THE EFFECT OF A LARGE PRESCRIPTION OPIOID DIVERSION EVENT ON OPIOID MORTALITY IN THE U.S.

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Abstract

Over a two-week period in December 2007, a massive spike of prescription opioids surged into retail pharmacies in 78 counties in five Southeastern U.S. states. These "spike counties" experienced an average 313% increase over baseline in opioid deliveries – representing more than 147 million excess opioid doses. The pattern of facts available is consistent with the hypothesis that Colombian drug cartels became suddenly unable to launder large amounts of physical cash at the end of 2007 at a time when their capacity to supply eastern US heroin markets was failing; they used their excess cash to acquire prescription opioid products which were diverted to the illicit drug market in the eastern US. This had the potential to change the proportion of prescription opioids (with precisely calibrated potency) relative to drugs like heroin (possessing uncertain potency) in the illicit drug market. We estimate novel difference-in-differences models of substance-specific opioid mortality and find that in the three years following the shock non-prescription opioid deaths fell and prescription opioid deaths rose in the eastern (Colombian cartel-controlled) US counties relative to western (Mexican cartel-controlled) counties. Further, we estimate that on net overall opioid mortality fell relative to the counterfactual.

Keywords: Opioid mortality, opioid diversion, pharmacy markets
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1 Introduction

The opioid epidemic has had a devastating impact on the United States. In the past 20 years, the rate of opioid use and mortality has increased more than sixfold. It is widely believed that one of the main drivers of this epidemic is the rapid proliferation of opioid pain medications prescribed by physicians and distributed by local pharmacies in the early 2000s (Simon 2012). Sales of OxyContin® prescriptions alone increased by almost an order of magnitude from about 670,000 in 1997 to about 6.2 million by 2002 (United States. General Accounting Office 2003). Overall, prescriptions for self-administered opioids rose throughout the first decade and a half since 1996, peaking in 2012 at more than 255 million prescriptions before falling to just over 142 million prescriptions by 2020 (CDC 2021). As opioid prescriptions increased, so have fatal opioid poisonings. The number of opioid-associated overdose deaths rose from just over 21,000 in 2010 to 68,630 accidental poisonings involving an opioid by 2020 (and rising again during the pandemic to more than 75,000 opioid deaths by 2022) (Powell et al. 2020; Ahmad et al. 2023). The strongly correlated trends between opioid prescribing and mortality suggest to many researchers that the diversion of prescription opioids into the illicit market is a key enabler of the opioid mortality epidemic (Janssen and Zhang 2023; Dart et al. 2015; King et al. 2014; Green et al. 2013; Donahoe 2022; Soliman 2022).

While there are a plethora of policy options to constrain the supply of opioids out of pharmacies – including prescription drug monitoring programs, limits on initial days supply, and limits on refills – interventions on the demand side have been less widespread. One option that has been explored in the face of potentially deadly risky behaviors like opioid abuse – usually on a single clinic or single city level – is promoting the use of less harmful alternatives. Needle exchange programs and safe use sites have been tested, with some success, as means of making opioid injection practices less risky (Strathdee and Vlahov 2001; Levengood et al. 2021). Harm abatement proponents assume that the prohibition of risky activity doesn't work and that in the face of *some* risky behavior persistence it's better to promote less risky, rather than more risky, activity. Harm abatement interventions are not limited to the problem of illicit opioid use. Some researchers advocate (controversially) that vaping or smokeless tobacco are less damaging nicotine ingestion strategies than smoking, even without asserting that they are themselves as safe as cessation (Marti et al. 2019; Pesko et al. 2020). The risk of unintended pregnancy may best be managed with regular oral contraception and/or condom use, but Plan B is offered as a better alternative than unprotected sex without any form of birth control. Automobiles are a major source of greenhouse gas emissions and even though electric vehicles do not eliminate emissions many argue that they do "move the needle" toward environmental improvement. During the COVID-19 epidemic masks were seen as

a less risky way to shorten lockdown periods even though they did not completely eliminate the risk of people gathering in large groups.

These harm abatement strategies are broadly applied and can be motivated by appealing to the theory of second best, a perspective with a long tradition in welfare economics (Lipsey and Lancaster 1956). Empirically, there are three hurdles to understanding the causal impact of harm abatement. First, in nearly all circumstances when the harm abatement option is sharply introduced (and thereby subject to clean identification) it occurs because of some government action; examples of this are the aforementioned needle exchange programs, the 2010 reformulation of Oxycontin® to make the drug less easily abused, or safe injection sites for intravenous drug users. It is not clear how well such deliberate harm abatement can translate into markets without governmental intervention. Second, when harm abatement does arise from innate market forces, it is rarely sharply introduced at a defined point in time which clouds identification; examples include the substitution of vaping or smokeless tobacco for cigarette smoking or the gradual replacement of internal combustion engine automobiles with electric automobiles. Third, when harm abatement interventions are deliberately designed to permit clean identification of a causal effect, often in the context of a clinical trial or program evaluation, they typically involve relatively small populations of affected people.

We explore a novel – indeed, we believe unique – example of a large-scale (unintentional) harm reduction event that impacted large sections of the United States east of the Mississippi River, which was initiated over one very compressed two-week period at the end of 2007, and which arose without government action. Thus, this event overcomes each of the three evaluation hurdles mentioned above. In what follows we present what we believe to be compelling evidence that there was an extremely large surge of prescription opioids into selected Southeastern U.S. counties in December of 2007 that almost certainly resulted from Colombian drug trafficking organization coordinated activity to divert prescription drugs into the illicit market as a substitute for heroin. For structural reasons that we discuss below, this diversion event impacted areas east of the Mississippi River and did not spill into areas west of the Mississippi. Further, since prescription medications are produced with very tight dosing tolerances, unlike illicitly manufactured drugs like heroin, the resulting illicit market drug supply became, for a time, safer. Using a novel spacial differences-in-differences strategy, we find that mortality from accidental drug poisonings did plausibly fall for heroin, and other non-prescription opioids by around 22%. At the same time, mortality associated with prescription opioids increased by about 16%. Ultimately we estimate that across all treated counties, mortality from any opioid poisoning fell by 5.4% in counties affected by the diversion compared to unaffected counties.

In addition to the evidence we provide regarding harm reduction, this article is the first one

to provide indicative evidence of how the involvement of large organized drug trafficking has permeated the opioid epidemic since. The current academic understanding of how illegal actors involvement into the opioid epidemic started, is thought to be triggered by the reformulation of Oxycontin (Evans et al. 2019; Alpert et al. 2018). However, the substituting patterns observed from the reformulation of oxycodone into heroin abuse, can only be observed if there was already an ongoing relationship between users and their dealers. The diversion events we argue occurred in this paper are indicative that drug trafficking involvement started earlier than the reformulation, and demonstrate channels through which legally produced opioids reached illegal markets well before it is currently understood. Considering the extent of the crisis entirely driven by illegal actors, we make one of the first contributions to this part of the opioid epidemic of illegal actors involvement that is less than well understood.

2 Background

Living with chronic pain is an extremely common problem for people in the United States. Chronic pain represents a major contributor to disability and can be exacerbated by adverse mental states (like depression and anxiety). Managing pain is not only a clinically challenging undertaking, it is also a public health problem. (National Research Council, 2011) Estimates in the literature suggest that between 11 to 30 percent of the U.S. population experiences chronic pain currently (Johannes et al. 2010; Kennedy et al. 2014; Nahin 2015; Volkow and McLellan 2016).

Historically, managing nerve pain has been very difficult as until the mid-1990s there were few drugs that could be easily self-administered by patients in the community. The introduction of Oxycontin® by Purdue Pharma changed that. Combined with marketing by the pseudo-professional American Pain Society and the adoption of "pain as the fifth vital sign" credo among many clinicians, new extended-release opioid formulations (dominated by Oxycontin®) flooded the market. This ushered in what has been called the "first wave" of the opioid crisis which was characterized by a rapid rise in deaths attributed to opioid compounds found in prescriptions drugs. Accidental opioid poisonings rose from 9,496 (3.3 deaths per 100,000) in 2001 to 21,089 (7.3 deaths per 100,000) by the end of the First Wave in 2010. As can be seen in Figure 1, the first wave of the epidemic was dominated by prescription opioids (the natural and semisynthetic class), with heroin contributing to a fairly steady 2,000 - 3,000 deaths each year even as deaths from natural and semisynthetic opioid rose rapidly. In response to the increased rates of misuse and abuse of Oxycontin®, Purdue Pharma reformulated their flagship product in 2010 to make it crush-resistant and then non-dissoluble (Evans et al. 2019).

These new formulations pushed many individuals with opioid use disorders (OUDs) away from

prescription products and initially toward heroin. This began the second wave of the opioid crisis, which was characterized by the rise of heroin to dominance on the illicit market (Alpert et al. 2018; Evans et al. 2019). The heroin market in the U.S. was geographically segmented with cartels or drug trafficking organizations (DTOs) in Mexico controlling the supply in the western part of the country and DTOs in Colombia controlling the eastern part of the U.S. This division, which was negotiated between the two groups of DTOs in order to minimize "ruinous competition" (i.e., fatal shootings) between the two, would turn out to have profound implications for the progression of the opioid crisis in the U.S.

Sometime around 2013 most observers agree that the third wave of the opioid crisis began. It is noteworthy that this happened at the same time that Colombian cartels who managed the eastern half of the U.S. illicit drug market faced a severe supply crisis. Unable to rely on Colombian-grown poppy crops (which had been in serious decline for almost a decade), Afghanistan-sourced heroin, or an accumulated stock of diverted prescription opioids, DTOs, with Chinese links, turned to a new, much more potent, alternative: illicitly-manufactured fentanyl. Fentanyl is a synthetic opioid approved for use in the United States for breakthrough pain, mostly for terminal cancer patients. It is an extremely potent compound; 4 micrograms (equivalent mass of about 4 grains of table salt) is enough to kill approximately 50% of opioid-naive adults. Fentanyl's potency means that a large number of effective doses can be transported in very small containers, making smuggling by mail feasible. Quickly non-prescription fentanyl became a common adulterant to extend dwindling supplies of heroin and eventually supplanted heroin almost entirely in illicit markets - first east of the Mississippi River and then eventually across the entire U.S. During the third wave of the crisis fentanyl-related deaths rapidly increased, even as deaths from prescription opioids began to fall. This phase of the crisis continued until the time of this writing and opioid deaths, which had shown some signs of decline overall, accelerated again with the 2020 COVID-19 crisis.

The broad sweep of the history of the opioid epidemic outlined above is widely agreed upon. There is, nonetheless, less direct evidence than might be expected that causally links opioid flows into brick-and-mortar pharmacies to overdose deaths, and there is nearly no evidence about how DTOs connect to the demand created by prescription opioids in the first wave of the opioid crisis. Popular discourse assumes, largely unchallenged, that prescription drugs funneled via licit pharmacy channels are the prime mover in the rise of opioid-related deaths (Kolodny and Frieden 2017). This popular view does have support in the academic literature (Manchikanti et al. 2012; Okie 2010; CDC 2012; Powell et al. 2020). Indeed, the assumed diversion of prescription opioids from legitimate to non-medical uses is often portrayed as a series of deliberate acts on the part of physicians, pharmacies, wholesalers, and manufacturers (Higham and Bernstein 2017; Bernstein and Higham 2017).

Further, research indicates that even deaths associated with illegal drugs such as heroin may also be linked to the use of prescription opioids (Compton et al. 2016; Jones 2013; Muhuri 2013). The association between prescription drug misuse and illicit opioid, like heroin, use is complex. One study from 2013 finds that less than 5% of opioid users turn to heroin within the first five years of initiating opioid abuse (Muhuri et al. 2013). However, the association is more striking for people who are observed to be current heroin users. Cicero and colleagues find that 75% of people in treatment for heroin abuse who started abuse since 2000 report that their abuse began with prescription opioid misuse (Cicero et al. 2017). Surveys of persons currently or recently using heroin suggest that 80% of heroin users (irrespective of treatment status) began with prescription medications (Jones 2013; Muhuri et al. 2013). Taken together evidence does *suggest* links between prescription and illicit opioid use.

In this paper, we investigate a late-2007 surge in opioid pharmacy sales that appears to be a coordinated diversion event. We show that during a two-week period in December of that year there was a surge of more than 147 million excess opioid doses into 78 Southeastern U.S. counties. Further, we argue, based upon further evidence, that the most likely reason for this surge is that Colombian DTOs, in an effort to bolster shrinking domestic heroin production and facing a looming constraint on their ability to launder money earned from the drug trade, used hundreds of millions of dollars of cash on hand in order to source the excess doses of prescription opioids for diversion to the illicit market that they controlled east of the Mississippi River. Bizarrely, this shift from non-prescription opioid (e.g. heroin) dominated markets to diverted prescription pill-dominated markets implies that the illicit drug supply actually became safer - or at least more predictable. Non-prescription illicit opioids have a much greater variance in strength per dose than pharmaceutical opioids and so are more likely to result in unintentional overdoses. We explore whether this theoretical harm-reduction shock changed the opioid mortality profile in impacted counties. But, before we model the effects of the shock it is necessary to establish the magnitude and origin of the diversion event.

3 The Opioid Surge

In this section we provide a brief overview of the magnitude and specific geographic scope of an unprecedented surge of opioids into specific Southeastern U.S. counties over an approximate two-week period in December of 2007. We also outline evidence strongly suggesting this surge was linked to the diversion of prescription opioids to the illicit drug market by Colombian drug trafficking organizations. A more comprehensive discussion of each step in this case can be found in Appendix Section A.1 below.

3.1 Release of Transaction-Level ARCOS Data

In response to the rapid spread of opioid use disorders and rising opioid mortality throughout the United States, by the late 2020s more than 2000 cases had been filed in state and federal courts by health systems, cities, counties, and states seeking civil damages against the major participants in the pharmaceutical industry that supplied opioids. The main targets were the opioid manufacturers (e.g., Endo, Insys, Mallinckrodt, and Perdue among others), the major wholesale distributors (AmeriSourceBergen, Cardinal Health, and McKesson), and major pharmacy groups (e.g., CVS, Eckerd, Walgreen, etc.). The range of defendants in the several thousand cases reflected the distribution system for pharmaceuticals in the U.S. For controlled substances like opioids, the entire chain of distribution from manufacture to local pharmacy is tracked by the Drug Enforcement Agency (DEA) using an electronic system called the Automation of Reports and Consolidated Orders System (ARCOS) - the raw data of which is usually considered highly confidential.

