substances were not reported. Ruhm (2017) argues that many of the drug poisoning deaths where specific drugs were not mentioned over this period were actually prescription opioid deaths; this result corroborates that. The end result is that each additional dose of prescription opioids that were disrupted per capita caused 0.41 fewer total drug poisoning deaths per 100,000 people. This implies an elasticity of enforcement with respect to overall drug poisoning deaths of -0.22.

Table 4 Panels B and **C** show results separately for counties in Florida and counties in the rest of the U.S. I show results separately for Florida and the rest of the U.S. because Florida accounted for a disproportionate amount of enforcement activity over this period (see section I.B). Thus, it is unclear a priori whether effects would be similar in Florida compared to the rest of the U.S., which experienced enforcement actions of a much more

[30]Specifically, let μ_d denote the mean rate of deaths and μ_s denote the mean doses of opioids supplied in the US. The elasticity I calculate is $e = \frac{\frac{\beta}{\mu_d}}{\frac{1}{\mu_s}}$.

limited scale. Results show that the relationship between the amount of opioids disrupted and mortality was virtually the same in Florida as it was in other areas (albeit, effects outside of Florida are imprecisely estimated). In Florida and in other areas, greater amounts of enforcement caused fewer prescription opioid deaths (elasticities were very similar, ranging from -0.39 in Florida to -0.42 outside of Florida). More enforcement also caused fewer deaths where specific drugs were not mentioned. Further, both in Florida and in other areas, there was no relationship between enforcement and heroin mortality. The results imply that disrupting opioid supply by one percent reduced total drug poisoning mortality by 0.35 percent in Florida and 0.28 percent in other areas.

B. Would increasing enforcement have continued to reduce mortality?

Figure 5 presents the estimated effects of enforcement on mortality within Florida and other areas graphically. The figure relates county rates of drug poisoning deaths per 100,000 people (on the y-axis) to the per capita doses of prescription opioids disrupted by enforcement actions in that county and time period (from equation 5). The data are collapsed into twenty equally sized bins and the figure is adjusted for county, time, and state-by-time fixed effects. Regression lines from **Table 4** are also overlaid on the figure.

Both panels show an approximately linear relationship between the amount of enforcement activity in an area and mortality. More enforcement resulted in fewer drug poisoning deaths, and the slope is essentially the same within Florida and for all other counties in the U.S. Furthermore, the figure also highlights the vast discrepancy between the amount of enforcement activities undertaken in Florida compared to other areas. The diagram for Florida (Panel A) includes a grey box depicting the range of the amount of opioids disrupted by enforcement interventions across all twenty bins of counties outside of Florida. Even the counties in the highest quantile of exposure to enforcement outside of Florida experienced less enforcement than counties in the second-lowest quantile of enforcement in Florida. However, within that narrow range, the slope in Florida and outside of Florida is essentially identical. This suggests that had other counties outside of Florida been treated by a similar amount of enforcement as the counties in Florida had, mortality would have fallen by a similar amount. Furthermore, enforcement reducing mortality over the much wider range of variation in Florida suggests that even very large increases in enforcement outside of Florida would have continued to reduce mortality.

One possibility is that similar levels of enforcement would not have been possible outside of Florida, due to there being less opioid supply and diversion outside of Florida. This seems unlikely for several reasons. First, relative to overall opioid supply, enforcement activities were extremely limited in all areas over this time period. This is illustrated in **Figure 6**, which shows a histogram of each state's average quarterly rate of shipments of 50 MME doses of opioids per capita from 2006 to 2014 and the average quantity of opioids disrupted by enforcement activities. Even in the state with the most enforcement (Florida), enforcement activities disrupted the equivalent of just 12 percent of total opioid supply. In the state with the next most enforcement (Delaware), enforcement disrupted just 3.2 percent of supply. Second, while it is true that Florida was an outlier with respect to opioid supply and diversion, there were several areas of the U.S. with similar amounts of opioid shipments or more compared to Florida (West Virginia, Kentucky, Delaware, and Tennessee all received more) but which experienced substantially less enforcement activity (see **Figure 6**). This is because the enforcement activities that did occur over this period were not particularly targeted towards areas that had the greatest need. As discussed in I.B, they were targeted towards areas that had need but were also proximate to major urban areas where the DEA had offices (such as Miami in Florida). Taking this argument a step further, **Appendix Figure A7** maps the locations of the top 1 percent of pharmacies with the highest predicted diversion risk (from the LASSO model of section IV.B) alongside the locations of the suspicious pharmacies and clinics that were actually shut down. There were large areas of the country with a high concentration of suspicious pharmacies and clinics, most notably the Appalachian corridor at the borders of Kentucky, Tennessee, Virginia, and West Virginia, but where the suspicious actors were not shut down. All this suggests there were many areas of the U.S. where enforcement could have been increased considerably and that it would have reduced mortality in those areas.

VII. Robustness checks

In this final section, I examine the robustness of the results reported above to alternative specifications and estimation strategies. First, I examine the robustness of the results to an alternative market definition: commuting zones instead of counties. I repeat the entire analysis using commuting zones as markets for estimation of equations 3, 5, and 6. Because commuting zones overlap states, in this analysis I do not include time-varying state controls or state-by-year fixed effects (just unit and time-fixed effects). **Appendix Table A3** shows results for supply, which are very similar to what I found in section V.A. The enforcement actions had high pass-through into local opioid supply, even when the market is defined at the broader commuting zone level. This shows that expanding the market catchment area did not lead to lower pass-through estimates, as would be the case if interventions were offset by other suppliers opening up in other areas that were nearby but not necessarily in the same counties as suppliers that were shut down.

Appendix Table A4 shows results for mortality, which shows similar patterns to what I reported above. Greater enforcement activity within a commuting zone reduced prescription opioid and total drug poisoning deaths. However, the effects of enforcement actions on mortality at the commuting zone level of aggregation are even larger. Overall, I estimate that disrupting one percent of opioid supply in a commuting zone reduced all-cause drug poisoning deaths in that commuting zone by 0.58 percent. This is more than twice as large as the -0.22 percent estimate in section VI. These larger effects could be the result of reduced measurement error at the commuting zone level of aggregation. Cross-county and even cross-state trafficking of prescription opioids was common over this period. This type of measurement error will lead estimates of the effects of enforcement on within-county mortality to be biased toward the null. It is possible that aggregating to commuting zones helps improve the situation if opioids are more likely to be consumed within the commuting zone they were shipped to compared to the county. However, a limitation is that at this level of aggregation, I am unable to control for state-by-time fixed effects. There may also be other state-level and time-varying factors (e.g., state opioid policies) occurring at the same time and in the same places as the enforcement actions and that are contributing to the larger estimates. Thus, the county-level specification with state-by-time fixed effects in section VI is my preferred specification.

Lastly, to supplement the regression analyses of section V and VI, I also prevent results from non-parametric event studies that exploit variation in the location and timing of the largest county-level supply shocks over this period. Studying enforcement actions in an event study framework is challenging due to the way that enforcement commonly unfolds: in particular, that it plays out over long periods of time and that many suppliers tend to end up being prosecuted in the same areas (see sections I.B and III). This means that any given enforcement event is likely preceded and followed by others—making it a challenge to isolate the effects of any single event. Smaller events (e.g., physician arrests) that precede larger ones (e.g., a distributor action) also affect pre-trends, a common visual test of the plausibility of the parallel trends assumption required for causal identification in event studies. Finally, most enforcement actions were very small relative to overall opioid supply and would not be expected to cause easily discernible changes in aggregate supply or deaths on their own. For all these reasons, the regression analyses which uses continuous exposure to enforcement is my preferred approach. However, to assess robustness to different approaches and, in particular, to probe the robustness of the finding of a lack of substitution from prescription opioids to heroin due to enforcement—I examine trends in opioid supply and death rates around the time of the 100 largest enforcement-driven opioid supply shocks that occurred anywhere in the U.S. If reducing prescription opioid supply were to cause significant and offsetting substitution to heroin, one would expect that to occur after these very large and abrupt supply shocks.

For each firm (pharmacy or distributor) that was shut down, I estimated how many opioids they supplied in every county prior to being shut down. Then, I selected the interventions that targeted the 100 largest county-firm pairs. Each of these interventions were due to one of the distributor closures. A map of the counties that experienced one of these large distributor enforcement actions, as well as a histogram of the times that they occurred, is shown in **Appendix Figures A8** and **A9**. Most of the counties were located in Florida (see section I.B). However, there were also scattered counties throughout other areas of the U.S. Most of the shocks occurred at the end of 2007 when Cardinal Health's three distribution facilities were initially shut down (see **Table 1**). There was also a clustering of large supply shocks from 2010 to 2012 when several Florida-based distribution facilities were shut down (see **Table 1**).

I use the estimator described in Callaway and Sant'Anna (2021) (robust to heterogeneous treatment effects in the presence of differential treatment timing) to estimate changes in opioid supply and mortality for up to two years after these shocks. Results for opioid supply are shown in **Figure A10**. Opioid supply fell sharply and significantly after these large enforcement actions. The pooled estimate implies opioid supply fell in affected areas by 1.32 50 MME doses per person in the county (29 percent relative to the pre-period mean).

Next, **Appendix Figure A11** shows results for mortality involving prescription opioids (panel A) and heroin (panel B). As in the regression analysis of section VI.A, mortality involving prescription opioids fell after the large distributor supply shocks (by 20 percent). Furthermore, heroin mortality did not change. The effect on heroin is a sharply estimated null and I can rule out any increase in heroin more than 8 percent as large as the decline in prescription opioid deaths with 95 percent confidence. The overall result is that these large enforcement actions caused significant reductions in total drug poisoning mortality (see **Appendix Figure A12**). Quarterly drug poisoning deaths fell by 0.81 deaths per 100,000 (31 percent) over the two years following the largest enforcement actions.