In December 2017 nearly all of the filed cases were consolidated by the United States Judicial Panel on Multi-District Litigation (MDL 2017) into a single venue, the Northern District of Ohio Federal Court under the oversight of Federal Judge Dan A. Polster into a multi-district litigation (MDL) titled the National Prescription Opiate Litigation. Throughout the course of the litigation, Judge Polster ordered that various documents (deposition, emails, etc.) be released publicly. Plaintiffs in the MDL requested and were granted access to the transaction-level ARCOS data from the DEA for 2006 – 2014 (inclusive). [1] The plaintiffs requested ARCOS unedited data in the native format for the following drugs: buprenorphine, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanal, meperidine, methadone, morphine, powdered opium, oxycodone, oxymorphone and tapendadol. Data requested included seller name, seller major business activity, seller street address, buyer name, buyer major business activity, buyer street address, specific drug identifiers (drug name and NDC code), packages in shipment, units per package, grams of base controlled substance per shipment, MME equivalents, and other key data. Judge Polster ordered that the entire database be publicly released in mid- July 2019. [2]

3.2 Identifying Unprecedented Surges of Opioids into Several States

We extract all ARCOS data elements for the entire time period, keeping all records associated with transactions for finished (non-bulk) opioids where the endpoint was to a retail pharmacy (brick and mortar or online); we exclude shipments of opioids where the final disposition was to

[1] The initial release by Judge Polster was for the 2006-2012 tranche of data. He subsequently released an additional two years of raw ARCOS data. At a later phase of the trial he ordered the release of additional data from 2015-2019. We are using the first round set of data encompassing 2006-2014.

[2] The raw data is very large - over 180 GB in total - and is available for download at: file.opioidanalytics.com

a hospital, practitioner or mid-level provider, central fill pharmacy, ambulance service, nursing home, or military outlet (including the VA).[3] We use quantities of opioids in morphine milligram equivalent (MME) units in each shipment, not total grams or counts of pills. Converting the amount of each shipment into MME units allows for adding shipment amounts of different drugs together in a meaningful way. We exclude shipments of buprenorphine that are approved for the treatment of opioid use disorder based on the product National Drug Code.[4] Observations are aggregated by total MME and then MME per generic drug name to the county (in which each pharmacy was located) and week level for the entire January 2006 through December 2014 time period for the purposes of identifying the spike event.

We examine flows of opioids into each state by month. First, we graph the total MME (the sum of MME across all drugs listed above) by month and state. There is an anomaly immediately obvious for the state of Florida, where total MMEs flowing into retail pharmacies for December 2007 are strikingly higher than in other months observable in the data (see Figure 2). We do not observe a similar spike in total opioid MMEs shipped for other comparably large states (California, New York, and Texas; see Figure 3). We also observe sudden excess opioid shipments in December 2007 for three other states: Alabama, Louisiana, and Mississippi (see Figure 4). This pattern appears in no other states.[5] We further examine the flow of opioids by specific drugs into each state. Figure 5 presents the flow of total MME by tracked drug into Florida, where the spike event in December 2007 is apparent across all substances. Note that while the spike appears for all opioids, the magnitude of the spike is much larger for oxycodone (at this time primarily Oxycontin®), the most commonly used prescription opioid at the time.(Evans et al. 2019) The patterns apparent in Florida are generally representative of the patterns apparent in Alabama, Louisiana, and Mississippi.

3.3 Were the Excess Opioids Purchased by Insured Customers?

One question that springs immediately to the fore is: "Who is purchasing these excess doses?" To address this question, we turn to three sources of data. Lozano-Rojas et al. (2022) examine the impact of cannabis laws on the use of opioid medications in a large commercial claims database

[3]We followed the processing rules from Craig McCann, who was retained to clean the raw ARCOS data and supply a dataset of record for assigning damages in the MDL, as outlined in McCann (2019). We make particular note that there was an issue found in the raw data where some records from Cardinal Health were duplicated during December 2007, as mentioned in Footnote 1 of Mougey and Committee (2019). We used data provided by the court after this duplication was discovered. In addition, we also deleted all records with duplicated seller DEA number, buyer DEA number, buyer ZIP code, drug code, drug quantity, transaction date, and transaction ID. Thus, our data is not corrupted by the issues raised in Mougey and Committee (2019).

[4]A list of excluded buprenorphine formulations is available upon request.

[5]While not apparent on the initial graphs of state-wide total MMEs, several counties in far western Tennessee are also involved.

on over 20 million enrollees on average per year nationwide. The appendix to their work presents time series flows of MMEs by month into each state. Bradford et al. (2023) examine the impact of cannabis laws on opioid use in, among other settings, a Medicare Advantage (MA) claims database from one of the largest third-party sponsors of MA plans. The appendix to their paper also contains a monthly time series of the total flows of opioids (in terms of MMEs) to each state. We also extract quarterly data on Medicaid payments for opioids by state over 2006 to 2010 from the State Drug Utilization Data (SDUD). We extract data for each of the opioid drugs listed above separately. (NDCs are not listed in SDUD data so we cannot convert to MMEs and so add all drugs together). Figure 6 and Figure 7 show the time series for Florida for these major sources of pharmacy payments. From this, we see that no major insurer experienced a spike in opioid claims, which means that the excess doses must have been purchased in cash transactions as no remaining payor source could absorb the volume of pills that surged into the state.

3.4 Identifying Specific Counties Involved in the Surge

Next we identify which specific counties are involved. The spike is visually apparent at the state level, but a sub-state assessment has several advantages. First, it may be that only some specific locations in the affected states are involved, and that could provide information that to suggest a reason for the surge. Second, while the spike is obvious at the state level for Alabama, Florida, Louisiana, and Mississippi, it is possible that similar spikes happened in counties in other states in December 2007 but those surges are not obvious at the state level. Third, we want to establish a systematic methodology for identifying counties that does not impose a December 2007 spike in the four states based merely on visual inspection.

As mentioned above, the transaction level ARCOS data was publicly released as part of a large federal MDL. Discovery in that MDL generated tens of thousands of pages of evidence including depositions by industry participants. One deposition was taken of a DEA agent who regularly examined ARCOS data to identify individual pharmacies with suspicious patterns of opioid acquisition or sales. As reported by the Washington Post: *"The DEA is purposefully vague in how it defines what is a suspicious amount of opioids ordered by a buyer. But in a recent lawsuit, a former DEA agent described five methodologies: Maximum Monthly, Trailing 6 Month Threshold; 2x Trailing 12 Month average; Extraordinary Order Method – 3x Trailing 12 Month Average; Maximum 8,000 Dosage Units Monthly; Maximum Daily Dosage Units."* (Washington Post 2021). Following this DEA practice, our primary analysis identifies a county as having a suspicious surge in opioid shipments by comparing each December 2007 week to the average

shipment volume for the 52 weeks preceding the first week of December 2007.[6].

We construct a data set for every county in the U.S. in 2007 with one observation per week. We then run 2,980 separate regressions, one for each county in the continental U.S., with the following form:

$$MME_{ct} = \beta_0 + \beta_1 Dec_{c,t} + \beta_2 t + \epsilon_{c,t} \tag{1}$$

where $MME_{c,t}$ is the total opioid MME received by all retail pharmacies in county c in week t, $Dec_{c,t}$ is an indicator variable for whether the week is in December of 2007, and t is a continuous calendar time (week) variable. Once all 2,980 regressions are run, each county in the United States is characterized as being a "spike county" if two conditions are met: 1) the coefficient on β_1 is statistically significant at the 5% level or better, and 2) there are at least two weeks in December 2007 where the total MME shipments into the county are 200% or more of baseline.

Figure 8 shows the 78 U.S. counties that meet these two criteria; these counties are indicated in red; all counties that meet the spike conditions are in the Southeastern U.S. Figure 9 zooms in on the Southeastern region of the U.S.[7]. It will be important below to note that without any criteria other than the two listed above, we see that all of the suspicious "spike" counties are east of the Mississippi River or in Louisiana.

3.5 Determining the Size of the December 2007 Surge

We estimate the magnitude of the surge event for these 78 counties. If a December week is at least 200% of that county's baseline then we designate that as a "spike week." All counties identified as having suspicious shipment volumes had at least two spike weeks, and many had three[8]. No county has spike volumes for all weeks in December 2007. As is evident from Figures 2 through 4 shipments of opioids trend steadily up in all states during 2007. To avoid over-estimating the magnitude of increases in MMEs shipped during the spike weeks, we calculate excess MMEs

[6]We do not directly apply the DEA standard of checking every county-week's shipment against the rolling 52-week average because some counties had such enormous increases in the first week of the spike - in one instance a more than 1,300% increase - that it artificially inflates the rolling 52-week lag average for the second week. Given the size of the spike, we measure each December county-week against the 52-week average immediately prior to the spike event.

[7]When we use the DEA "Extraordinary Order" criterion, we identified 30 counties with more than 300% of the trailing 52-week average opioid MME deliveries. The higher threshold identifies fewer counties, but they have the same pattern as the baseline criteria and do not change the conclusions of subsequent analyses. Results from the secondary analysis are available on request.

[8]The spike event appears to have lasted between 10 and 14 days, with some variation around the first day. In some counties those 10-14 days spanned three calendar weeks and in some counties the spike days spanned only two calendar weeks.

shipped during the surge as the difference between the actual MMEs shipped during spike weeks and the average weekly shipments to those same counties during September, October, and November 2007. We estimate the excess number of doses using the average ratio of 23.43452 MME/dose in the ARCOS data[9]. We estimate the dollar value of excess shipments by assigning a wholesale price of $0.034 per MME taken from Food and Drug Administration (2018).

The estimated excess MME, doses, and wholesale value for the December 2007 surge appear in Table 1. We find that the volume of excess shipments of opioids ranges from 113.87 million MME (about 4,86 million doses) in Tennessee to 2.4 billion MME (about 102.43 million doses) in Florida. Altogether, we estimate that the suspicious surge in opioid shipments to select counties in these five states amounts to an excess of more than 3.4 *billion* MMEs, or over 147 million doses. Pharmacies would have had to spend approximately $117.17 million to acquire those doses from manufacturers, which would then be sold to patients who came into the pharmacies with prescriptions. Recall that since we find no evidence of this spike in opioids in commercial, Medicare, or Medicaid claims we conclude that they were purchased from the pharmacies in cash transactions; retail cash prices for drugs are much higher than wholesale costs. Thus, the number of dollars required to actually purchase this volume of drugs with cash is a multiple of the $117.17 million estimated wholesale (pharmacy) cost.

One question that arises is whether this volume is feasible. Could corrupt (as we will argue below) physicians write enough excess prescriptions *on top of the volume of prescriptions they were already writing* to allow pharmacies in these counties to fill 147 extra doses in only around two weeks? As we explain in Appendix Section A.1.6 in much more detail, it seems that this would have been easily managed in late 2007. Court documents from DEA and FBI raids on Florida pill mills in 2011 reveal that corrupt physicians were just beginning to pump high volumes of prescriptions intended for diversion into the illicit market around 2007. Pill mills were growing rapidly during this time, so expansion of corrupt prescriber capacity would have posed little constraint. Academic research finds that around this time it was not uncommon for "patients" to leave pill mills with multiple prescriptions for 200-300 high-dose Oxycontin and Roxicodone (Rigg et al. 2010). Just a single pill mill in Florida (raided in 2011) had 13 physicians who saw up to 500 patients per day. If we assume for the sake of illustration that just those corrupt pill mill physicians were operating at the maximum reported capacity (300 pills per prescription, 4 prescriptions per visit, 500 patients per day per physician) then the entire spike event across all counties in each of

[9]While in principle we can use the number of doses reported in the raw ARCOS data, MME/dose field is missing for 7,333,276 observations out of a total of 35,931,593 transactions in 2007. Rather than base the excess dose calculation on a different set of observations than we use to calculate excess MME, we use the average non-missing MME per dose ratio to impute the number of excess doses from the volume of excess MME. The MME per dose = 23.43452 using non-missing observations.

the five states could have been supported by the prescriptions that those 13 physicians could have written in only 13.6 days. Of course, many more physicians would have been involved than that - at least one would be required per state. Many "patients" would have been needed too; we will argue below that circumstantial evidence suggests this event was undertaken by Colombian drug trafficking organization whose U.S. workforce of illicit drug dealers could have easily supplied the needed manpower. The primary lesson from accounts and legal documents at the time is that, as remarkable as it may seem, it would have been trivially easy for as few as two or three dozen corrupt physicians scattered across the five states to provide sufficient prescriptions to allow the purchase of all 147 million excess doses associated with the December 2007 spike event.

A second question that the magnitude of the spike poses is how local pharmacies came to have adequate stock on hand to supply the surge in demand over such a short time frame in December of 2007. We explore this issue in detail in Appendix Section A.1.7. As we explain there, drugs make their way to the pharmacy to be sold to patients presenting (apparently) valid prescriptions through several stages. Manufacturers produce opioids (subject to DEA quotas); distributors take possession of opioids (either wholesaling pharmacies like CVS which operate their own warehouses or independent wholesalers like AmeriSourceBergen which purchase drugs and then resell them to independent pharmacies); finally, local pharmacies receive drugs from a warehouse or wholesaler for sale to the final customer. We calculate the share of total shipments delivered to pharmacies in the 78 spike counties (Figure 9) before and during the spike event by each manufacturer; comparing changes to market shares we find no evidence of movement or disproportionate gains in shipments from any manufacturer associated with the excess MME shipments during December 2007. Similarly, we compare market share of opioid sales for each pharmacy in the spike counties before and after the event; ultimately, we conclude that no player in the retail pharmacy sector disproportionately benefits from the spike, in terms of systematically capturing a large portion of the sales. Finally, we compare changes in market shares for the three largest independent drug wholesalers (which we label Wholesaler A, B, and C - not in alphabetical order). Here, we find there is a dramatic pattern: Wholesaler C goes from a stable one-third of opioid shipments before the spike event to almost 85% share during the spike event before returning to baseline thereafter (looking at weekly data for all of 2007 and 2008). When examining Wholesaler C's acquisition of opioids preceding the spike event, we find evidence of three very large and statistically anomalous purchases of opioids (different from Wholesaler C's overall patterns of acquisition and from the patterns for the other two wholesalers as well) that began in the last week of March of 2007. The importance of this pattern will be discussed below.

3.6 Historical Context for the Illicit Drug Market in 2007

To appreciate the importance of the location of the spike counties east of the Mississippi River plus Louisiana and of the timing of the anomalous opioid acquisitions by Wholesaler C it is necessary to understand the illicit heroin market in the U.S. around the time of the spike event. During 1990s and early 2000s, the U.S. illicit drug market, at least for cocaine and heroin, was dominated by two groups of DTOs, those headquartered in Mexico and those headquartered in Colombia. According to Ciccarone et al. (2009), the Mexican DTOs were able to gain a foothold in the western heroin market due to the weakening of the Colombian DTOs in the 1990s, which had previously dominated the entire US market. The Colombian DTOs more easily defended their hold on the eastern U.S. market, where they had established supply and distribution networks and were able to offset declines in Colombian-produced heroin via connections with suppliers in Southeast Asia. Throughout this period of disruption, the Mexican and Colombian DTOs sought to minimize violent competition between themselves. By the 1990s the DTOs arrived at a detente where the Mexican DTOs controlled the illicit heroin market west of the Mississippi River and the Colombian DTOs controlled the heroin market in Louisiana and east of the Mississippi. This was well documented at the time by interviews on the ground and by chemical analysis of seized drug samples (The White House, The Office of National Drug Control Policy 2023; Castillo et al. 2020; Ciccarone et al. 2009).

Both groups sourced raw materials (coca leaves and opium poppy latex) primarily from farms in their respective home territories. Mexican, Colombian, and U.S. authorities waged a decades-long battle against the DTOs that was multi-pronged in nature. Authorities attempted to eradicate the agricultural source of raw materials, interdict finished drugs before they could be sold in the U.S., and cut off access to international banking systems that allowed the DTOs to launder profits. U.S. and Colombian authorities cooperated in opium poppy eradication projects that sought to destroy the agricultural base for opium latex production in Colombia itself. Bureau of International Narcotics and Law Enforcement Affairs (2002) According to the U.S. Department of State, between 1996 and 2001, the amount of land dedicated to opium poppy cultivation in Colombia decreased by over 90%. This was largely due to the Colombian government's eradication efforts, which were supported by the U.S. As illustrated in Figure 13 these efforts to eliminate opium poppy crops and opium latex production depressed Colombian production and increased heroin prices, straining Colombia DTO's capacity to meet heroin demand in their half of the U.S. market. These eradication efforts created shortages of illicit drug production of both cocaine and heroin and some of their repercussions over prices and purity, especially in the more developed cocaine market, have been referenced often in reports made by the United Nations Office on Drugs and Crime, as well as in reports made by the U.S. Department of Defense (National Drug Intelligence

Center 2009; 2011; United Nations Office on Drugs and Crime 2012; Castillo et al. 2020). [10].

A second front in the war on drugs, and perhaps the more significant one for this research, was waged on the Colombian DTOs' capacity to launder profits from the drug trade. During the 1990s and early 2000s, Colombia was the major hub for illegal money laundering activities in the Western hemisphere. DTOs used various methods to launder their money and avoid detection by law enforcement authorities (Kar and Cartwright-Smith 2009; Kar and Spanjers 2015; Reuter 2012; Thoumi and Anzola 2010; 2012). One common method was for DTOs to buy or create businesses that have predominately cash transactions, such as restaurants, hotels, casinos, or foreign currency exchange companies, and use those to launder drug money. DTOs would mix illicit cash with legitimate revenue from the business and deposit the cash into Colombian bank accounts. This method was particularly difficult for authorities to detect, as the businesses appeared to be legitimate and the money appeared to be from legal sources. The DTOs then set up front companies and shell corporations in countries known to be tax havens and transferred the laundered cash from Colombia to those offshore businesses (United Nations Office on Drugs and Crime 2002). The shell companies would often have no real business operations and would exist solely to move money, making them difficult for authorities to trace.

The Colombian government, with the assistance of international organizations such as the United Nations, made significant strides in the early 2000s to combat money laundering activities in the country. In April of 2007, the Superintendence of Finance of Colombia announced the final language for regulations requiring all financial institutions under its authority to bring monitoring and financial processing procedures to international standards by January 1, 2008 (Colombian Government 2007) This regulatory change aimed to increase transparency and combat money laundering and other financial crimes. One of the key impacts of this regulatory change was that it made migrating large amounts of U.S. currency out of Colombia using the domestic and international banking system much more difficult. This regulation automatized reporting of suspicious activities, tightened the scope of the regulator across all financial institutions, and over foreign currency transactions and foreign exchange houses in particular, which before the reform produced more than half of the reports of suspicious activities (UIAF 2011; Caballero et al. 2016) As mentioned above, drug traffickers and other criminal organizations were able to use the financial system to launder their profits and move large amounts of cash across borders prior to the implementation of these regulations (Bureau of International Narcotics and Law Enforcement Affairs 2019) However, the new regulations made it much harder for these organizations to move their money

[10]For instance the Department of Defense National Drug Threat Assessment by 2011 stated: "The availability of South American heroin is declining and will continue to do so as a result of sustained reduced poppy cultivation in Colombia" National Drug Intelligence Center (2011)

undetected. According to the U.S. Department of State, the implementation of these regulations helped to disrupt the flow of drug money from Colombia to the U.S. As a result, many drug traffickers were forced to find new ways to move their cash and achieve positive returns on investment from it.

We emphasize the following fact: these new Colombian anti-money laundering regulations were set to take full effect (and did take full effect) on January 1, 2008 – three weeks after 147 million excess doses of opioids were purchased with cash in 78 Southeastern U.S. counties, *all* of which are located in the Colombian DTOs' heroin sales territory.

3.7 What the Evidence Suggests

In summary, we observe the following broad facts, some of which are illustrated in Figure 12.

- A large, unprecedented, spike in (apparent) cash purchases of just over 147 million opioid doses took place in December 2007.
- The excess shipments were concentrated in counties that were: 1) east of the Mississippi River or in Louisiana, and 2) largely along navigable waterways and routes known to be used in smuggling illicit drugs within the U.S.
- Colombian DTOs controlled the heroin market east of the Mississippi River and Louisiana at this time.
- Only one US pharmaceutical distributor pre-positioned itself to fill this demand, and so supplied around 86% of the spike demand.
- The timing of the start of inventory accumulation by this distributor coincided with the release of the final language for the Colombian Ministry of Finance about reforms that would make money laundering very difficult.
- The actual cash purchase of excess opioids from Southeastern US pharmacies came just before the new Colombian banking regulations took effect that prevented Colombian DTOs from migrating cash out of the country.
- This features occurred at the same time that Colombian DTOs were experiencing pressure and the production levels of heroin were estimated in historical lows.

This evidence is consistent with the following narrative. In 2007 the Colombian DTOs faced a shortage of opioids to sell in the eastern U.S. illicit drug market. At the same time, they faced

a looming threat to their ability to launder large amounts of cash through the Colombian banking sector. They responded by moving cash to, or leaving cash in, U.S. counties which were easily accessible via navigable waterways (where the DTOs had long-standing smuggling infrastructure) and purchased around 147 million doses of prescription opioids over a 2-week period in December 2007. The wholesale value of the purchases would have been around $117 million; the cost to purchase that many doses in cash from retail pharmacies would have been a multiple of that number. This sudden spike in purchases had the effect of directing 86% of the wholesale demand to Distributor C, whose acquisition of opioids stood out as an aberration, in terms of magnitude and timing, compared to Distributors A and B. Given the evidence that these purchases were made in cash – bypassing any monitoring that would have occurred if third-party payers were involved and taking place in states without mandatory PDMPs – and that the spike in purchases/shipments occurred no more than three weeks before the Colombian anti-money laundering banking rules went into effect, we believe these prescription opioids were diverted to the illicit market to replace depleted Colombian heroin supplies. The purchases happened along waterways and roadways commonly used by Colombian drug smugglers, facilitating the smuggling of physical cash into the U.S. to bankroll the purchases.

The importance of the accumulated evidence and most likely conclusions are twofold. First, the December 2007 spike in opioid shipments into 78 select Southeastern U.S. counties represents Colombian DTOs combating the twin challenges of reduced heroin production and sharply increasing money laundering costs by purchasing prescription opioids that could be resold in the illicit opiate market they controlled. Second, sales of those diverted opioids would have occurred only east of the Mississippi River (plus Louisiana); locations west of the Mississippi River (under Mexican DTO control) would have been unaffected. Thus, we present strong evidence of a shock to the illicit market east of the Mississippi that made heroin harder to obtain and prescription opioids easier to obtain, which would have altered the substance mix in illicit markets. But, only illicit markets east of the Mississippi river were affected. This sets up the possibility of assessing the impact of this large, real-world, shock to illicit markets that replaced non-prescription (illicitly manufactured) opioids which are more risky (high variance in dosage strength) products, with a less risky (low dosage variance) product (prescription opioids). The data-generating process aligns with a near-ideal difference-in-differences framework.

4 Estimation of the Surge Effect over Mortality

In general, if our interpretation of the facts outlined above is correct, we expect to find reductions in mortality rates for opioids that were not manufactured by prescription pharmaceutical manufac-

turers (such as heroin) and increases in mortality rates from opioids that were manufactured by the pharmaceutical industry (such as oxycodone and hydrocodone). For convenience, we will refer to the former group (illicitly produced and distributed) as "non-prescription drugs" (non-Rx) and the latter group (pharmaceutical industry manufactured) as "prescription drugs" (Rx)[11]. In addition, given the costs and risks of transporting bulk illicit drugs across the U.S., we expect these effects are strongest nearer to "spike" counties. We illustrate our initial expectation in Figure 14. As the diversion alters the mix of opioids, DTOs induce net substitution from non-Rx to Rx opioids. We expected to find decreasing mortality from non-Rx opioid misuse in counties east of the Mississippi River (compared to counties west of the Mississippi River) that are close to spike counties, and this effect should diminish the further an eastern county is from a spike county (Figure 14 - top panel); at the same time, we expect to find a positive relationship between the exposure to the diversion and poisoning mortality from Rx opioids in counties east of the Mississippi River (compared to counties west of the Mississippi River) - with a treatment effect that falls for eastern counties further away from a spike county (Figure 14 - bottom panel).

In this section, we describe the empirical strategy we follow to establish the effects as measures of the diversion treatment as measures of distance to identified spike counties.

4.1 Additional Data

We use the DEA-ARCOS data described above to identify the spike diversion event and the counties involved. We extract travel distance between the geographic centroids of each county and the closest spike county from Google Distance Matrix API, which allows us to obtain measures for driving mileage as well as driving time.[12] We classify counties based on the distance to their closest spike county. Figure 16 illustrates the classification exercise for treatment and control counties using different distance-to-spike County-bins (50 mile wide). Analogously, Table 2 presents the number of counties in each distance bin in intervals of 100 miles per bin. These are number of

[11]This classification is approximate, and largely for descriptive purposes. There are drugs, like fentanyl, which are manufactured by the legal prescription drug industry and distributed through pharmacies, but which are also manufactured by illicit production facilities associated with drug trafficking organizations. Since most forms of fentanyl produced to be sold by prescription are more difficult to abuse, currently most fentanyl deaths are from forms of the drug sold on the illicit market. So, we classify fentanyl as a non-Rx drug for the purposes of our analysis. Ultimately, we choose to categorize deaths from natural and semi-synthetic opioids (ICD-10 code T40.2) - being more likely to be manufactured legally and then diverted - as being from Rx products and deaths from all other forms of opioids - having both legal and illicit manufacturing options - as non-Rx in origin.

[12]We queried the system in September of 2022, and January 2023, using the *ggmap* package from *R* and rely on its functionality that allows querying the Google Maps API given two reference points. We use the counties' population centroids from the Census, available at: www.census.gov. There are restrictions in the use of Google Maps of about 40,000 queries per month. Thus, to obtain the driving distance, we first calculate the geodetic distance for all additional counties to the identified spike ones. We select the closest 20 on the basis of the geodetic distance for the continental U.S. counties and calculate the driving distance and time on this subset.

counties that will contribute to the identification of distance specific treatment effects of the diversion. Control counties are all U.S. counties west of the Mississippi River (excluding Louisiana parishes) within 1,000 miles (driving distance) of their closest spike county. Treatment counties are all U.S. counties east of the Mississippi River plus Louisiana parishes (some of which are slightly more than 1,000 miles away from their closest spike county).[13]

For the difference-in-difference models of the effect of the spike event on mortality, we use the Restricted-Use Multiple Cause of Death Vital Statistics Data from the National Center for Health Statistics at the Center for Disease Control and Prevention. These data are abstracts from all U.S. death certificates, and they record up to 20 multiple causes of death. For the purpose of our analysis we identify drug poisonings related to the specific substances in question[14]. We represent county mortality as rates per 100,000 inhabitants. We analyze mortality data from 2006 through 2010, the year in which the reformulation of oxycontin kicked off the third (fentanyl-based) wave of the opioid epidemic (Evans et al. 2019).

We present pre-diversion mean-adjusted mortality rates in Table 3 for our treatment (east of the Mississippi River and Louisiana) counties for different opioids. In 2007, prior to the diversion event, the average quarterly Natural or Semi-synthetic (T40.2) opioid mortality was 0.85 deaths per each 100,000 people across eastern U.S. counties. This category includes most prescriptions opioids, such as oxycodone and hydrocodone. This mortality rate represented 40.2% of all opioid poisoning deaths (at 2.12 deaths per 100,000 people). Mortality from opioids not including natural and semi-synthetic (Non-Rx Op.), accounted for 59.8% of opioid mortality at the time. In this category we find heroin, synthetic opioids (mostly fentanyl and tramadol during this time period), methadone (also synthetic, but classified separately in the mortality data), and unclassified opioid mortality. Heroin was only a fifth of non-prescription opioid mortality and just over 10% of total opioid mortality. This could be seen from Figure 1 above, as heroin mortality did not contribute to the epidemic until the 2010 diversion.

Before moving to estimated difference-in-difference models, we check to see whether our expectations are observable in the raw series of opioid mortality. Figure 15 presents the raw average opioid mortality series for counties across different "distance to spike county" bins up to 800 miles. Panel A of Figure 15 showcases the mortality rates for non-prescription opioid mortality, and Panel

[13] We use the travel distance for our main results, and we test the sensitivity our results to this choice by conducting a series of robustness exercises using the geodetic distance instead and find this choice does not substantially affect our findings.