VIII. Conclusion

This paper provides the first systematic evidence of the effects of supplier enforcement in markets for prescription opioids, a major way that policymakers have responded to the U.S. opioid crisis. I find that supplier enforcement actions had high pass-through into local opioid supply. I also find that interventions targeting distributors were well-targeted at disrupting high-risk use, with limited effects on the broader medical market. Broadly, these results show that enforcement policies play a large role in affecting how much diversion there is in markets for harmful and addictive prescription drugs. Furthermore, results show that the limited amount of enforcement while opioid supply was at its peak, and in areas where diversion was the greatest, played a large role in the development of the opioid crisis.

With respect to health outcomes, enforcement actions reduced prescription opioid and all-cause drug poisoning mortality. Reducing prescription opioid supply and deaths also did not cause increased deaths from heroin, as previous literature suggested it might. Evidence of limited or harmful effects of enforcement and other supply-side interventions has led drug policy advocates to increasingly focus their attention away from supply-side drug control strategies. However, these findings show a much larger role for targeting the availability of drug supply to reduce mortality than was previously thought. An important area for future work is to examine the role of supplier enforcement in reducing deaths from illicit fentanyl and its analogues, which are responsible for most opioid deaths currently.

The implications of these findings for other addictive prescription drugs (e.g., stimulants, for which prescriptions have been rising sharply in recent years) and for preventing future epidemics are also important. In the aftermath of the enforcement actions analyzed in this paper, the landscape for successfully prosecuting and shutting down prescribers, pharmacies, and pharmaceutical distributors that supply controlled substances recklessly is even more difficult than it was before. In 2015, Congress passed the "Ensuring Patient Access and Effective Drug Enforcement Act," which raised the standard of proof that is required before the Drug Enforcement Administration can shut down pharmaceutical distribution facilities.[31] In 2022, the U.S. Supreme Court also increased standards for prosecuting pre-

[31] See S. Higham and L. Bernstein, "The Drug Industry's Triumph over the DEA," 2017. Prior to the Act, the DEA had to prove the distributors posed a threat to public health before revoking their licenses, e.g., by showing they shipped unusual quantities of opioids to pharmacies that had been found to be dispensing them inappropriately. Now, the DEA must show that distributors pose an "imminent" threat to public health, which rules out using

scribers, requiring evidence that they intentionally prescribe opioids in a harmful manner (rather than negligently). Both of these factors limit the ability to respond effectively to future crises involving diverted prescription drugs with supplier enforcement interventions. Examining the implications of this is an important area for future research.

retrospective data on opioid shipments to suspicious pharmacies to demonstrate harm.

REFERENCES

Alpert, Abby, David Powell, and Rosalie Liccardo Pacula. 2018. "Supply-side drug policy in the presence of substitutes: Evidence from the introduction of abuse-deterrent opioids." *American Economic Journal: Economic Policy*, 10(4): 1–35. ISBN: 1945-7731.

Alpert, Abby, William N Evans, Ethan M J Lieber, and David Powell. 2021. "Origins of the Opioid Crisis and its Enduring Impacts*." *The Quarterly Journal of Economics*, qjab043.

Arteaga, Carolina, and Victoria Barone. 2021. "A Manufactured Tragedy: The Origins and Deep Ripples of the Opioid Epidemic." *Working Paper*, 72.

Balestra, Simone, Helge Liebert, Nicole Maestas, and Tisamarie B. Sherry. 2021. "Behavioral Responses to Supply-Side Drug Policy During the Opioid Epidemic." National Bureau of Economic Research Working Paper 29596. Series: Working Paper Series.

Callaway, Brantly, and Pedro HC Sant'Anna. 2021. "Difference-in-differences with multiple time periods." *Journal of econometrics*, 225(2): 200–230.

Cutler, David M., and Edward L. Glaeser. 2021. "When Innovation Goes Wrong: Technological Regress and the Opioid Epidemic." *Journal of Economic Perspectives*, 35(4): 171–196.

Evans, William N., Ethan MJ Lieber, and Patrick Power. 2019. "How the reformulation of OxyContin ignited the heroin epidemic." *Review of Economics and Statistics*, 101(1): 1–15. ISBN: 0034-6535 Publisher: MIT Press.

Kennedy-Hendricks, Alene, Matthew Richey, Emma E. McGinty, Elizabeth A. Stuart, Colleen L. Barry, and Daniel W. Webster. 2016. "Opioid overdose deaths and Florida's crackdown on pill mills." *American journal of public health*, 106(2): 291–297. ISBN: 1541-0048 Publisher: American Public Health Association.

Kim, Bokyung. 2021. "Must-access prescription drug monitoring programs and the opioid overdose epidemic: The unintended consequences." *Journal of Health Economics*, 75: 102408.

Mallatt, Justine. 2022. "Policy-induced substitution to illicit drugs and implications for law enforcement activity." *American Journal of Health Economics*, 8(1): 30–64. ISBN: 2332-3493 Publisher: The University of Chicago Press Chicago, IL.

McGuire, Thomas G. 2000. "Physician agency." *Handbook of health economics*, 1: 461–536.

Meinhofer, Angelica. 2016. "The war on drugs: Estimating the effect of prescription drug supply-side interventions." *Available at SSRN 2716974*.

Powell, David, and Rosalie Liccardo Pacula. 2021. "The evolving consequences of oxycontin reformulation on drug overdoses." *American Journal of Health Economics*, 7(1): 000–000. ISBN: 2332-3493 Publisher: The University of Chicago Press Chicago, IL.

Ruhm, Christopher J. 2017. "Drug involvement in fatal overdoses." *SSM - Population Health*, 3: 219–226.

Schnell, Molly. 2022. "Physician behavior in the presence of a secondary market: The case of prescription opioids." *NBER Working Paper No. 26095.*

Soliman, Adam. 2022. "Disrupting Drug Markets: The Effects of Crackdowns on Rogue Opioid Suppliers." *Available at SSRN.*

Table 1: Enforcement actions against pharmaceutical distribution facilities, 2006 to 2014.

	Type	MM/YY	Status
AmerisourceBergen Drug			
Orlando FL	ISO	04/2007	License re-instated in 08/2007.
Anda, Inc.	Administrative action*	06/2010	Resumed shipments to pharmacies in 07/2010 but not pain clinics.
Bellco Drug Corporation	ISO	05/2007	License surrendered in 04/2007. Fined $800,000.
Cardinal Health			
Auburn WA, Lakeland FL, Swedesboro NJ	ISO	12/2007	Licenses re-instated in 10/2008. Fined $11 million.
Lakeland FL	ISO	05/2012	License re-instated in 05/2014. Fined $34 million.
Harvard Drug Group	ISO	06/2010	License re-instated in 04/2012. Fined $8 million.
Keysource Medical	ISO	06/2011	License surrendered in 09/2011.
Medical Arts	Indictment	08/2011	Firm closed. Owner sentenced in 08/2012.
Paragon Enterprises Inc.	Administrative action*	06/2010	Resumed shipments to pharmacies in 07/2010 but not pain clinics.
Richie Pharmacal	ISO	03/2007	License surrendered in 04/2007.
Southwood Pharmaceuticals	ISO	11/2006	License revoked in 06/2007
Sunrise Wholesale, Inc.	ISO	06/2010	Never re-opened.
Walgreens			
Jupiter FL	ISO	09/2012	License surrendered in 06/2013. Fined $80 million.

Notes: Some enforcement actions affected entire companies, while others affected only particular facilities. When the enforcement affected particular facilities, I indicated their locations below the company in *italics* and presented the information about the enforcement in the same row as the facility locations. ISOs are Immediate Suspension Orders which prevented affected companies/facilities from supplying controlled substances while active. The indictment was a criminal indictment against the owner of Medical Arts and several affiliated business partners. *Anda, Inc., and Paragon Enterprises, Inc., were part of a coordinated administrative action that shut down their shipments to pain clinics in Florida. However, they were never prosecuted or shut down overall.

Table 2: All types of enforcement activity passed through to aggregate opioid supply.

	(1)	(2)	(3)
Pharmacy shutdown ($\hat{\alpha}_1$)	-3.207	-3.206	-3.198
	(0.420)	(0.420)	(0.420)
Distributor shutdown ($\hat{\alpha}_2$)	-2.484	-2.484	-2.487
	(0.041)	(0.041)	(0.040)
Other pharmacies shutdown in county ($\hat{\gamma}_1$)	-2.710	-2.594	-1.463
	(0.796)	(0.793)	(0.794)
Other distributors shutdown in county ($\hat{\gamma}_2$)	-0.416	0.161	1.548
	(0.142)	(0.133)	(0.228)
Number prescribers shutdown in county ($\hat{\rho}$)	-0.034	-0.029	-0.029
	(0.003)	(0.003)	(0.003)
Pass-through [95% confidence intervals]			
Pharmacy enforcement actions ($\hat{\theta}_1$)	185	181	146
	[126, 243]	[124, 238]	[93.0, 198]
Distributor enforcement actions ($\hat{\theta}_2$)	117	93.5	37.8
	[106, 128]	[83.0, 104]	[20.0, 55.6]
Controls:			
Post state PDMP		-0.140	
		(0.009)	
Post state pain clinic law		-0.131	
		(0.013)	
2004-09 state *OxyContin* misuse×Post-2010Q3		0.159	
		(0.029)	
Pharmacy-distributor fixed effects	X	X	X
Time fixed effects	X	X	X
State-by-time fixed effects			X
Within R-squared	0.005	0.005	0.004
N (pharmacy-distributor pairs × quarters)	16,953,910	16,953,802	16,953,802

Notes: Results are estimates of equation 3 and the implied pass-through. The dependent variable is thousands of 50 MME doses of opioids, from ARCOS. Standard errors are clustered at the firm level and reported in parentheses. 95% confidence intervals for pass-through use the delta method. See section IV.A for more details.

Table 3: Enforcement reduced total U.S. opioid supply by four percent from 2006 to 2014.