[14] Following the CDC (Ahmad et al. 2023), we use ICD10 codes to identify drug-poisoning deaths as accidental poisoning (X40-X44); intentional self-harm poisoning (X60-X64); assault by drug poisoning (X85), poisoning of undetermined intent (Y10-Y14); and legal intervention involving gas (Y352). We use these poisonings in combination to the identified substances in the Poisoning by narcotics (T40 sub-classification), which allows to identify different opiates derivatives, such as heroin (T40.1) or naturally occurring opioids (T40.2).

B shows the rates for prescription poisoning mortality. Each graph presents two series, the one for those identified treated counties (in blue) and those in the west that serve as a control (gray) within the distance threshold, and we have included dashed lines with their linear fit. The vertical red dashed lines indicate the fourth quarter of 2007 (diversion moment) and the fourth quarter of 2008, as reference for the initial diversion period.

For the top row of Figure 15 including data for Non-Rx opioid mortality, it is clear that there is a noticeable change in trend, or even a drop, on other opioid mortality compared to prescription opioid mortality, as the gap between East and West closes after the diversion for most distance bins. This widening happens in all the figures of the top panel irrespective of the distance considered. With respect to prescription opioid mortality (Rx), on the other hand – the bottom panel of Figure 15 – there is a widening space after the diversion, although in some instances (up to 200 miles to spike), the widening arguably starts before the diversion. The gap between East and West is considerable by the end of our time frame for those bin up to 600 miles. These figures illustrate that for the majority of counties identified by distance to spike counties, by the time of the diversion, there was a marked drop in the mortality from non-prescription opioids, or at least a break in an increasing trend of these poisonings. Simultaneously, there was an increasing trend in the mortality from prescription opioids in those counties. That increasing trend diverged from what the Western U.S. was experiencing, specially for counties closest to the spike.

4.2 The effect of the diversion on mortality

We hypothesize that Colombian DTOs used the diverted opioids to substitute diverted Rx drugs for illicit non-Rx opioids east of the Mississippi River and in Louisiana, consistent with the territorial agreement with the Mexican DTOs, which was well-documented by the authorities at the time (National Drug Intelligence Center 2007). We lever this variation to identify treatment and control units of our analysis. Control counties are west of the Mississippi (except Louisiana) and treatment counties are east of the Mississippi and also Louisiana. Figure 16 presents in grey the counties that we classify as controls and in red the counties we classify as treated, with the intensity of the color dropping in the distance from the closest spike county.

We use travel distance from a spike county to capture the intensity of treatment for a treated county. Figure 16 shows this intensity fading the color as the proximity to the spike counties increases. We follow 2,628 counties in our analysis. We present information on how many counties are included in the analysis according to their distance to the spike counties in Table 2. The table reports 1,670 counties from Louisiana and the East of the Mississippi in the treatment and 958 counties from west of the Mississippi states. There are fewer counties in the control set be-

cause counties west of the Mississippi tend to be geographically larger. We don't include western counties further than 1,000 miles from the Mississippi river.

Our aim is to estimate average treatment effects over poisoning mortality across separate distance bins in a heterogeneous difference in difference framework using Equation 2 below:

$$y_{it} = \sum_{d \geq 0} \beta_d \cdot \mathbf{1}[D_d = 1] \cdot \mathbf{1}[Treat_{t \geq 2007Q4}] + \chi_{it} + \chi_{st} + \eta_i + \eta_t + \epsilon_{it} \tag{2}$$

Equation 2 is specified in a panel setting, where i indexes county and t quarter periods. For outcomes, we follow different opioid poisoning mortality measures (y_{it}) and each β_d in this model captures a before and after comparison between treatment units in the given distance bin, d, and control units west of the Mississippi. The exercise considers a post-period starting in 2007-Q4, the quarter we observe the diversion happening. The interactions of interest are constructed as a set of indicator variables that identify treated units for each distance bin ($\mathbf{1}[D_d = 1]$) and the post period ($Treat_{t \geq 2007Q4}$). To make the estimation more accurate, we include a set of covariates describing time-varying characteristics in χ_{it}, such as the demographic composition in the county (i.e. share of black population, Hispanic, Asian and Native American, all as separate variables), general labor market and economic conditions (i.e. unemployment rate, participation rate, and per capita income), and more specific exposition to automation and foreign competition by including the manufacturing share of employment in the county, which has found to drive opioid mortality as well (Pierce and Schott 2020; Hollingsworth et al. 2017; Ruhm 2000). We also consider a series of state policy files that have been found to have an effect over the extent of the opioid epidemic (i.e. Good Samaritan Laws, Naloxone Access Laws, Must Access PDMPs, and access to a medical cannabis dispensary). We include county fixed effects (η_i) to account for any time-invariant characteristics across localities, and also include period (quarter) fixed effects (η_t) to account for common temporal shocks.

The β_d coefficients from this exercise have a causal interpretation as long as the model complies with the assumptions of a difference-in differences framework: 1) that no other "dormant" factor occurs at the same time as the treatment in question, affecting treated or control units at the same time, and 2) that the control units exhibit a relatively similar trend in the outcomes prior to the intervention. For the first assumption, we believe that the potential to identify the counties by means of the spike event is as good as random as in principle there are no contemporaneous competing alternative shocks that also affect opioids poisoning mortality. An alternative explanation might be that the effects we hypothesize are driven by particular momentum within the pharmaceutical industry-induced opioid epidemic; for instance, if the effects we find were driven by places that had a disproportional exposure to the opioid epidemic as opposed to exposure to DTOs activity.

We test for this possibility explicitly in a separate robustness test.

As is standard, we run a set of event study analyses to partially test for conformity to the parallel pre-trends embedded in assumption 2:

$$y_{it} = \sum_{t \neq 2007Q3} \beta_{d,t} \cdot \mathbf{1}[D_d = 1] \cdot \mathbf{1}[Treat_{T=t}] + \chi_{\mathbf{it}} + \chi_{\mathbf{st}} + \eta_i + \eta_t + \epsilon_{it} \rightarrow \text{ for each } D_d \quad (3)$$

For each distance bin, we evaluate the parallel trends assumption separately. While in the previous equation the interaction with time identified all observations in the post-treatment period, ($Treat_{t \geq 2007Q4}$), in Equation 3 the interaction with time identifies each time period independently ($Treat_{T=t}$), with the exception of the reference period, which we define as the third quarter of 2007, the last quarter prior to the diversion. In this exercise, the coefficient $\beta_{d,t}$ measures the difference between treatment and control units, and how that difference evolves over time relative to the last quarter prior to the diversion. As long as we do not observe consistent and statistically significant differences in the pre-treatment period, the parallel trend assumption holds, and we assume that the differences between treated and control counties would have remained constant in the absence of the diversion. In the next major section we walk the reader through findings from these estimation exercises.

4.3 Heterogeneity and Robustness Exercises

4.3.1 Heterogeneity

Prior to discussing the findings, we specify a series of robustness checks. While heroin is the most common illegal opioid in the pre-spike period, our main specifications estimate models for all non-Rx opioid mortality as these encompass a substantial share of the total opioid mortality at the time. These analyses are presented together with the main results. In addition to different opioid categories, we also follow the categories associated with the literature often referred to as *Deaths of Despair*. Case and Deaton (2015) point to specific sub-populations that between 1999 and 2013, were disproportionately affected by the rise in drug-poisoning mortality. Middle-age white non-Hispanic men are found to be disproportionally represented in drug overdose deaths. Finally, we analyze the effects of the diversion across sub-populations divided by sex, race, and age. We present results from these sub-analyses in the next major section.

4.3.2 Robustness

We make several modeling decisions that could be seen as favorable to our arguments and so which must be evaluated.

First, our primary model uses risk-adjusted mortality estimates following Ruhm (2018), and the socio-economic adjustment weights could impact our results. We therefore run versions of all of our models using unadjusted mortality weights (and obtain qualitatively identical results). Another robustness exercise is to consider Louisiana as part of the control group. Our main models define Louisiana parishes as being in the treatment group, since the U.S. Department of Justice identifies the state as part of the trafficking network of Colombian DTOs close to the time of our analysis (National Drug Intelligence Center 2001). However, since Louisiana is west of the Mississippi River and the River is widely cited as a demarcation line between Colombian and Mexican DTOs, we run a versions of our models where we classify all Louisiana parishes as being in the control group. We also estimate our difference-in-differences models without including covariates to illustrate that the effects we find are not an artifice of the added controls. To evaluate the sensitivity of our findings to how we classify spike counties (using the DEA "200% of baseline" criterion), we replicate our models using the DEA "300% of baseline" threshold to identify spike counties (finding nearly identical results). Finally, we test the impact of an alternative definition of distance to spike localities (which defines our treatment bins). We find driving distance to be a better measure, but we cannot observe the driving times of the given years, as GIS information systems were not as developed during the timeframe of our analysis. Accordingly, we estimate alternative models that use the geodetic distance between counties, which is time-invariant. Our main results are robust to each of these exercises, as we discuss in Section 5.

Earlier we mentioned that there might be a potential competing explanation, that states that the particular changes in opioid mortality we find, are part of the pharmaceutical-industry induced opioid epidemic. Various studies have pointed to the role of the pharmaceutical industry in the increase in prescription opioid mortality starting in the mid-90s (Arteaga and Barone 2022; Alpert et al. 2022). This influence has been present in the design of supply deterrent policies, such as the reformulation of Oxycontin, introduced with the aim of making the medication abuse-deterrent, and in turn, researchers found that the decrease on prescription opioid poisonings was offset by an increase in heroin mortality (Evans et al. 2019). At this point in time, DTOs were already in control of the supply of both regulated and illegal opioids.

By the time of the reformulation of Oxycontin, DTOs were already well in control of the illicit opioid distribution networks. Further, the academic understanding of the opioid epidemic suggests that cancer patients, terminal patients, and those with acute and chronic pain diagnoses were the initial recipients of prescription opioids, but these drugs quickly spread from these legitimate

patients into the hands of otherwise healthy individuals, predominantly middle age white men; this diversion was fueled by organized DTOs. We argue that the December 2007 diversion event was a pivotal moment in the opioid epidemic, because from this point onward Colombian DTOs were able to confront heroin supply restrictions with product sourced from the prescription opioid industry. Their influence continues up to this day with more perverse innovations, including the introduction of fentanyl to illegal markets (third wave), and its mixing with stimulants (fourth wave) which in turn has driven the overall opioid mortality to three times what it was in the mid-2000s (CDC 2021; Jenkins 2021; Ciccarone 2021).

To assess these competing explanations (pre-existing secular trends in the opioid epidemic or Colombian DTO activity where heroin was supplanted by diverted prescription pills) we explore the extent to which the diversion affected counties with different pre-event exposures to prescription opioid mortality compared to counties with different pre-event non-prescription opioid exposure. If the effects we find are largely and exclusively driven by the group of counties represented by high pre-diversion prescription opioid mortality, this would be a challenge to our argument. If, on the other hand, the effects are mainly driven by counties where the pre-diversion exposure to non-prescription opioids was more important, this would constitute suggestive evidence that the effects were driven by DTOs instead of the general opioid epidemic which up to the mid-200s was largely driven by pharmaceutical industry efforts.

We run Equations 2 and 3, across four separate groups based on whether they had high or low pre-event prescription opioid mortality and/or high or low pre-event non-prescription opioid mortality. We define a county to have *high* pre-diversion exposure, if the poisoning mortality across Rx (or alternatively Non-Rx) opioids, was in the top 30% of the distribution of pre-diversion Rx Mortality across Eastern U.S. counties. We measure pre-diversion mortality as the average mortality from 2005 to 2007. The idea of this exercise is to compare how counties with high pre-diversion Non-Rx opioid mortality, mainly driven by DTO activity, compared to low Non-Rx opioid mortality, conditional on the level pre-diversion prescription mortality.

5 Results

5.1 Evaluating the Design Assumptions

Before estimating a model of heterogeneous effects on a difference in differences setting, we evaluate the compliance of our models to design assumptions. One of the most important is the assumptions of as-good-as random assignment of the treatment among the different units under study. We argue that the spike (diversion) event meets this standard for the localities under the control

of Colombian DTOs. In general, the events that increased the stringency of money laundering in Colombia, or the series of seizures and hits to Colombian drug production, are not a matter of significant choice for policy makers in eastern U.S. counties or their citizens. While we do not observe the extent of the DTO actions, it is clear that Colombian heroin and illegal opioid production eventually withered and, in the years that followed the time period we study, gave way to Mexican drug organizations to take over the eastern U.S. market. This fact is pointed by the later reports from the DEA-DoD, as heroin availability across the U.S. increased even as South American heroin availability decreased (National Drug Intelligence Center 2011).

However, there might be other relevant actions that drive changes in U.S. opioid mortality. For instance, economic shocks such as automation and competition to foreign imports (Ruhm 2000; Hollingsworth et al. 2017), or the pharma-industry driven opioid epidemic itself (Alpert et al. 2022; Arteaga and Barone 2022). To address this concerns, we include in our specifications a series of covariates that account for local employment, exposure to foreign competition, and policies focused on addressing the opioid epidemic, all of which would account for this kind of variation. Furthermore, we conduct a robustness test where we try to make comparisons across counties according to their pre-diversion DTO prevalent activity (where Non-Rx mortality is relatively higher), conditional on the level of their pre-diversion prescription opioid mortality. If our results are driven by counties were DTO activity are less than prevalent, that would be a challenge to our hypothesis. On the other hand, if our findings are strong among those counties were DTO activity pre-diversion was greater, then, this would be suggestive evidence that DTOs' activities are the drivers behind our results. We condition on the extent of pre-diversion prescription opioid mortality, as it is impossible to distinguish cleanly DTO activity from the overall pharmaceutical industry opioid epidemic that was already under way. We present results from this analysis in the Robustness subsection below.

Another assumption is that in the absence of the policy, the difference between treatment units and control would have remained constant. This is the parallel trends assumption which can be partially tested following the specification of Equation 3. We estimate individual distance bin regressions to prevent the over-saturation of the models that would occur if we tested this assumption for all distance bins in a single regression. Each individual regression includes control and treatment counties in each distance bin d and the coefficients $\beta_{d,t}$ capture the relative difference between treatment and control for any period, in comparison to the third quarter of 2007, which we use as the reference period in our main specifications.