	Impact (million 50 MME doses)	Impacts as % of supply
Pharmacy enforcement	-102.4	-0.4
	[-137.7, -67.2]	
Distributor enforcement	-270.7	-1.1
	[-421.5, -119.9]	
Prescriber enforcement	-600.0	-2.5
	[-711.6, -488.3]	
All enforcement	-973.1	-4.0
	[-1,895, -51.0]	
Total supply (million doses)	24,485	

Notes: Aggregate impacts implied by **Table 2** model 3. 95% confidence intervals are presented in brackets.

Table 4: Greater exposure to enforcement activity reduced drug poisoning deaths.

	Impact on overdose deaths per 100,000 involving:			
	Rx opioids	Heroin	Unknown drugs	Any drug
Panel A. All counties				
Doses disrupted per capita (β)	-0.13	-0.01	-0.21	-0.41
	[-0.39, -0.03]	[-0.09, 0.07]	[-0.45, -0.004]	[-0.72, -0.23]
Implied elasticity	-0.27	-0.05	-0.44	-0.22
N (counties × quarters)	109,324	109,324	109,324	109,324
Panel B. Within Florida				
Doses disrupted per capita (β)	-0.16	-0.02	-0.25	-0.46
	[-1.54, -0.03]	[-0.08, 0.14]	[-0.98, 0.35]	[-2.16, -0.23]
Implied elasticity	-0.39	-0.25	-0.59	-0.35
N (counties × quarters)	2,412	2,412	2,412	2,412
Panel C. Excluding Florida				
Doses disrupted per capita (β)	-0.20	-0.003	-0.25	-0.53
	[-0.45, 0.35]	[-0.24, 0.23]	[-0.76, 0.42]	[-1.07, 0.57]
Implied elasticity	-0.42	-0.01	-0.51	-0.28
N (counties × quarters)	106,912	106,912	106,912	106,912

Notes: Estimates from 6. A county-level block bootstrap of equations 3, 5, and 6 with 1,000 iterations was used to construct 95% confidence intervals (shown in brackets). Implied elasticities estimate the change in deaths resulting from disrupting one percent of local opioid supply with enforcement actions.

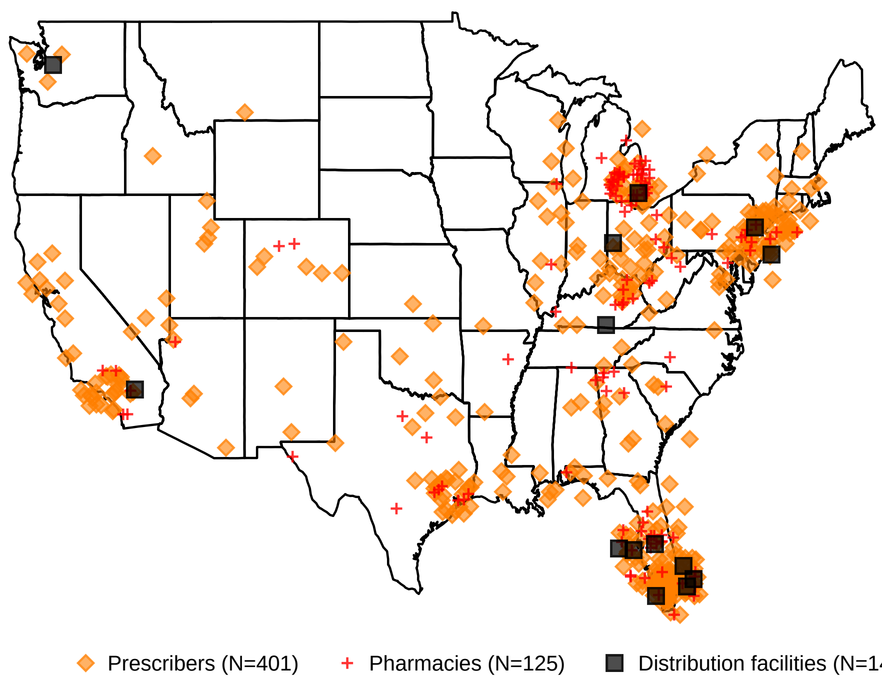

Figure 1: Map of suppliers shut down by enforcement interventions, 2006–2014.

Notes: Uses geocoded data provided by the Washington Post and (where geocoded data were not available) each supplier's 5-digit zip code. Spherical random noise was added to each location to highlight clusters.

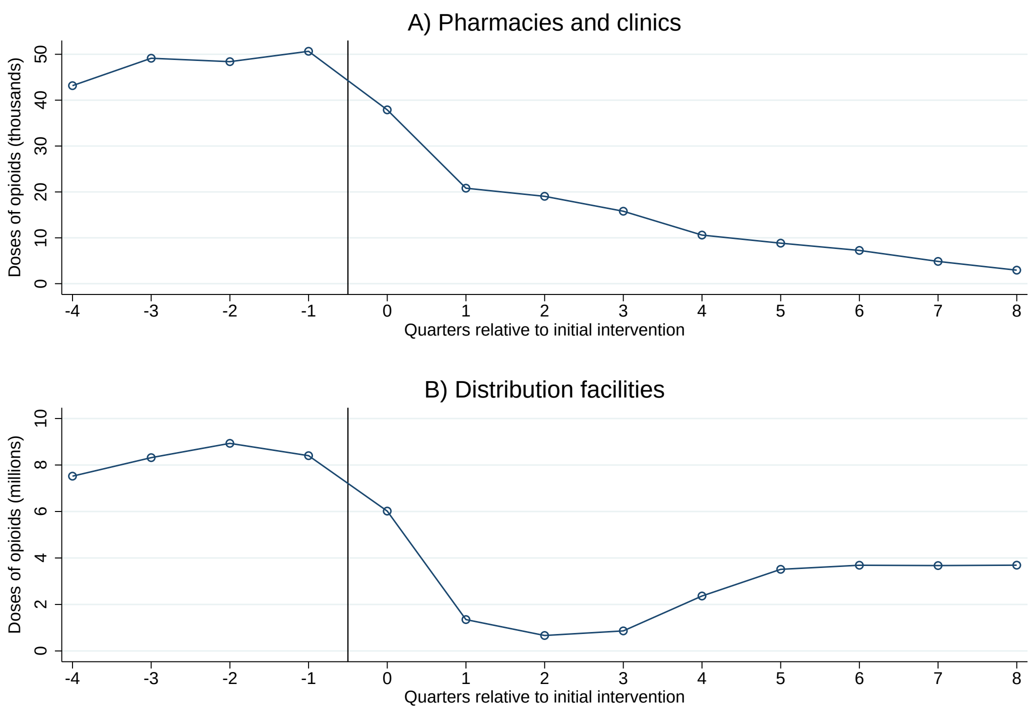

Figure 2: Targeted pharmacies and clinics (distributors) received (distributed) fewer opioids immediately after initial interventions that ultimately led to them being shut down.

Source: Author's analysis of the Automation of Reports and Consolidated Orders System.

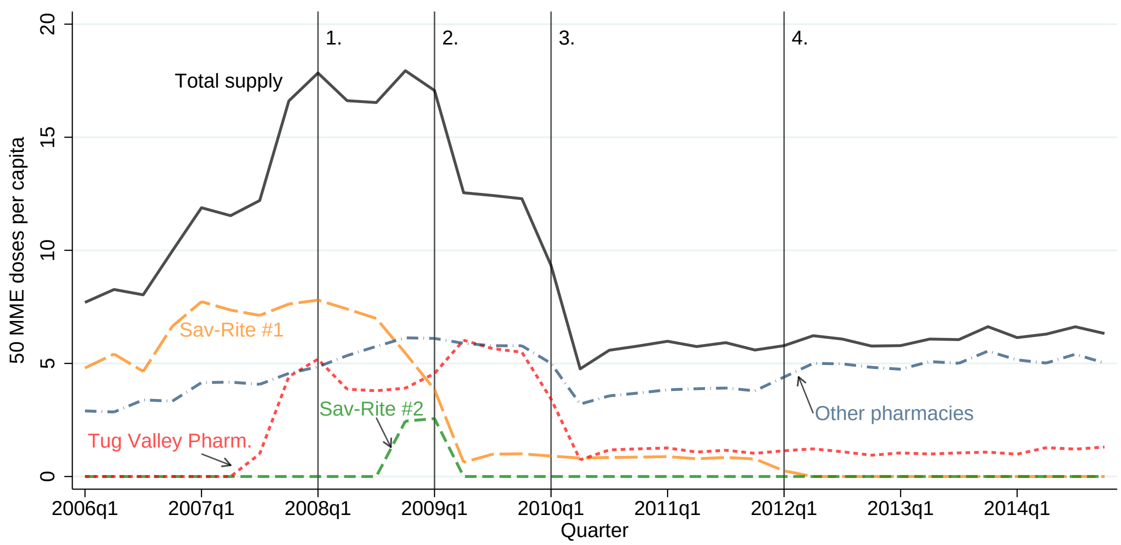

Figure 3: Supplier enforcement actions reduced opioid supply in Mingo County, W.Va.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS). Figure legend: 1. Drug Enforcement Administration begins undercover investigation in the area. 2. The Drug Enforcement Administration raids and closes Sav-Rite Pharmacy #2 and Justice Medical Complex, arresting two physicians. 3. The Drug Enforcement Administration raids Mountain Medical Care Center and an orthopedic physician's practice, arresting two physicians. 4. The owner of the two Sav-Rite pharmacies is indicted.

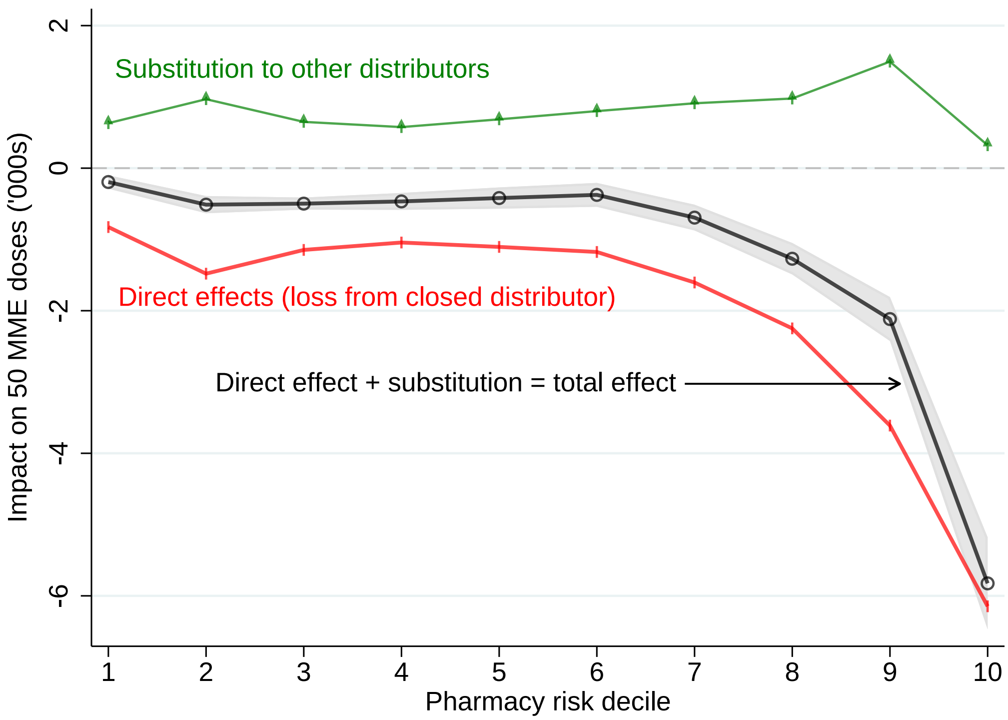

Figure 4: Distributor enforcement had greater pass-through for the most suspicious pharmacies.

Notes: Estimates from equation 4. See sections IV.B and V.B for more details.

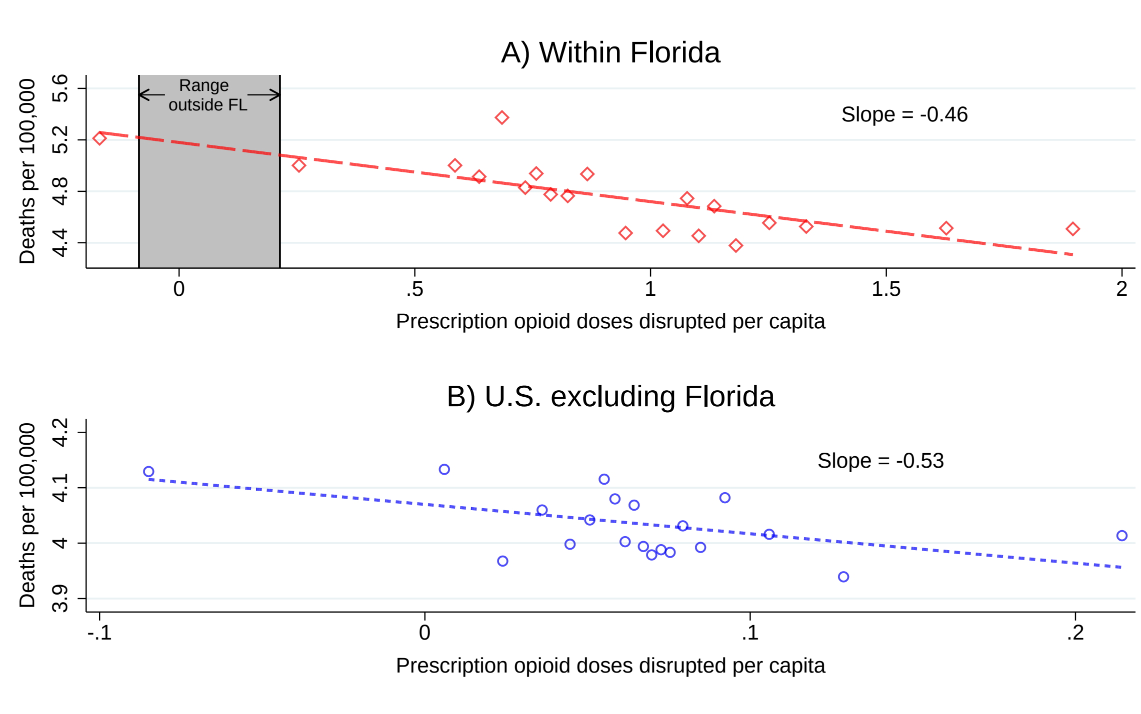

Figure 5: Greater intensity enforcement resulted in fewer drug poisoning deaths.

Notes: Binned scatter plot of data from ARCOS and NVSS. Controls for county and state-by-time fixed effects.

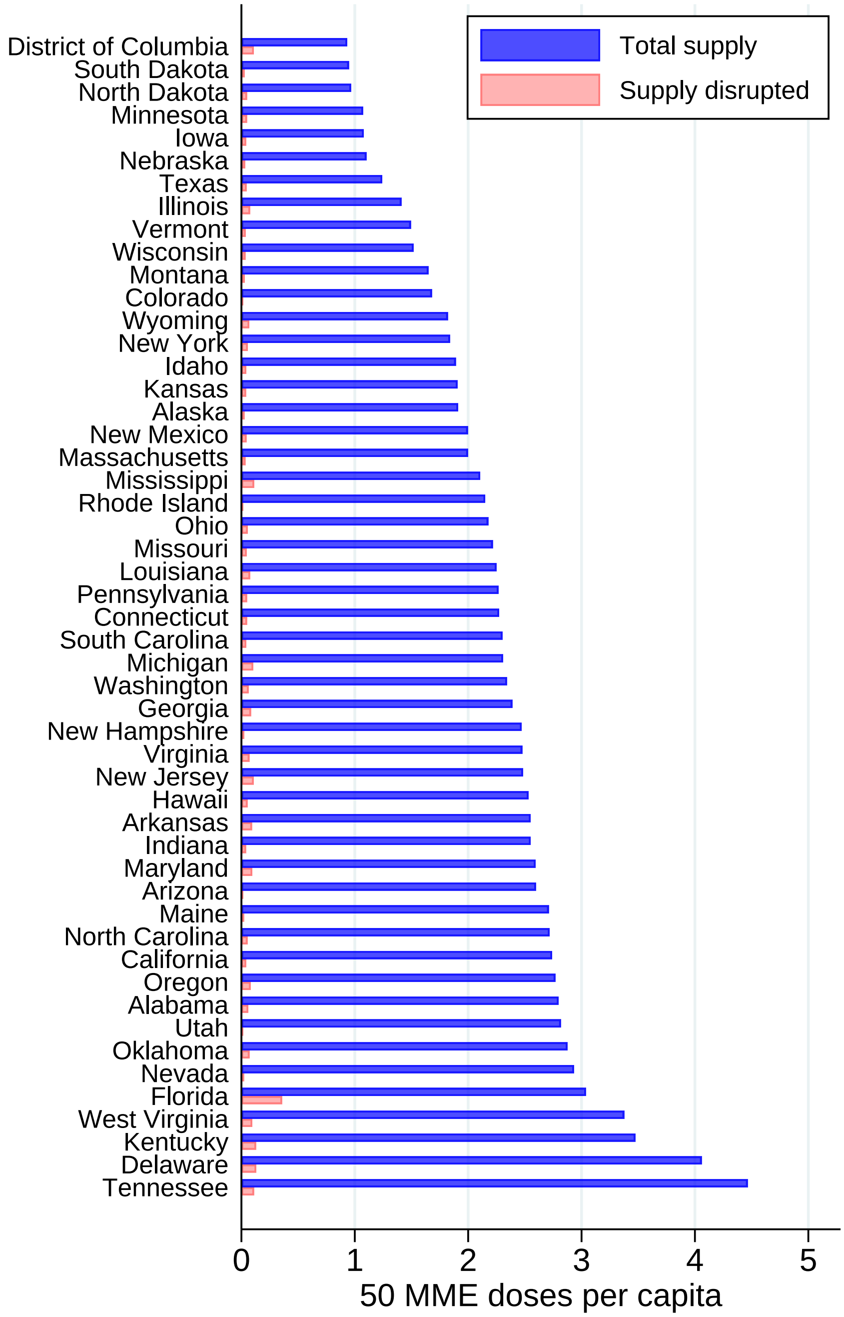

Figure 6: Enforcement activities were extremely limited relative to U.S. opioid supply.

Notes: Histogram of doses of 50 MME opioids supplied from 2006 to 2014 and doses disrupted by enforcement. Author's analysis of ARCOS.

Appendix A. Additional Tables and Figures for Online Publication

Table A1: Supplier obligations under the Controlled Substances Act.

Type of supplier	Obligations	Customer red flags
Manufacturers	Produce below DEA assigned quota	Orders of unusual size
	Report sales data to ARCOS	Orders deviating from a normal pattern
	Design systems to detect suspicious orders	Orders of unusual frequency
	Not sell to customers placing suspicious orders	
	Report customers placing suspicious orders to DEA	
Distributors	Report sales data to ARCOS	Orders of unusual size
	Design systems to detect suspicious orders	Orders deviating from a normal pattern
	Not sell to customers placing suspicious orders	Orders of unusual frequency
	Report customers placing suspicious orders to DEA	
Dispensers	Keep accurate inventories and records	Many customers present similar prescriptions
	Report data on sales to DEA	Customers paying in cash
	Ensure prescriptions are for legitimate medical purpose	Customers visit in groups
	Not dispense prescriptions of suspicious origin	Customers traveling long distances
Prescribers	Keep accurate inventories and records	Patient requests specific drug
	Prescribe for legitimate medical purpose	Patient has no treatment records
	Act in the usual course of medical practice	Patient cites textbook symptoms

For more information, see the following resources:
1. Congressional Research Service, "Legal Authorities Under the Controlled Substances Act to Combat the Opioid Crisis," 2018, available at: https://sgp.fas.org/crs/misc/R45164.pdf.
2. Prevoznik, "Distributor Initiative: A National Perspective," 2013, available at: https://web.archive.org/web/20220418181747/https://www.deadiversion.usdoj.gov/mtgs/distributor/conf_2013/prevoznik.pdf.
3. Georgia Office of the Attorney General, "Red Flags for Physicians," available at: https://law.georgia.gov/key-issues/opioid-abuse/3-red-flags-physicians.