The event studies for non-prescription opioid (Non-Rx) opioid mortality suggest the difference-in-difference effects are well identified overall. Figure 17 presents the exercise for Non-Rx opioid mortality for groups of counties across "distance to spike counties" bins from zero miles (top left

panel) to over 1,000 miles (bottom right panel). In nearly all the "distance to spike" bins the parallel trend assumption appears to hold, with minor exceptions for individual periods. There are two exceptions, 401-500 and 801-900 miles bins, and still in those figures most pre-diversion coefficients are not statistically significant. Hence, we cannot reject the parallel trend assumption for most distance bins. These models suggest that the pre-treatment trends are no different between treatment and control counties and thus the difference-in-differences treatment effects we present in our main analysis below are well-identified. While the raw series in Figure 15, were already suggestive of the parallel trends in the bins we presented, Figure 17 provides a formal test across each individual distance bin. The comparison group is always conformed by the counties West of the Mississippi within 1,000 miles from a spike county.

Each graph also presents the dynamic coefficients from extending Equation 2, and letting β_d vary by year after the diversion. The coefficients and the graphs reveal that the effect in 2008 was usually the smallest and oftentimes not statistically significant. We included in Figure 17 two vertical solid red lines to denote the diversion timing as well as a plausible transitional period, as we see that the effects do not take place immediately following the diversion. This could be driven by the fact that the diversion counties we use are not the sites for the illicit sales and consumption, but are rather the sources of the product that must then be transported and distributed throughout the eastern U.S. We do not observe directly the timing of when the diverted opioids were substituted for non-prescription illicit opioids in each place, nor when the misuse among consumers happened. Finally, it is worth noting that the effect of the diversion on Non-Rx mortality does not dissipate along the distance gradient as we hypothesized. Even in counties over 900 and over 1,000 miles, there are still important treatment effects.

Figure 18 shows the same exercise but modeling mortality from prescription (Rx) opioids. From the standpoint of the parallel trends assumption, all bins offer a parallel trend with the exception of the bin over 0 to 100 miles, where the graph captures a pre-trend instead. Again, our specification largely identifies valid comparisons for most distance bins. From the standpoint of the timing of the treatment effects, several bins showcase immediate effects, but the delay is less uniform with some instances requiring more than two years to see significant increases in mortality. We reiterate that we did not expect to find an immediate effect, as we are not able to observe final consumer use, but only pharmacy transactions, and from there we do not know what other mediation occurs on how the prescription drugs are distributed and abused. Another feature of Figure 18 is that the diversion treatment effect that increases Rx mortality does decline along the distance gradient and even shows decreases in Rx mortality for some distance bins over 500 miles.

For both categories of opioid mortality, some of the effects we find take a certain time to emerge. We can compare those times with analogous studies that use instruments and exogenous

shocks to infer the drivers of the opioid epidemic. Evans et al. (2019) present trends in the series of heroin mortality that do not deviate from each other until after more than 15 months. In studies analyzing annual data statistically significant differences often take several years to appear; for instance, the introduction of oxycontin causing mortality across different levels of pre-oxy launching cancer-prevalence (Arteaga and Barone 2022) takes nearly 3 years before becoming statistically significant. Analogously, analysis of opioid mortality across states by their triplicate status shows differences after five years, which become statistically significant after the seventh year of comparison (Alpert et al. 2022). In comparison, the DTO-driven diversion we study here appears to have driven changes in mortality relatively faster than these other treatments.

We also analyze heroin mortality series individually. Heroin is an important sub-category of Non-Rx opioids, and one of the most commonly associated opioids to the illegal trade. Even if this association was prevalent at the time, heroin mortality was not among the most important drivers of opioid mortality by the mid-2000s in the Eastern U.S. counties, with only 0.25 deaths per each 100,000 people. This number only accounted for 11.7% of any opioid mortality in 2007, and for 19.9% of the Non-Rx mortality (see Table 3). We present the results for heroin mortality starting in Figure 19. For some distance bins the event studies show parallel trends (for example, the 201-300, 301-400, 701-800, 901-1,000, and over 1,000 mile bins) and subsequent significant long-term decreases in heroin mortality for most of them. Still, several cases showcase a pre-trend that would indicate that heroin mortality was decreasing in treated counties prior to the diversion. While this might be a challenge to the causal estimates of the diversion effect over heroin mortality, it is consistent with the scarcity of this substance among Colombian DTOs' controlled markets, which started earlier. Additionally, while the event studies show occasional signs of such a pre-existing trend, starting in 2009 some of them show a deepening in the decrease in heroin mortality (including the distance bins for zero, 101-200, 401-500, and 801-900 miles).

Looking at the diversion effect on mortality from any opioid in Figure 20, we observe that the majority of the distance bin graphs showcase pre-diversion coefficients for which the parallel trends assumption holds. We also see that several of the effects in Non-Rx mortality decreases are offset by the effects in Rx mortality increases. While this is true in the majority of distance bins closer to the spike counties, the diversion is associated with decreases in mortality in all counties with distances over 800 miles to the spike.

The results from Figures 17 and 20 support our identification strategy for the effects over mortality of Non-Rx and Rx opioids. While any individual post-diversion period treatment effect may estimated with noise, the joint estimation of a post-treatment parameter does in fact yield statistically significant effects, which we explore in Table 4 in the following sub-section.

5.2 Difference in differences - Distance-to-Spike Counties and Mortality

We proceed by estimating a model of heterogeneous spatial effects in our difference-in-differences models using Equation 2. Figures 21 and 22 present the different estimated values of β_d for several of the mortality outcomes we follow. The point estimates are presented in Table 4.

From Figure 21 and 22, we find the spatial patterns for the treatment effect we expect based on our conceptual framing. The top panel of Figure 22 shows the diversion effect over Non-Rx mortality rates. We find statistically and economically significant effects of the diversion event in reduced Non-Rx mortality for all distance bins. The magnitude of these effects ranges between 0.106 deaths to 0.435 deaths avoided per 100,000 population, with that highest mark occurring at the spike counties (0 miles). Even beyond the 800-mile distance group of counties, we find clusters of counties where Non-Rx opioid mortality falls significantly after the diversion event. Indeed, beyond the 900-mile distance bin (which corresponds to passing the central Appalachian region) we again observe generally statistically significant numbers of lives saved from Non-Rx opioids - with effects ranging over 0.3 deaths avoided per 100,000 population on those distance bins. The patterns observed in Figure 22 and Table 4 resemble our expectation from Figure 14. If there is any difference, it is related to the fact that we observed more lives saved than we originally expected, as even in the furthest areas served by Colombian DTO, we still observe declines in Non-Rx opioid mortality. Among those highly impacted localities, the diversion effects represent between 25% and 30% over the baseline of 2007 mortality.

The middle panel in Figure 21 and column (2) in Table 4 presents the estimation for β_d from Equation 2 for Rx opioids (T40.2). We again find a pattern consistent with our expectations, though the effects are less often statistically significant compared to the difference-in-differences estimates for Non-Rx opioids. We estimate a statistically significant increase in lives lost from Rx opioids of 0.259 deaths per 100,000 population for counties within 1 to 100 miles of a spike county, and we find statistically significant effects again when counties are between 201-300 and 301-400 miles away, where the diversion effects range between an increase of 0.135 and 0.227 additional deaths per 100,000 population, respectively. There are occasional distance bins beyond 500 miles from the nearest spike county which exhibit statistically significant effects from the diversion, 701-800 miles, and the last distance bin group of counties even experiences a decrease in its Rx mortality. Among those highly impacted localities, the diversion effects represent about 12% and 25% of the baseline mortality rate.

Column 3 of Table 4 and the bottom panel of Figure 22 presents the diversion event effects isolating heroin (T40.1). Heroin was an important component of the illicit drug trafficking in the U.S. during the period we are studying, and (as discussed above) a substance that the Colombian DTOs were particularly focused on distributing; so, it is worth examining whether there were

effects on that individual substance that mirror that found in other Non-Rx opioids. As can be seen from the Table and Figure, the answer to that question is "Yes". We find statistically significant reductions in deaths involving heroin (either alone or as a poly-substance death) for counties up to 300 miles away from the closest spike county. Estimates of the impact of the diversion range from 0.077 fewer deaths per 100,000 population up to 0.116 fewer deaths per 100,000 population. The results are largely analogous to those found for Non-Rx opioid mortality although they can represent only up to 25% as a share of the baseline in the highest affected distance bin.

As a sensitivity analysis, we examine substance-specific effects by estimating individual substance mortality in the same way as we did for heroin and Rx opioids, adding mortality related to synthetic opioids (T40.4, including Tramadol and Fentanyl) and methadone (T40.3) and estimating mono- and poly-substance mortality. We present the additional individual substance analysis in Appendix Figure A2.1 and the point estimates in the Appendix Table A2.1 for the interested reader.

Restating our findings of this subsection, the spike (diversion) event is associated with drops in overall Non-Rx opioid mortality and increases in mortality from Rx opioids. However the former are present along the entire distance gradient, whereas the latter fade with distance. The question is whether those opposing effects work to net each other out to zero change, or whether when the entirety of the eastern U.S. market is taken into account more or fewer lives are lost to opioids overall.

5.3 The extent of the effect

One approach to answering the question of whether there is a net positive or net negative effect of the diversion event on mortality is to simply measure the impact of the diversion on total opioid deaths from any substance (mono- or poly). Those results are presented in Figure 22 and the final column of Table 4. The two effects do often appear to offset each other as far as the marginal effect goes - as is perhaps best seen in Figure 22. Even so, there are many distance bins for which the marginal effect of deaths avoided from Non-Rx opioids dominates the marginal effect of additional deaths incurred from Rx opioids in a large and statistically significant way, especially further away from the spike counties. Also of note is the fact that it is rarely the case that the marginal effect on Rx opioid deaths algebraically offsets the marginal effect on Non-Rx deaths such that the net effect is positive. Nearly all of the average marginal effects are negative, even when not statistically significant.

More importantly, the comparison of marginal effects does not tell the whole tale, since the bases are different across distance bins so the actual magnitude of the net deaths avoided (or ad-

ditional deaths incurred) is not obvious from comparing a series of net effects. In order to better understand how large the net effect is, we estimated a series of back-of-the-envelope calculations to frame the magnitude of the effect of the spike (diversion) on overall opioid mortality, leveraging the linear form of our approximation. We estimate the instantaneous number of lives saved in each distance bin d by multiplying the population in the bin (in 100,000s) by the bin-specific coefficient β_d from Equation 2. Table 5 presents the results of the exercise.

As an example, according to Table 4, the coefficient $\beta_{d=0}$ for Non-Rx opioid mortality implies -0.435 fewer deaths per 100,000 inhabitants. In 2010 these counties had a population of 11.48 million, so our estimates imply that 49.9 lives were saved from Non-Rx poisoning deaths per quarter, or 199.6 lives annually in these counties alone. For the next bin, the annual specific number of lives saved is 246.11 (-61.53 additional deaths per quarter), which combined with the previous 199.6 lives, gets a cumulative number of lives saved equal to 445.71 in localities between zero and 100 miles from the spike counties.

Table 5 presents the quarterly and annual estimate of lives saved (lost) due to the diversion event for each distance bin (Quarterly Effect per bin Distance) and cumulative across all prior distance bins as you move down the rows - i.e. further from the closest spike county (Annual Effect Cumulative). Note that the cumulative difference in mortality for the "greater than 1000 miles" distance bin (final row of Table 5) corresponds to the total effect across all treated counties. In addition to this estimation, Table 5 presents the total number of cumulative actual deaths for 2007 (Deaths 07 Cumulative) as a reference baseline, and the share of that baseline that the forecast of changed mortality represents. The effect of the diversion in deaths avoided for Non-Rx mortality represents, on average, -21.4% of baseline deaths (from a high of -35.7% in the spike counties down to around -19% for the areas within 800 miles to the spike counties). On the other hand, the diversion led to an increase mortality of, on average, 9.1% over baseline Rx mortality (from a high of 18.5% to a low of 9.1%). These results are also presented graphically in Figure 23.

Finally, the bottom of Figure 23 illustrates the estimated net treatment effect of the diversion event on mortality from any opioid by distance bin. The effect of increased mortality associated with Rx opioids is generally only statistically and economically significant for areas close to the spike counties (up to 400 miles), while the reduction in mortality from Non-Rx opioids associated with the diversion persists even to the areas furthest from the spike counties. This is reflected in the net lives saved/lost estimates in the final panel of Table 5. We find generally small and statistically insignificant effects (sometimes positive, sometimes negative) until we arrive at bins at least 500 miles away from the closest spike county where the deaths avoided from Non-Rx opioids start to dominate additional deaths incurred from Rx opioids. Across the entirety of the treated counties east of the Mississippi River, our calculations suggest the diversion led to 1,434.8 fewer

"any opioid" deaths overall (compared to a counterfactual world where the diversion spike had not occurred). We thus estimate opioid mortality would have been approximately 9.2% higher without the diversion.

5.4 Heterogeneity and Robustness Exercises

5.4.1 Heterogeneity across Genders

We begin this section by presenting estimates for separate regressions in which we model deaths separately by gender. The marginal effect derived from estimating Equation 2 by sex for each of our mortality groups are presented graphically in Figure 24. One thing that is immediately apparent when examining Figure 24 is that whichever group of substances we examine, and for any distance from a spike county group, the effect of the diversion event is larger for men than for women. The top panel of Figure 24 shows the mortality effect associated with Non-Rx opioids by sex. As with the main results, Non-Rx opioid deaths fall (for all distance bins) in response to the diversion event, but the magnitude of the effect for men is as much as two to five times larger than for women. (This same pattern is also present for heroin deaths - the third row of Figure 24, though because of the scale of the figure the effects on women are hard to visualize). This pattern of larger effect for men than for women in most distance groups holds true for Rx opioid mortality (the second panel of Figure 24), though the differences are not nearly as stark. The differences are at most twice as large for men compared to women, and the confidence intervals on the estimate often overlap. The final panel in Figure 24 presents the net "any opioid death" marginal effects. Again, the effects are sometimes statistically significant for women (and suggests lives saved from the diversion event when so) but the marginal effects by distance bin are much more commonly statistically significant, negative (implying lives saved), and always much larger for men compared to women.

Table 6 presents the estimated change in mortality associated with the diversion by substance and distance, calculated separately for men and women. In addition, each panel compares the change in deaths from the diversion to actual deaths in each cell. Note that these mortality effects are estimated cumulatively moving out from the closest to the furthest counties from the spike event, such that the last row of each panel captures to total national effect. Looking at the leftmost panel (women on the upper, men on the lower) we see the differential effect of the diversion by sex: women average about a 17.7% reduction in estimated mortality from Non-Rx opioids compared to actual deaths whereas men average about a 23.4% reduction. In total we estimate there were 533 fewer Non-Rx deaths for women and 1,484 fewer Non-Rx deaths for men nationally because of the diversion. The middle panel of the Table presents the same calculations for Rx opioid mortality;

again, the effect is larger for men than women though by a smaller margin than for Non-Rx opioids. Cumulatively we estimate that the diversion led to 190 additional deaths involving Rx opioids for women and 423 additional deaths involving Rx opioids for men, nationally.

The final panel in Table 6 presents the estimated change in mortality from the model of any opioid-involved deaths. On net, women are predicted to have 246 fewer deaths from all opioid causes, while men are predicted to have 811 fewer deaths nationally from all opioid causes. Thus, our findings of net lives saved overall hold when the models are estimated separately for men and women, but it is clear that the "benefits" of the diversion accrue disproportionately to men compared to women. In part, this stems from higher prevalence of opioid mortality among men, however while the difference in the baseline mortality is two-fold, the difference in the diversion effects is nearly three times higher for men across Non-Rx, Rx and any opioid. This is consistent with the deaths of despair literature which generally finds men are more impacted by the opioid epidemic.

5.4.2 Heterogeneity across Races and Ethnic groups

We conduct the same exercise counting the number of deaths for each county for different classifications of race (Non-Hispanic White and non-Hispanic Black) and ethnicity (Hispanic).

We present these findings in Table 7 and Figure 25. Looking at the estimated numbers of deaths caused or avoided by the diversion, the greatest magnitude effects are always for non-Hispanic Whites in accordance with the figure (Panel A). Our models predict that for Whites nationally around 1,440 Non-Rx opioid deaths were prevented (18.1% over the baseline) by the diversion event and an additional 525 (9.1%) deaths were induced from Rx opioids. The net effect is less consistent, but when all treated counties are included in the estimate, the diversion appears to have prevented 915 (6.7%) deaths among the White population.

The diversion event also had statistically significant effects on the Black population, though the number of prevented deaths is smaller. Cumulatively, we see consistent reductions in Non-Rx mortality as we move to each more distant county bin away from the spike counties; across all treated counties, we estimate that there were 229 (23.2%)) fewer Black deaths associated with Non-Rx opioids as a result of the diversion. The cumulative effect on Rx opioid mortality is less significant in comparison to estimates of white mortality. Cumulatively we estimate that there were 85 (25.7%) additional Rx opioid deaths associated with the diversion. On net, however, we find no statistically significant effect of the diversion on opioid mortality among the Black population when all treated counties are taken into account (a drop of 126 deaths - 10.2%). Thus any decrease in Non-Rx mortality is statistically offset by increases in Rx mortality for the Black population.

Finally, for the Hispanic population, the impact of the diversion event on opioid mortality ap-

pears to have been wholly beneficial (at least from a statistical sense). We estimate consistently significant reductions in Non-Rx opioid mortality cumulatively for all distance bins, with an estimated 168 (38.9%) fewer deaths in treated counties as a result of the diversion. There is no statistically significant increase in Rx opioid mortality from the diversion in any county group, and the next effect on any opioid deaths - when all treated counties are included - is for 145 fewer any-opioid deaths. This represents a 23.6% reduction from baseline.

In conclusion, the diversion event has a general net effect of reducing mortality, but most of the effect is driven by the impact on non-Hispanic Whites, which has been historically the group disproportionately affected by increased opioid mortality during the opioid epidemic. Hispanics experienced decreases in their overall opioid mortality (any opioid) as well, stemming from the decrease in Non-Rx opioid mortality effect that was distributed across all the distance-to-spike counties' bins. It is noteworthy that there was no increase in Rx mortality for Hispanics as was observed for the other two subpopulations.

5.4.3 Heterogeneity across Age Groups

The final exercise across age subpopulation groups is summarized in Figure 26 and Table 8. Each column of Figure 26 represents different age groups from the youngest we follow (24 years of age and less), up to the most senior (65 years of age and more), while each row represents each of the substance mortality subcategories we have followed in the article. On Table 8, each panel represents an age category. Lives saved in Non-Rx mortality are concentrated among young and middle aged groups as the 414 lives saved among those under 24, represent 31.4% of the cumulative Non-Rx mortality in 2007. This number is 569 lives saved and 25% of the mortality for the age group 25 to 34 years of age. More lives are saved among those aged 35 to 44 years, with 588 lives and 24% of the cumulative mortality. For the age group 45 to 54, the cumulative effects are on the order of 362 lives saved and 14% of cumulative deaths. Non-Rx opioid mortality is rare among the two eldest groups, and among the most senior, the small numbers in lives saved with 40, account still for 29% of the cumulative mortality.

Whereas most groups experienced lives saved from Non-Rx mortality, in the case of Rx mortality most groups experienced some degree of increased mortality, with the exception of the most senior group. In this case, the effects of the diversion were concentrated mostly among the middle age subpopulations. Age ranges from 35 to 44 and 45 to 54 years of age experienced an increase in Rx opioid mortality in the order of 214 and 220 additional poisonings, respectively. These numbers represented 13% and 11% of the cumulative mortality observed in 2007.

The distribution of the offsetting effects, tilts the balance in favor of lives saved especially among the youth, although there are lives saved across all age ranges. The extent of lives saved

among the youth groups was a net 338 and 511 lives saved annually for those under 24 and those from 25 to 34 years of age, respectively. These numbers averaged about 17 and 15% of the cumulative mortality in each age range. The offsetting effect of the diversion on increased Rx mortality was stronger among middle-age subpopulations, where mortality from any opioid decreased only 9.1%, 3.3% and increased 2.5% for the age groups with 35 to 44, 45 to 54, and 55 to 64 respectively. Finally, back to a marginally significant effect of lives saved among the most senior group, although with smaller numbers of only 57 lives saved, that still represented 19% of the cumulative mortality.

In conclusion, lives saved from Non-Rx seemed to be reaching most age group subpopulations with the exception of the 55 to 64 year olds; however, the increased mortality from Rx opioids largely offset the effect for those in the middle age subpopulations, where the opioid epidemic has manifested itself most strongly, according to the literature describing the deaths of despair.

Taken together, these heterogeneity analyses are consistent with the interpretation that the diversion created substitution patterns across subpopulations that favored less risky prescription-sourced illicit use. On the one hand, we have patterns of lives saved in Non-Rx opioids that reach a wide population, including men and women, several race/ethnic subgroups (White, Black, and Hispanic), and younger age groups. On the other hand, Rx mortality increased disproportionately among middle-age white men. Thus it appears that the diversion event accelerated the entrance of DTOs into the provision of prescription opioids for illicit markets in time to meet to the surging demand traditionally associated with the opioid epidemic.

5.4.4 Robustness Exercises

Earlier in Section 5 we mentioned that we want to address the question if there are confounders that otherwise would drive opioid mortality challenging our hypothesis that our findings are driven by DTOs activity following the diversion. We cannot entirely distinguish counties where the opioid epidemic was primarily driven by the pharmaceutical industry, or where it was primarily driven by DTO activity. But, we can get a first approximation of each by focusing on the pre-diversion (i.e., pre-December 2007) *intensity* of opioid mortality across both Non-RX (which we associate with DTO activity) and Rx mortality (which we and several studies associate with the pharmaceutical industry) driven opioid epidemic up to that moment (Evans et al. 2019; Pierce and Schott 2020; Arteaga and Barone 2022).

We want to compare counties by their level pre-diversion Non-Rx opioid mortality, as we associate those counties with higher DTO activity, and their pre-diversion Rx opioid mortality, as we associate those with a pharmaceutical company driven epidemic. However, there is a concern that the ongoing opioid epidemic might bias the comparison. Hence we compare the diversion

effects across counties with four different levels of opioid mortality according to their pre-diversion exposure to Rx and Non-Rx mortality and the geographic classification in Figure 27. Panel A presents the two comparisons we focus on, with the left map showcasing counties that conditional on having a *High* Rx mortality pre-diversion also have a *High* Non-Rx counties (*High Rx - High Non Rx* in solid red), and we want to compare those counties to those pre-diversion *Low Non-Rx*, also conditional on *High Rx* pre diversion mortality (*High Rx - Low Non Rx in solid navy blue)*. The right map shows the analogous comparison conditional on counties with *Low Rx* pre-diversion mortality. We defined counties on the top 30% of the population weighted distribution of the 2005-2007 average opioid mortality in question to be *High*, and *Low* for the remainder of the distribution. Panel B of Figure 27 consolidates the two maps and displays an interesting pattern as three solid focal geographic points become evident: 1) The Gulf of Mexico and Florida, 2) Appalachia, and 3) the North East at more than 1,000 miles from the spike counties, all of them with deep red centers. Surrounding those centers solid navy blue shows DTOs dominant prevalent counties trailing the opioid epidemic driven by High-Rx and High Non-Rx pre-diversion mortality counties.

Table 9 and Figure 28 present the results of splitting the sample across these subgroups of counties. Panel A presents the estimation of the marginal effects of the diversion on Non-Rx mortality. Labels in the Table state the subgroup by their pre-diversion opioid mortality prevalence. Conditional on the prevalence of pre-diversion Rx mortality, Non-Rx counties drive our results considering that the point estimates are higher for *High Non-Rx* irrespective of the status of pre-diversion Rx mortality. For *High Rx* pre-diversion, we have Column 2 (*High Non-Rx* pre-diversion) exhibiting greater decreasing effects than Column 3 (*Low Non-Rx* pre-diversion) in each single distance bin. And equivalent the same happens when we compare Columns 4 and 5, which are conditional on *Low Rx* pre-diversion. This constitutes suggestive evidence that the DTO activity is the most important driver of the main results presented above, which are also displayed in the first column of the Table. These differences in the effects over Non-Rx mortality across pre-diversion Non-Rx mortality prevalence are statistically significant as shown by Figure 28. Each graph shows a comparison across the effects of the diversion across the level of Non-Rx pre-diversion mortality, conditional on Rx mortality. Especially for the effects over lives saved, the main driver counties are those with High Non-Rx, which we associate with high DTO activity in relative terms.

The opposite proposition is also relevant. Starting from conditional on DTO exposure (*High Non-Rx* pre-diversion), how different are the diversion effects across counties where the pharmaceutical industry driven opioid epidemic (*High Rx* pre-diversion) has been more prevalent. If *High Rx* pre-diversion counties are driving the results, this would constitute a challenge to our hypothesis. This entails comparing Columns 3 and 4, and also Columns 3 and 5 from Table 9. The first comparison conditional on *High Non-Rx* pre-diversion, *High vs Low Rx* pre-diversion, does not

yield a consistently positive or negative treatment effect ; counties with *Low Rx* pre-diversion evidence higher mortality in most bins (8 out of 12), while counties in *Low-Low* exhibit no consistent effect.

Panel B of Table 9 and the second row of Figure 28 present the results of the effect of the diversion over Rx mortality. In this case, the effects of the diversion over Rx mortality are more evenly driven across subgroups. Conditional on *High Rx* pre-diversion, there is not much of a significant difference in the effect over Rx mortality across *High vs. Low Non-Rx* pre-diversion counties. Conditional on having a *Low Rx* mortality prevalence pre-diversion, at least two distance bands experience a significantly higher increase in Rx mortality following the diversion.

As part of this exercise we evaluate the sensitivity of the results to the choice of the threshold for defining *High* pre-diversion prevalence. We focused on the top 30% to emphasize the top of the distribution while still having enough within distance-bin power. We also repeated the exercise for different cutoffs from top 25, 40, and 50 percent of the distributions. While the point estimates vary, the two main findings of the exercise remain qualitatively identical. First, the larger decrease in Non-Rx follows the diversion among counties were DTO mortality was more prevalent before the diversion, irrespective of the level of prevalence of pre-diversion Rx mortality. Second, Rx mortality increases following the diversion are more evenly split across subgroups, with some specific distance bins experiencing significantly higher levels of lives sacrificed among those with higher prevalence of DTOs activity prior to the diversion. These results are available upon request.

Overall, this exercise shows that the effects of the diversion were largely driven by the lives saved from Non-Rx mortality in counties where DTO activity was more prevalent prior to the diversion. On the other hand, while the diversion effects on lives lost from Rx mortality were more evenly split across subgroups, with particular distance bins where DTO prevalence was higher exhibiting significantly higher increases in mortality. Still, the main take away of this exercise is that the effect of the diversion on Non-Rx and Rx opioid mortality, is not driven by counties where the pre-diversion prevalence of the pharma-industry driven opioid epidemic was higher, as it would have been the case with confounders that mostly had affected the prevalence of prescription opioid mortality up to the point in time of the diversion. To the extent that we can associate Non-Rx opioid mortality prevalence prior to the diversion to DTO relative prevalence, the effects we find are largely driven by those localities.

Finally, as mentioned in Section 4, we conduct several exercises trying to see if the results are sensitive to our most important modeling choices. Following, Figure 29 and Table 10 both present the main results from the estimation of Equation 2 stress testing our choices. Each panel of the Figure presents a different category of substance mortality following the structure of the last section, whereas each column presents the results for each different exercise. The Table presents

first the main results of the article under Column 1, which we introduced earlier in Table 4, along with the coefficients for the robustness exercises omitting the results for any opioid in interest of space.

The first exercise, estimating the effect of the diversion event for unadjusted mortality in Column 2 of Table 10, implies disregarding mortality from poisonings that cannot directly be attributed to opioids. In turn, this implies an undercount of the number of deaths (Ruhm 2018). Focusing on those results (column one), we observe that the coefficients for Rx and Non-Rx opioid without the adjustment are generally lower in absolute terms with few exceptions. None of the results of this exercise implies a change in the sign nor decreases substantially the significance of our results.

Our second exercise of moving Louisiana to the control counties presented in Column 3 of Table 10 generally attenuates the magnitude of estimated lives saved from the diversion event. We test including Louisiana as part of the control group in consideration of the customary consideration of splitting the country East-West, along the line of the Mississippi River. However, we consider the state in the treated group for our primary models given that we find spike counties in the state and the substantial documentation from the Department of Defense and the DEA confirms that illegal heroin distributed in the state belongs to Colombian DTOs at the beginning of the 2000s and the years that followed National Drug Intelligence Center (2001; 2007). If the state is treated and we, mistakenly consider it part of the control, this should attenuate our results. That is what we find for the effect of the diversion event on Non-Rx opioid mortality. In contrast, the coefficients for Rx opioid mortality are higher in magnitude. When we consider the net effect across any opioid mortality, some coefficients become positive specifically in the closest vicinity of the spike counties. Again, none of these results changes the main direction of our results.