Table A2: Variables that predict pharmacy and clinic enforcement actions.

	Standardized coefficient
Max quarterly MME × clinic	0.0079882
Max quarterly MME	0.0046973
Max quarterly MME × chain pharmacy	0.0027799
Max quarterly pills	-0.0019251
Max quarterly MME × 2004-09 state *Oxy* misuse	0.0019032
Max pills × chain pharmacy	-0.0017757
Max $\frac{\text{Quarterly MME}}{\text{pills}}$× chain pharmacy	-0.0007961
Max quarterly MME × retail pharmacy	0.0005168
Max $\frac{\text{Quarterly MME}}{\text{pills}}$× retail pharmacy	0.0004182
Max quarterly pills × 2004-09 state *OxyContin* misuse	0.0001914
Max $\frac{\text{Quarterly MME}}{\text{pills}}$× 2004-09 state *OxyContin* misuse	-0.0001855
Max quarterly pills × retail pharmacy	0.0001689
2004-09 state *OxyContin* misuse	-0.0000604
R-squared	0.07
N (pharmacies and clinics)	139,731

Notes: Table presents the selected coefficients and their standardized impacts, from a LASSO linear regression of the probability that the pharmacy was shut down by the DEA between 2006 and 2014. Variables that were included are maximum quarterly pill and morphine milligram equivalent (MME) shipments, maximum growth in pill and MME shipments across periods, maximum MME and pill shipments per capita in the pharmacy's or clinic's county, the maximum quarterly ratio of MME to pills (i.e., potency per pill), business type (whether chain pharmacy, retail pharmacy, or a practitioner clinic), state 2004-09 state *OxyContin* misuse rates from the National Survey on Drug Use and Health, and two-way interactions between the historical opioid shipments variables, business type, and state *OxyContin* misuse rates.

Table A3: The timing and intensity of enforcement was not related to pre-enforcement deaths.

	D.V.: doses of opioids disrupted per capita.			
	(1)	(2)	(3)	(4)
Log 2010 population	0.0554	0.0568	0.0393	0.0017
	(0.0145)	(0.0144)	(0.0100)	(0.0005)
Miles to TDS office ('00s)	-0.0030	-0.0022	-0.0300	-0.0012
	(0.0014)	(0.0011)	(0.0094)	(0.0004)
2006Q1 opioid doses per capita	0.0835	0.0731	0.0495	0.0020
	(0.0329)	(0.0271)	(0.0192)	(0.0008)
2006Q1 prescription opioid deaths	-0.0076	-0.0068	-0.0017	-0.0000
	(0.0061)	(0.0057)	(0.0040)	(0.0002)
2006Q1 heroin deaths	-0.0257	-0.0194	-0.0046	-0.0001
	(0.0182)	(0.0167)	(0.0122)	(0.0006)
Post state PDMP		0.0144		
		(0.0161)		
Post state pain clinic law		0.2266		
		(0.0708)		
2004-09 state *OxyContin* misuse×Post-2010Q3		0.0249		
		(0.0930)		
Lagged dependent variable				1.0128
				(0.0024)
Time fixed effects	X	X	X	X
State-by-time fixed effects			X	X
R-squared (within)	0.13	0.20	0.10	0.97
N	109,260	109,260	109,224	106,190

Notes: See section IV.C for details.

Table A4: Distributor enforcement had greater pass-through for higher-risk pharmacies.

	Direct ($\hat{\psi}_r$)	Substitution ($\hat{\chi}_r$)	Pass-through ($\hat{\theta}_r$)
Risk percentile			
1–10	-0.826	0.631	23.5
	(0.024)	(0.055)	[12.0, 35.1]
11–20	-1.480	0.968	34.6
	(0.034)	(0.067)	[26.4, 42.8]
21–30	-1.147	0.650	43.4
	(0.035)	(0.046)	[36.4, 50.3]
31–40	-1.043	0.576	44.7
	(0.045)	(0.063)	[33.9, 55.5]
41–50	-1.105	0.685	38.0
	(0.061)	(0.081)	[25.2, 50.8]
51–60	-1.176	0.801	31.9
	(0.060)	(0.096)	[17.8, 46.0]
61–70	-1.604	0.910	43.2
	(0.059)	(0.102)	[32.0, 54.5]
71–80	-2.248	0.977	56.5
	(0.063)	(0.121)	[46.6, 66.4]
81–90	-3.611	1.494	58.6
	(0.085)	(0.166)	[50.1, 67.1]
91–100	-6.146	0.322	94.8
	(0.163)	(0.316)	[84.7, 104.8]

Notes: Estimates from equation 4. See sections IV.B and V.B for more details.

Table A5: Robustness of opioid supply results to commuting zone market definition.

	(1)
Pharmacy shutdown ($\hat{\alpha}_1$)	-3.24
	(0.42)
Distributor shutdown ($\hat{\alpha}_2$)	-2.48
	(0.04)
Other pharmacies shutdown in CZ ($\hat{\gamma}_1$)	-12.02
	(1.60)
Other distributors shutdown in CZ ($\hat{\gamma}_2$)	-0.54
	(0.15)
Number prescribers shutdown in CZ ($\hat{\rho}$)	-0.01
	(0.001)
Pass-through [95% confidence intervals]	
Pharmacy enforcement actions ($\hat{\theta}_1$)	471
	[325, 617]
Distributor enforcement actions ($\hat{\theta}_2$)	122
	[110, 134]
Controls:	
Pharmacy-distributor fixed effects	X
Time fixed effects	X
Within R-squared	0.005
N (pharmacy-distributor pairs × quarters)	16,953,912

Notes: Results are estimates of equation 3 and the implied pass-through. The dependent variable is thousands of 50 MME doses of opioids, from ARCOS. Standard errors are clustered at the firm level and reported in parentheses. 95% confidence intervals for pass-through use the delta method. See section IV.A for more details.

Table A6: Robustness of mortality results to commuting zone market definition.

	Impact on overdose deaths per 100,000 involving:			
	Rx opioids	Heroin	Unknown drugs	Any drug
Doses disrupted per capita (β)	-0.31	-0.18	-0.24	-0.85
	[-0.53, -0.15]	[-0.31, 0.03]	[-0.51, -0.09]	[-1.33, -0.47]
Implied elasticity	-0.81	-0.99	-0.62	-0.58
N (CZs $\times$ quarters)	25,340	25,340	25,340	25,340

Notes: Estimates from 6. A commuting zone-level block bootstrap of equations 3, 5, and 6 with 1,000 iterations was used to construct 95% confidence intervals (shown in brackets). Implied elasticities estimate the change in deaths resulting from disrupting one percent of local opioid supply with enforcement actions.

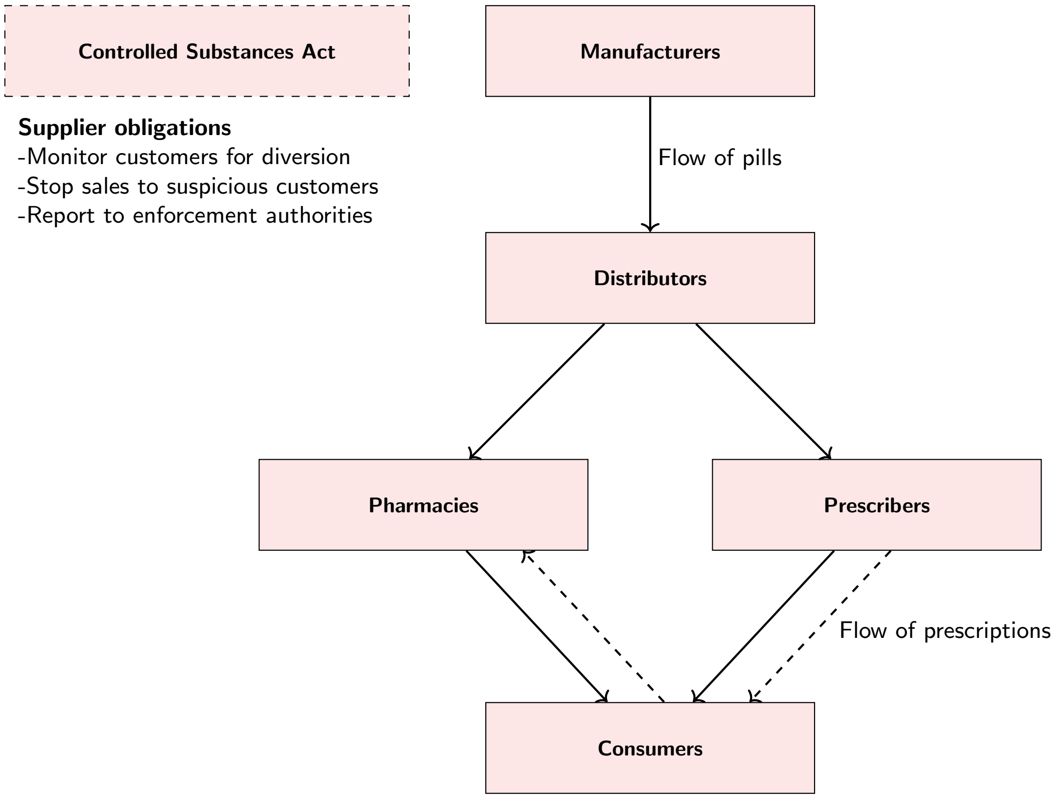

Figure A1: Flow of pills and prescriptions in the prescription drug industry.