The third exercise is to estimate the models without other covariates that account for time-varying socioeconomic characteristics of the counties nor state policies to address the ongoing opioid epidemic at the time. In general, the inclusion of covariates should produce more precise estimates. Leaving other independent variables out of our analyses attenuates the results for Non-Rx mortality in most distance bins. In contrast, it increases the effects on Rx mortality. Once again, none of these results changes the main direction of our results.

The last two exercises alter substantially the sample we use in the analysis. First, when we use the DEA “300% of baseline" rule to identify spike counties we end with a smaller set of spike counties, and thus, from the limited sample extending 1,000 miles renders fewer counties in the total sample. The exercise attenuates some of the results across Non-Rx opioid mortality, and Rx opioid mortality without changing the direction of the coefficients or the overall net effects.

Finally, we use the geodetic distance (equivalent to the Euclidean distance over the curved surface of the Earth) to create our distance bins of treated counties. This extends the sample as

1,000 miles on a straight line has a wider reach in comparison to 1,000 miles of driving distance (which must go around mountains and adjust to the landscape). We use this measure also to address any consideration about the time-variant nature of driving distance we use in the main results of our analysis. Using the geodetic distance rather than driving distance does not change our results in a relevant way. If anything, using the geodetic distance we find statistically significant results along all but one of the distance bins for Non-Rx lives saved, and we also find more significant results for Rx. This choice does not significantly alter our results, but increases the order of magnitude of lives saved following the comparison of the coefficients for Any opioids in Panel C.

Across all our robustness exercises we find very similar results to the ones reported in the main specification with very specific changes that do not alter the fact that the diversion led to a decrease in Non-Rx opioid mortality and to an increase in Rx mortality, with overall lives saved. From thses robustness exercises, we conclude that our results are generally robust to these different specifications.

6 Discussion and Conclusion

In this paper, using data from a complete census of manufacturer-wholesaler-pharmacy opioid shipments we present evidence that there was an aberrant surge of 147 million excess opioid doses into retail pharmacies in 78 Southeastern U.S. counties over two weeks in December 2007. To the best of our knowledge, this surge has not been documented in the literature, nor has its effect on illicit opioid markets been studied. Ancillary evidence on the illicit drug market in the U.S. and Colombia at the time supports a compelling narrative that this spike in opioid sales represented a diversion of prescription opioid products from pharmacies to the illegal drug market east, but not west, of the Mississippi River in the U.S. The apparent intent of the diversion was to allow Colombian drug trafficking organizations to maintain control of the illicit opioid market east of the Mississippi during a period when domestic Colombian production of heroin was collapsing.

One unintended consequence of this large shock was that the portfolio of illicit drugs east of the Mississippi River became relatively safer, in the sense that the variance in the typical dosage strength would have fallen as tightly controlled dosage prescription opioids supplanted high-variance dosage non-prescription street drugs (i.e., opioids, like heroin or illegal fentanyl, largely manufactured illicitly). We find that non-prescription opioid deaths (Non-Rx) fell by about 2,006 deaths per year in the treated counties (compared to western U.S. control counties) for several years following the spike event. Commensurate with the expectation that more people were consuming prescription opioids after the diversion event, we find increases in prescription opioid mortality of around 571 deaths annually for treated counties compared to controls. The net effect is

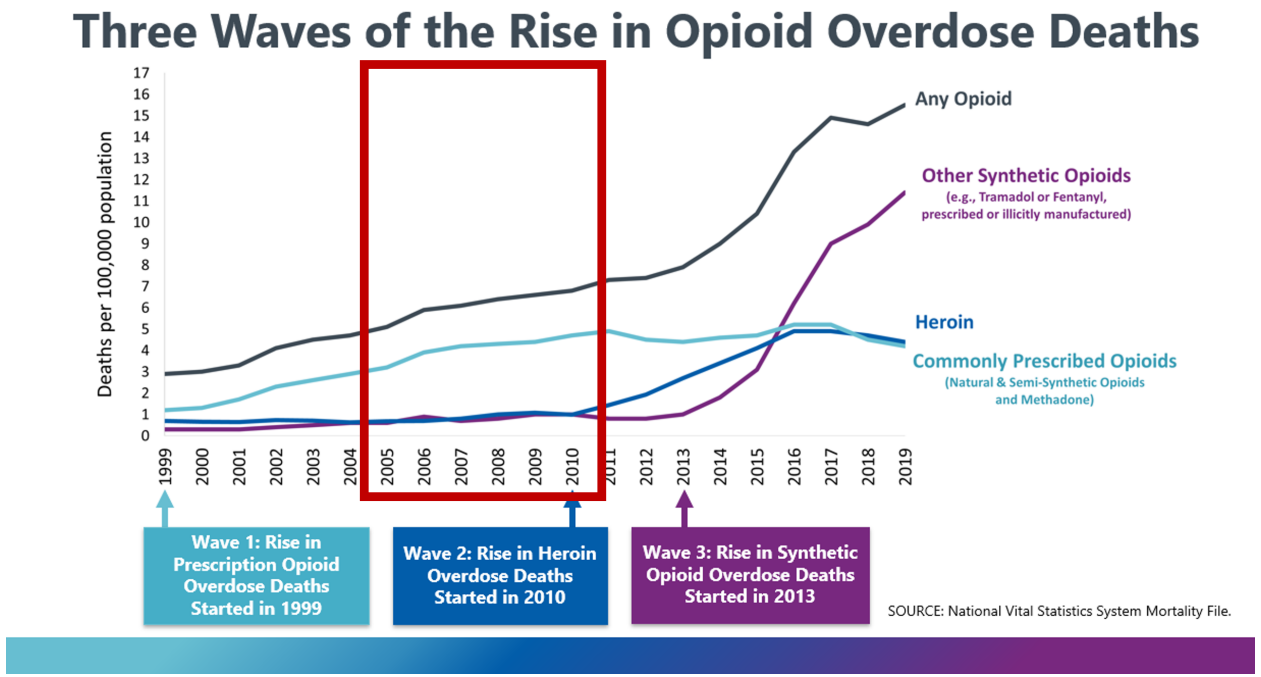
estimated to be 1,435 fewer deaths from any opioid east of the Mississippi River compared to west. It seems clear that the diversion event - which was almost certainly intended to extend Colombian drug trafficking organizations' hold on the illicit drug market - in practice resulted in a substantial, if temporary, tempering of the opioid mortality epidemic in affected counties.

Ultimately, this unique large-scale criminal diversion event provides several lessons for policymakers as they contemplate strategies to combat negative externalities - be they from the prescription opioid market or global pandemics. The first lesson is that large-scale harm reduction events can have significant effects in the real world, even when they aren't initiated and maintained by government fiat. Altering the terms of markets (even highly unregulated markets like those for illicit drugs) can have sustained effects. Second, "harm reduction" may not be universal. In the case of our study, mortality from non-prescription opioids clearly fell; however, mortality from prescription opioids increased. Thus, even with "harm reduction" there are winners and losers. Whether, for example, a heroin user who would have died in the counterfactual world actually survived long term or whether their cause of death was only shifted to another substance, is unknowable. But, our findings do emphasize a point that is known but often unmentioned: harm *reduction* is not harm *elimination*. Nevertheless, incremental gains are preferable to no gains - a lesson that bears repeating in the specific context of the U.S. opioid epidemic.

This is one of the first articles that provide evidence on the interaction transition from a pharmaceutical industry ignited opioid crisis, to one that is mostly driven by illegal actors. Hence, a key take-away from our analysis is that we need to change the focus of the understanding of the opioid epidemic. As opioid mortality has surpassed 100,000 poisoning deaths annually and keeps growing exponentially, mainly driven by the irruption of illegal fentanyl and its combination with other substances, a focus on the understanding of the illegal markets could help to think about solutions to the crisis.

7 Figures

Figure 1: U.S. CDC Three Waves of the Opioid Crisis



Note: Taken from the CDC webpage, consulted May 24, 2023. Available at: www.cdc.gov. The diversion event we document and its effect are located in the time framed by the red rectangle.