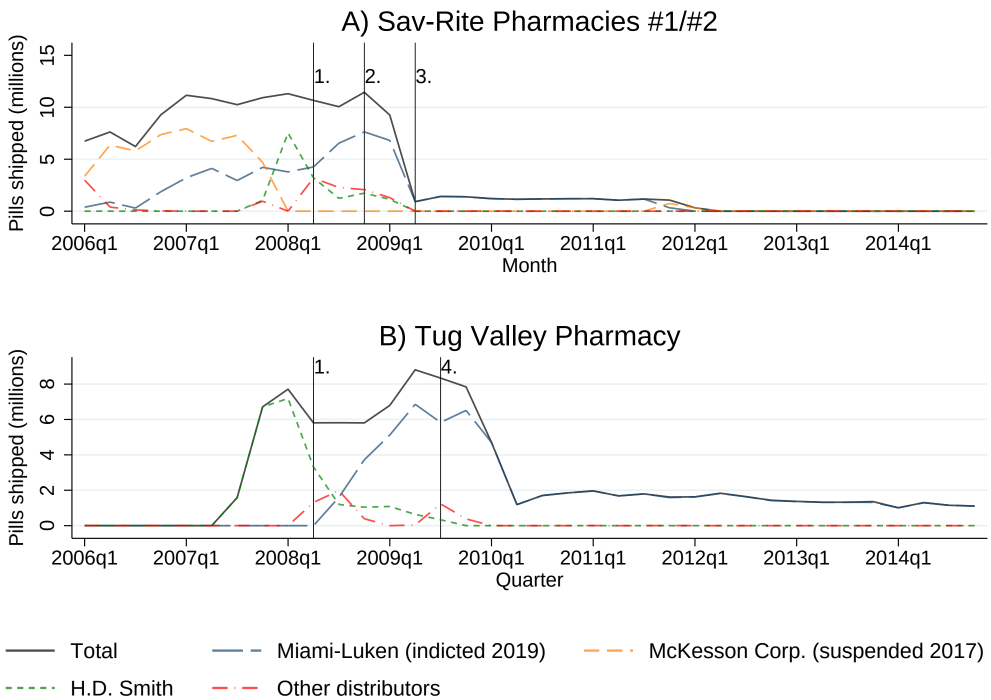

Figure A2: Trends in opioid shipments to Sav-Rite and Tug Valley pharmacies by distributors.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS). Figure legend: 1. H.D. Smith reports data on the Sav-Rite and Tug Valley pharmacies to the DEA. 2. H.D. Smith visits Sav-Rite. 3. Sav-Rite #2 is raided by the DEA; H.D. Smith terminates business with Sav-Rite #1. 4. H.D. Smith visits and terminates business with Tug Valley Pharmacy. See section V of the text for more details.

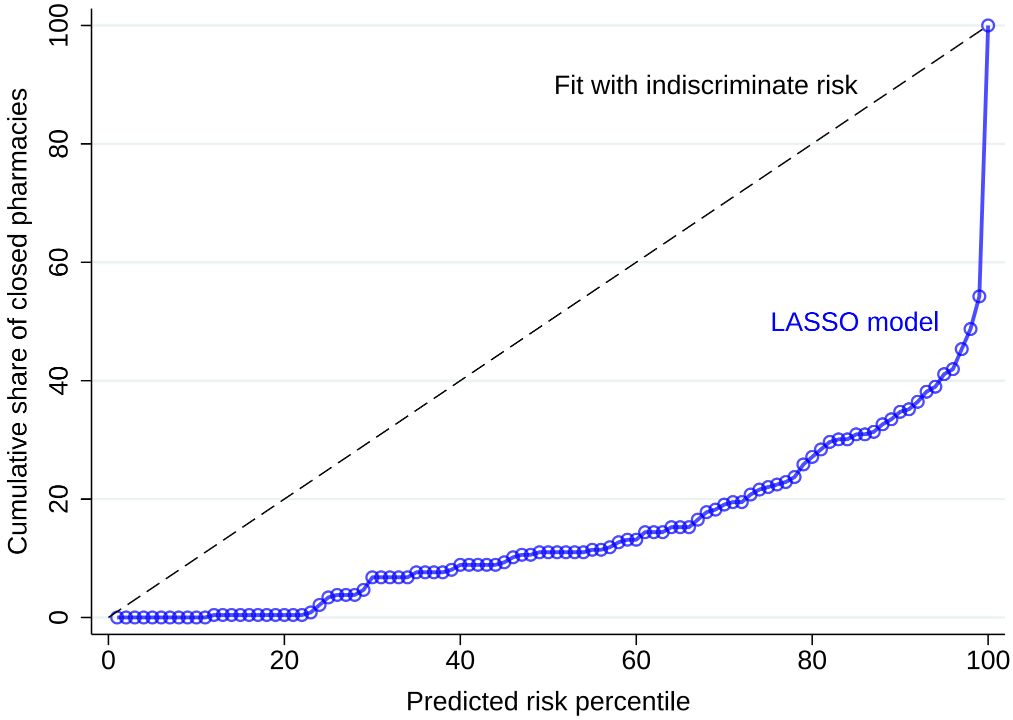

Figure A3: Power of LASSO model to predict pharmacy enforcement actions.

Notes: See section IV.B for more details.

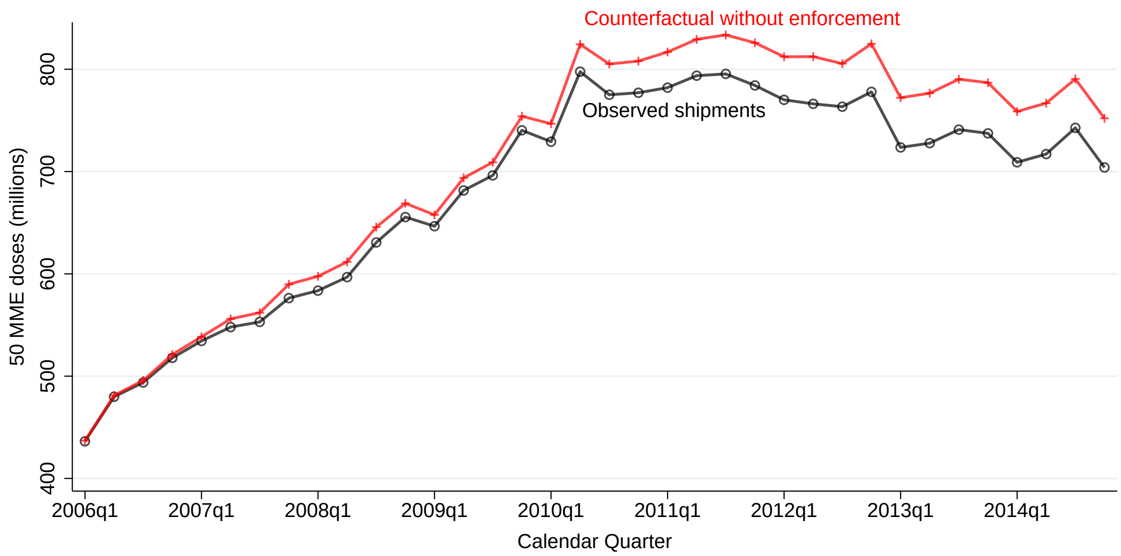

Figure A4: Trends in national opioid shipments and impacts of enforcement.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS). See section V.A.

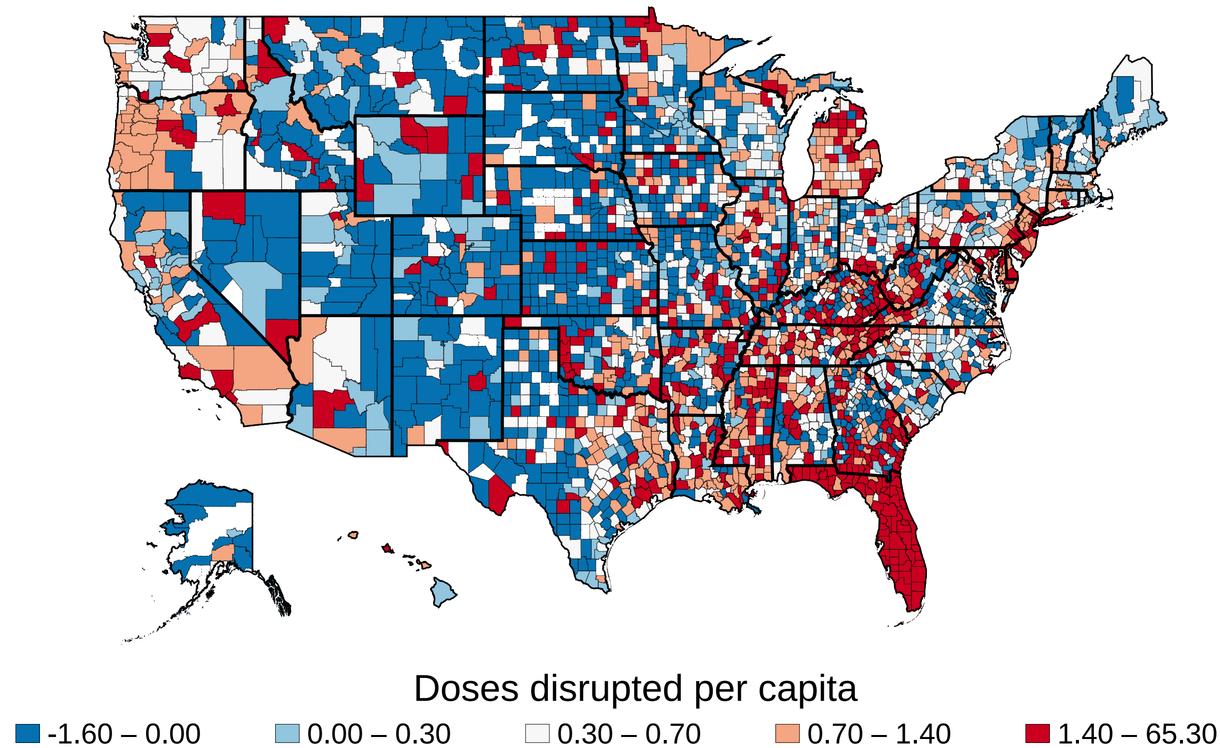

Figure A5: Map of enforcement impacts on supply across counties.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS). See section V.A.

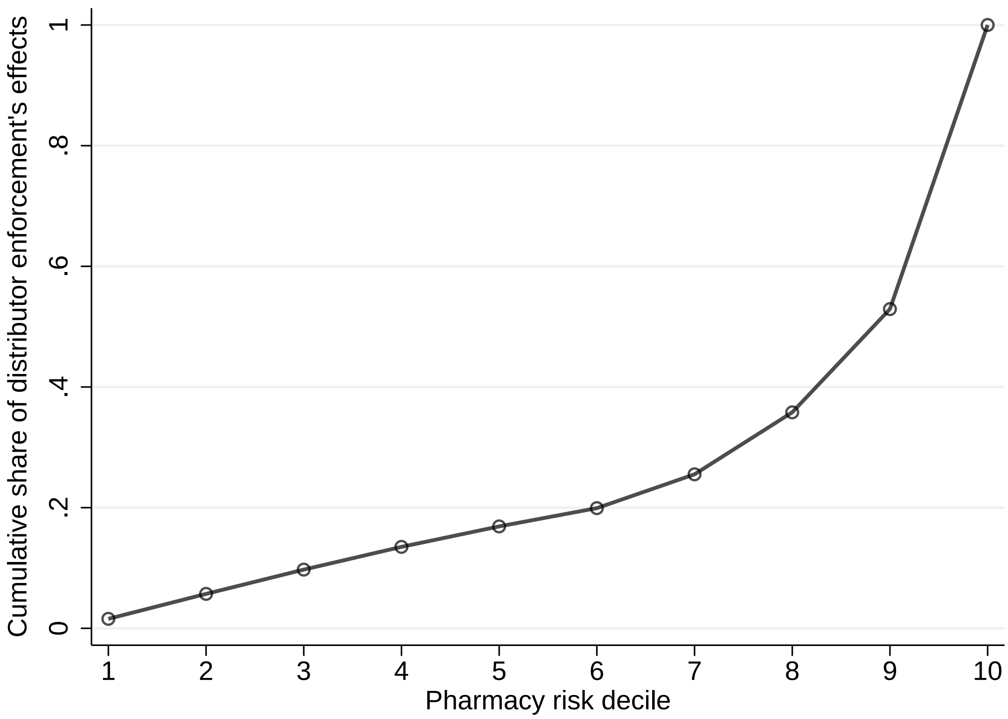

Figure A6: Most of the effects of distributor enforcement actions came from reducing opioid supply to the highest-risk pharmacies.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS).

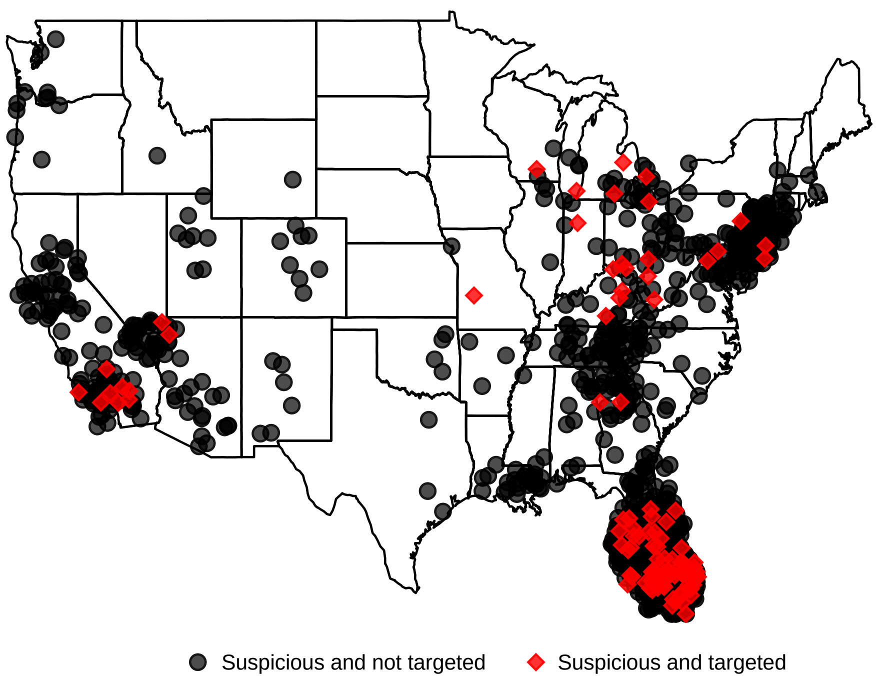

Figure A7: Map of suspicious pharmacies and clinics that were and were not targeted by DEA enforcement actions.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS).

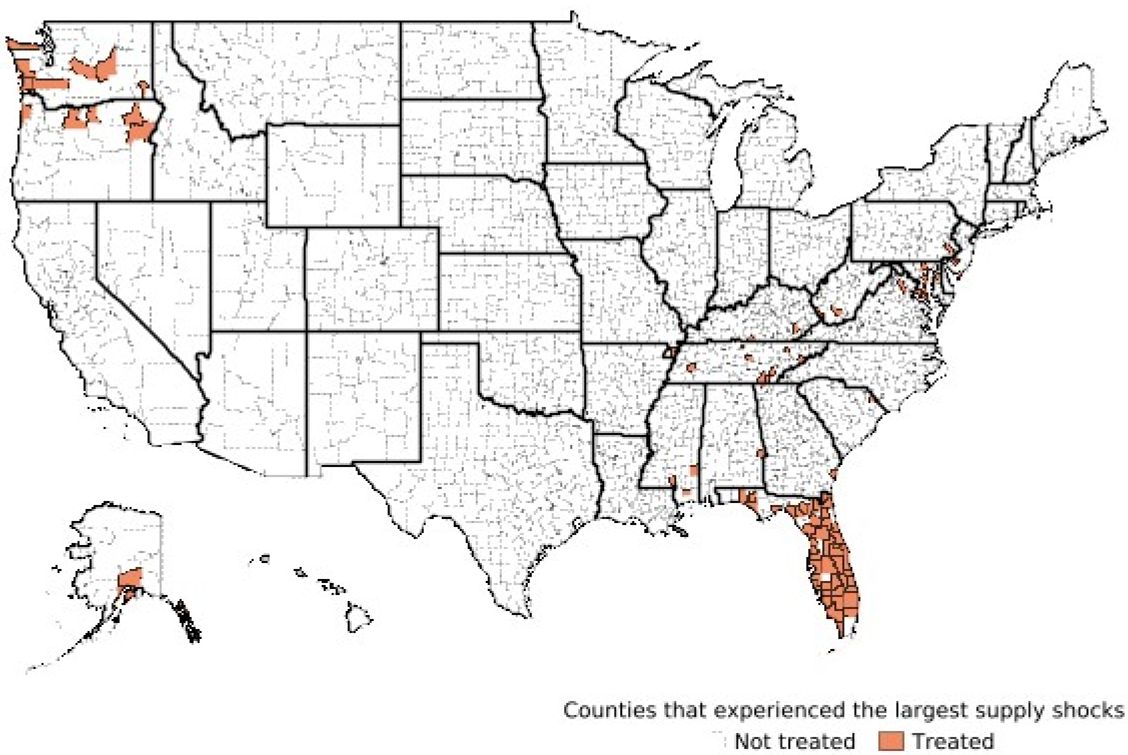

Figure A8: Map of counties that experienced the 100 largest distributor supply shocks.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS).

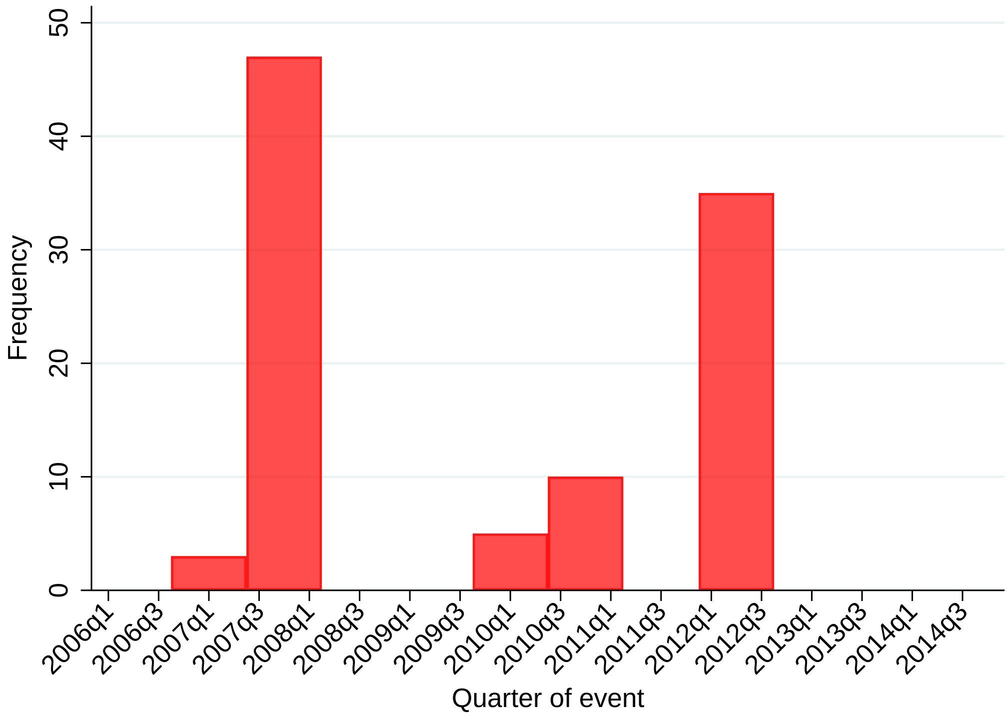

Figure A9: Timing of the 100 largest distributor supply shocks.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS).

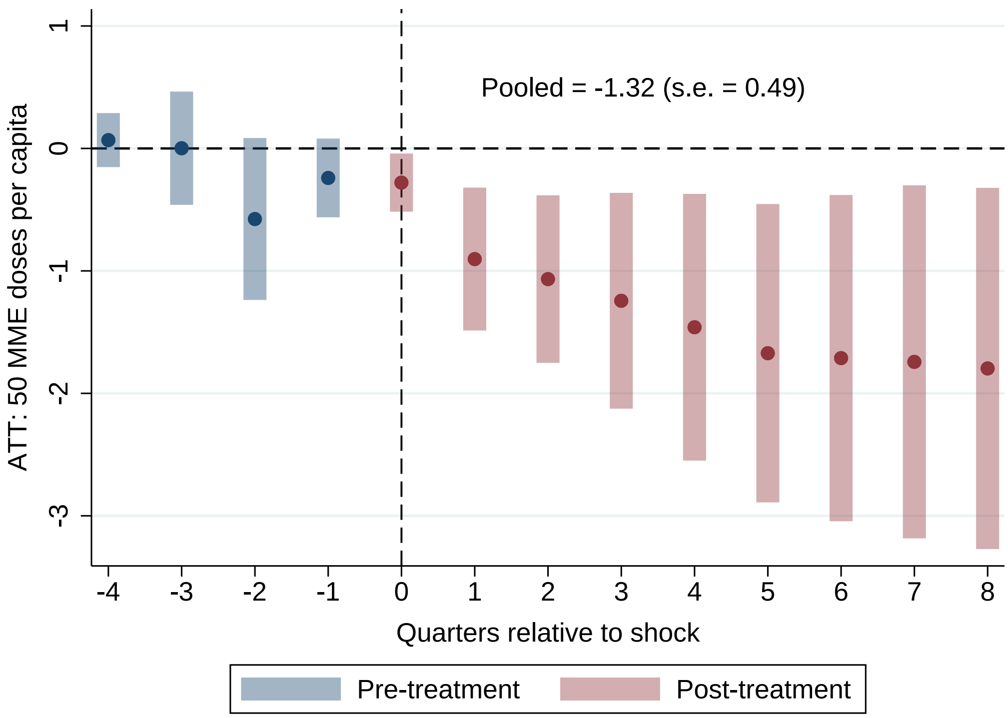

Figure A10: Opioid supply fell significantly after the 100 largest enforcement actions.

Notes: Data are from the Automation of Reports and Consolidated Orders System (ARCOS). Figure plots event study estimates of changes in opioid supply for up to one year before and two years after the 100 largest supplier enforcement actions in the U.S. Uses the Callaway and Sant'Anna (2021) estimator that is robust to heterogeneous treatment effects when treatment timing is differential. "ATT" denotes average treatment effect on the treated.

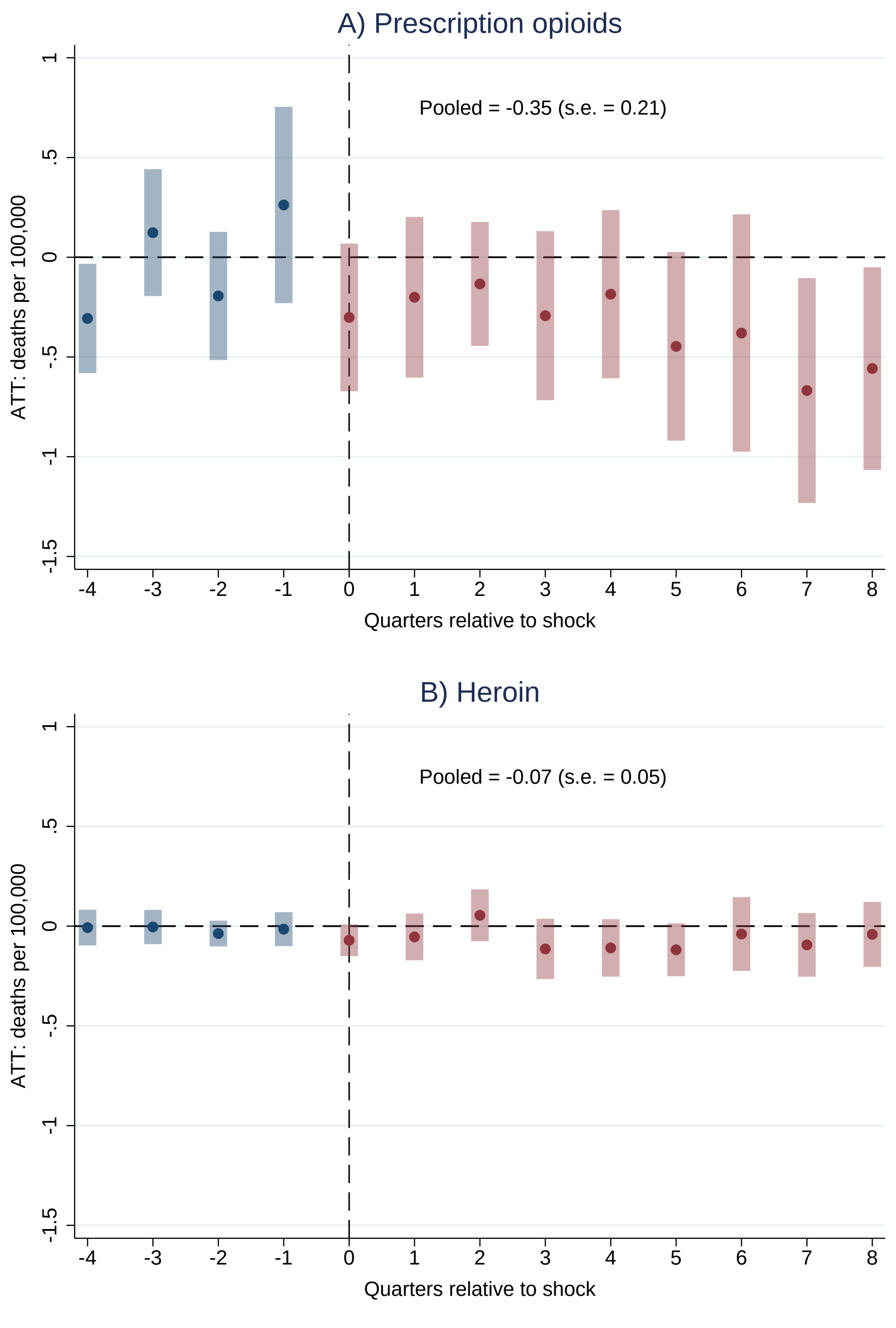

Figure A11: Prescription opioid mortality fell after the 100 largest enforcement actions; heroin mortality did not change.

Notes: Data are from the National Vital Statistics System (NVSS). Figure plots event study estimates of changes in prescription opioid and heroin poisoning death rates for up to one year before and two years after the 100 largest supplier enforcement actions in the U.S. Uses the Callaway and Sant'Anna (2021) estimator that is robust to heterogeneous treatment effects when treatment timing is differential. "ATT" denotes average treatment effect on the treated.

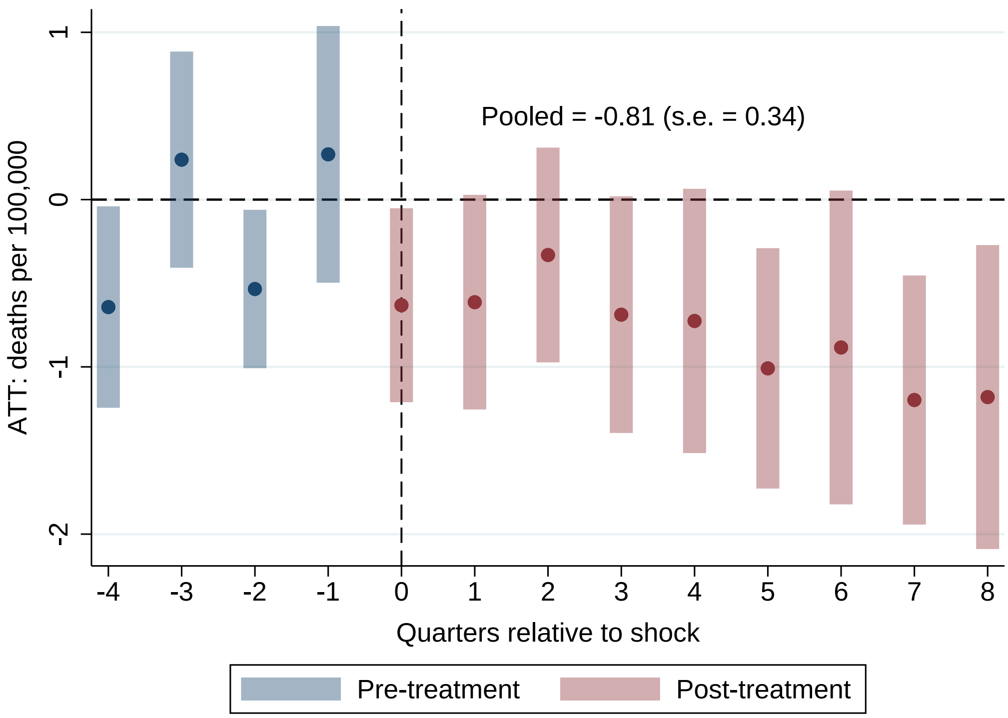

Figure A12: Total drug mortality fell significantly after the 100 largest enforcement actions.

Notes: Data are from the National Vital Statistics System (NVSS). Figure plots event study estimates of changes in all-cause drug poisoning death rates for up to one year before and two years after the 100 largest supplier enforcement actions in the U.S. Uses the Callaway and Sant'Anna (2021) estimator that is robust to heterogeneous treatment effects when treatment timing is differential. "ATT" denotes average treatment effect on the treated.