Figure 2: Total MME Spike into Florida

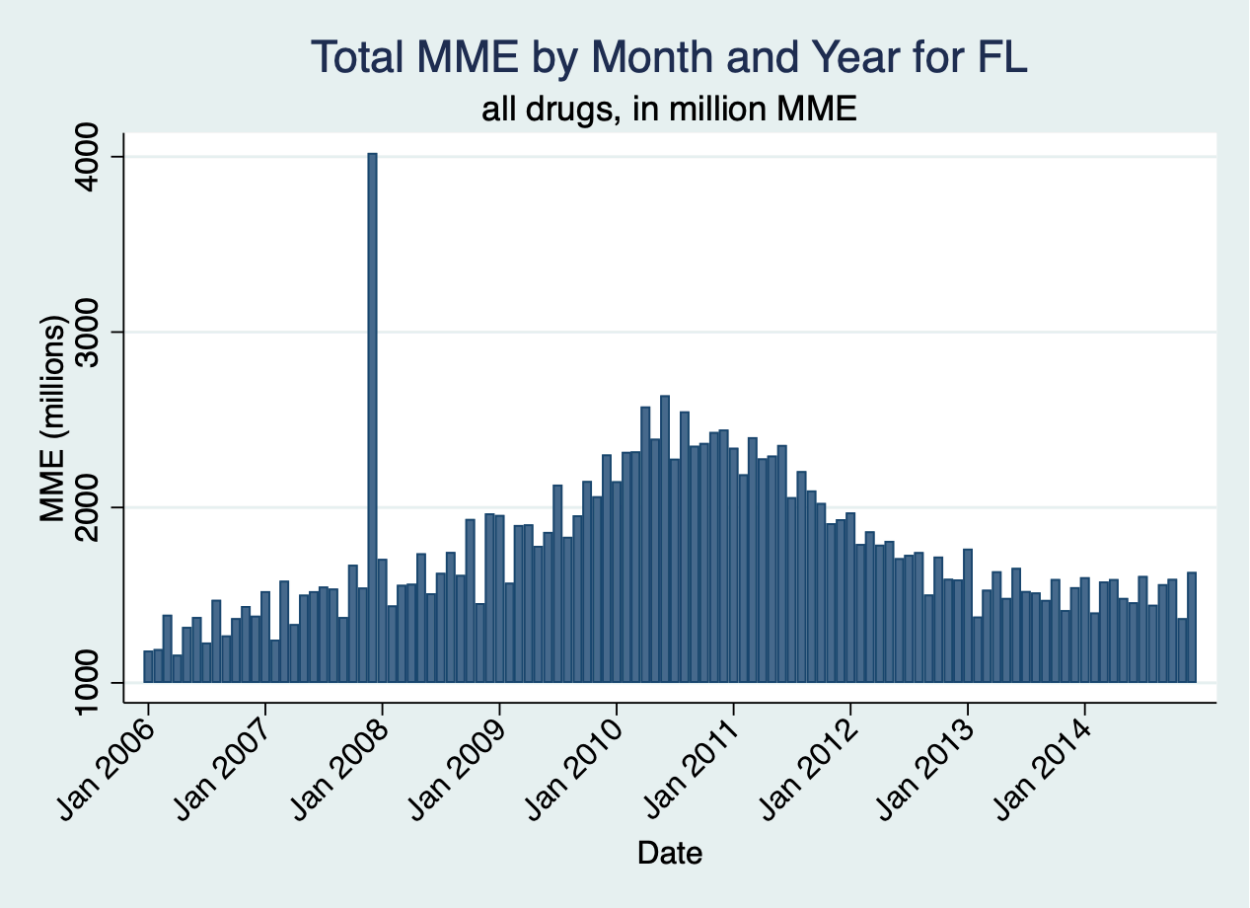


Figure 3: Total MME into California, New York, and Texas

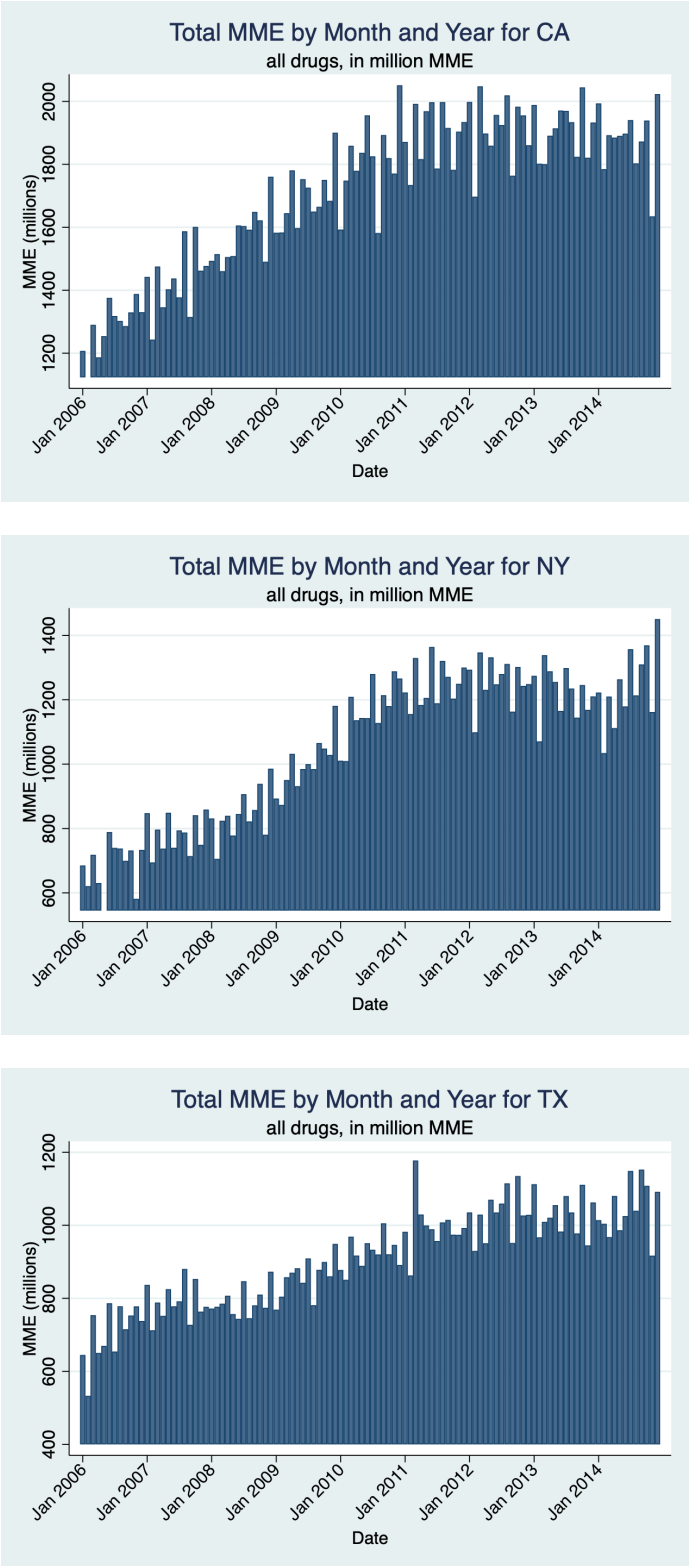


Figure 4: Total MME into Alabama, Louisiana, and Mississippi

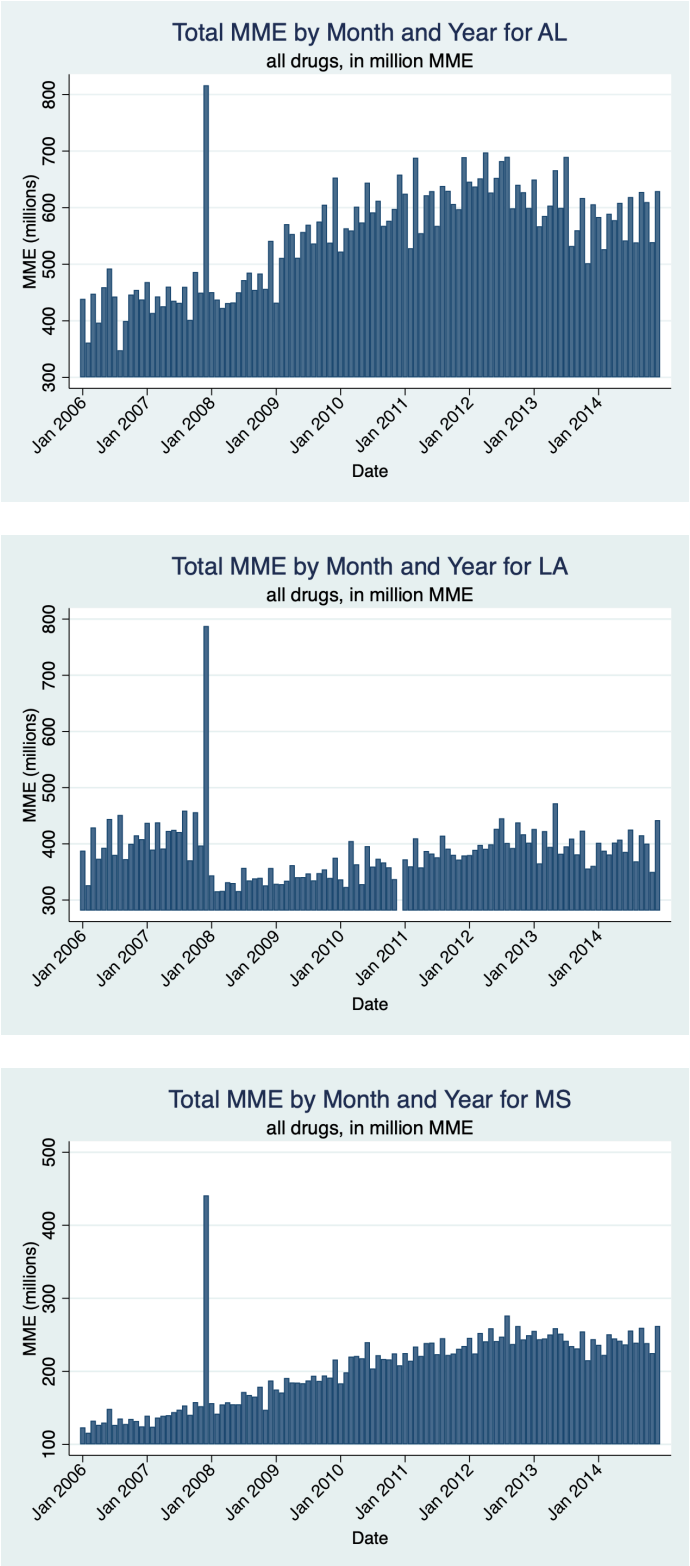


Figure 5: Total MME Spike into Florida

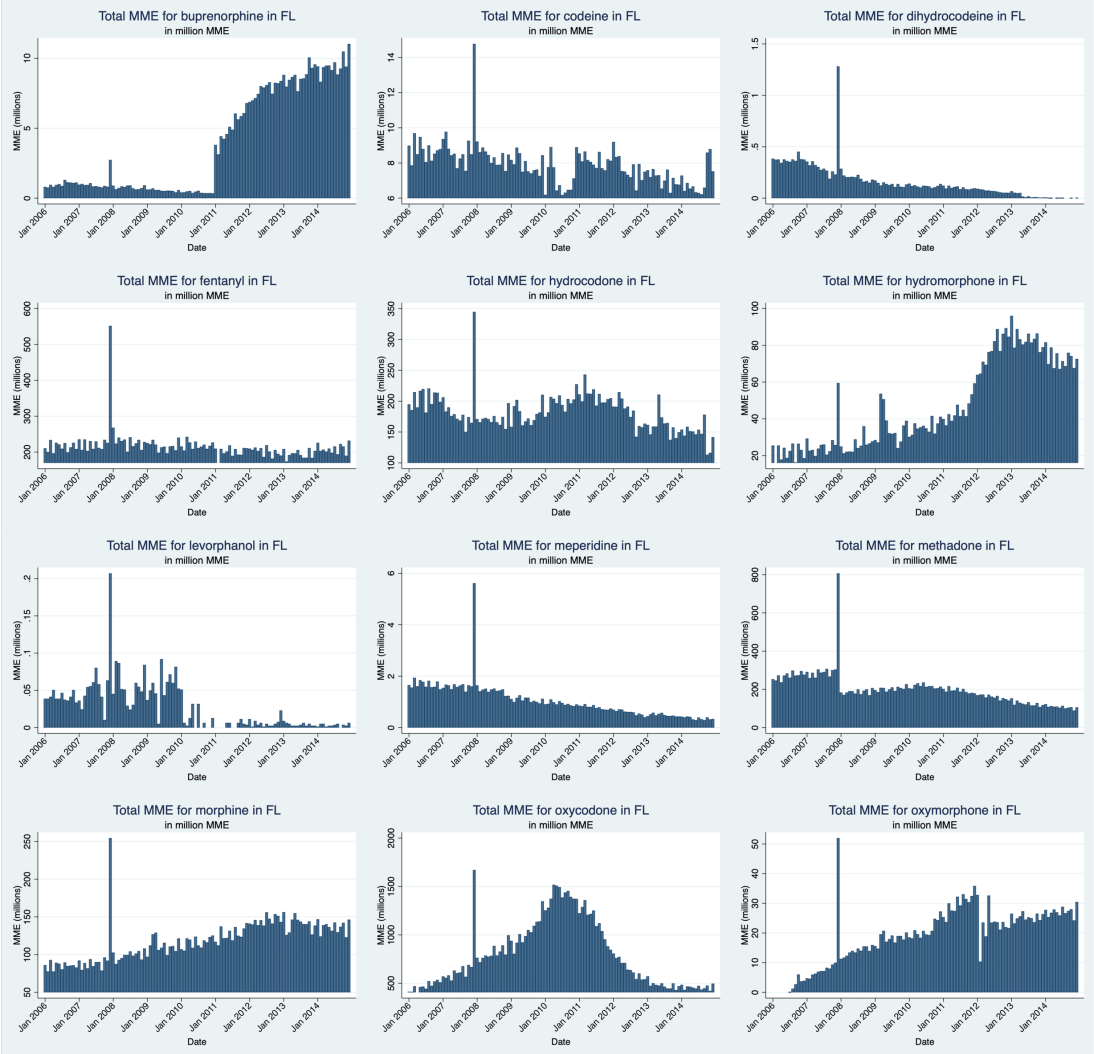
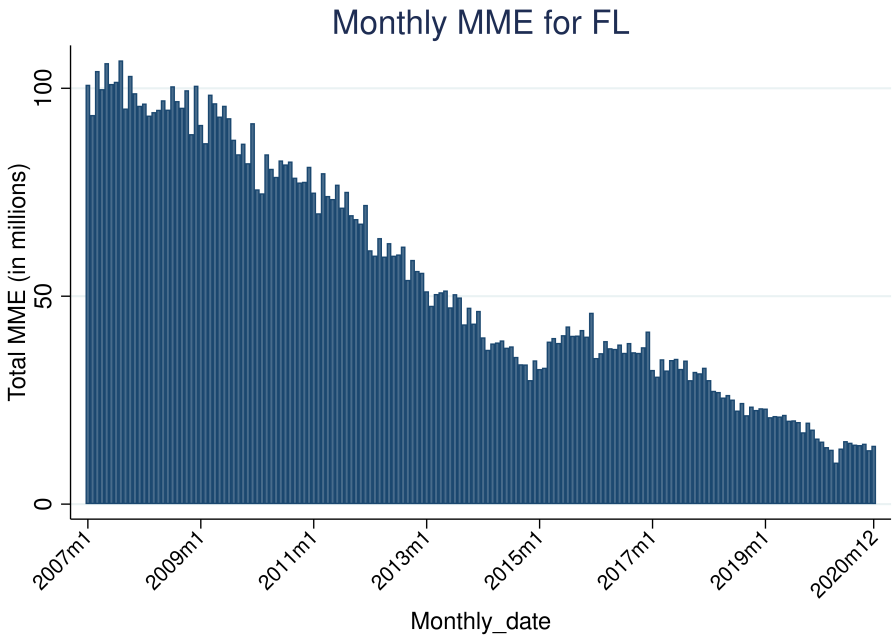
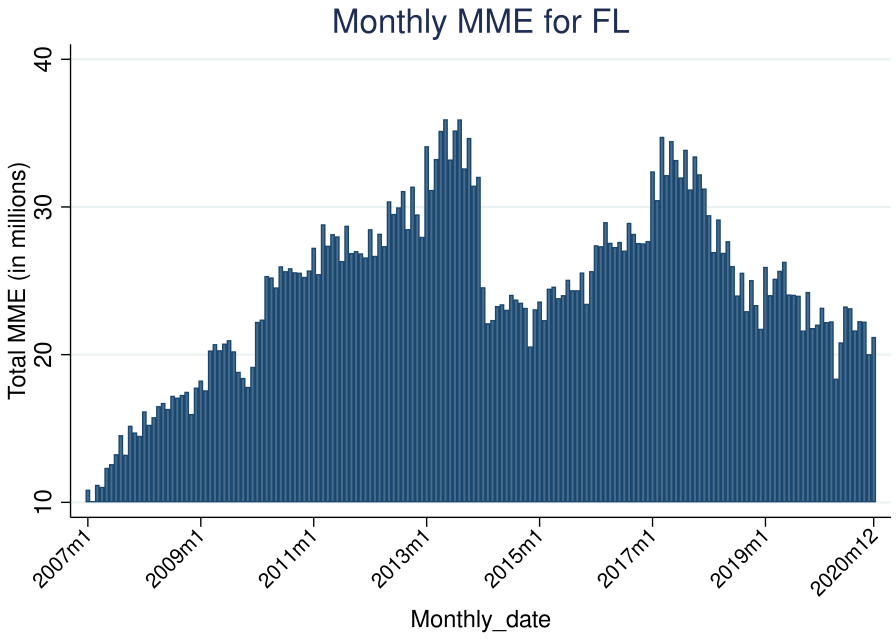


Figure 6: Total Prescription MME reimbursed by Commercial and Medicare Advantage Plans in Florida



(a) Commercial Claims



(b) Medicare Advantage Claims

Figure 7: Total MME Reimbursed by Florida Medicaid, 2006-2010 (quarterly)

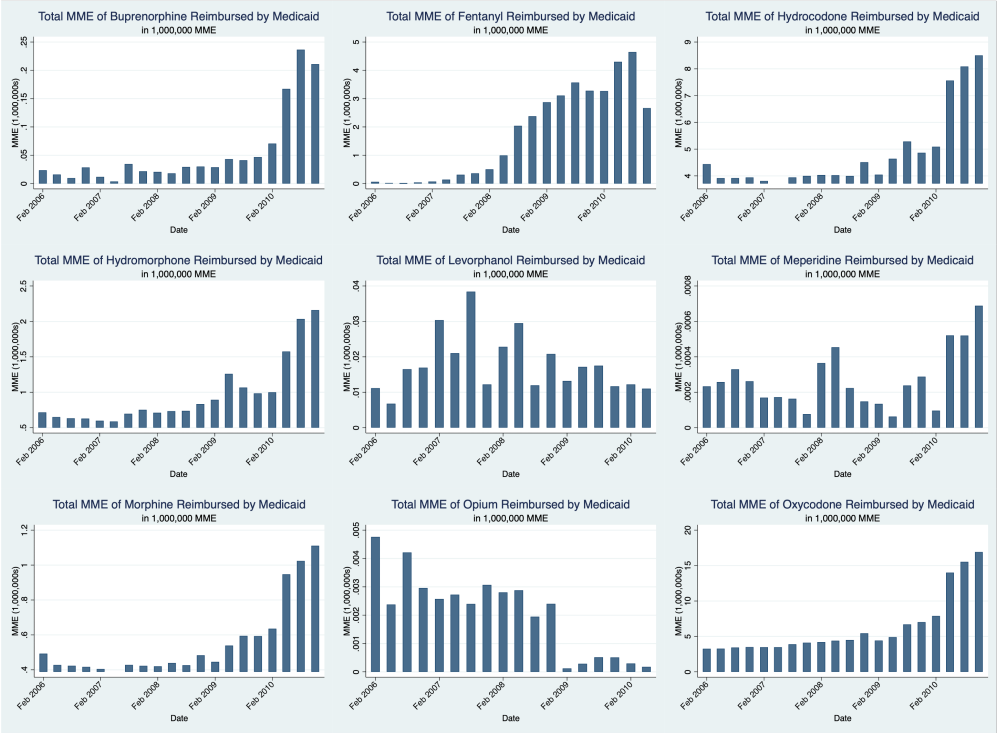


Figure 8: Counties Classified as Having Suspicious Shipments in December 2007

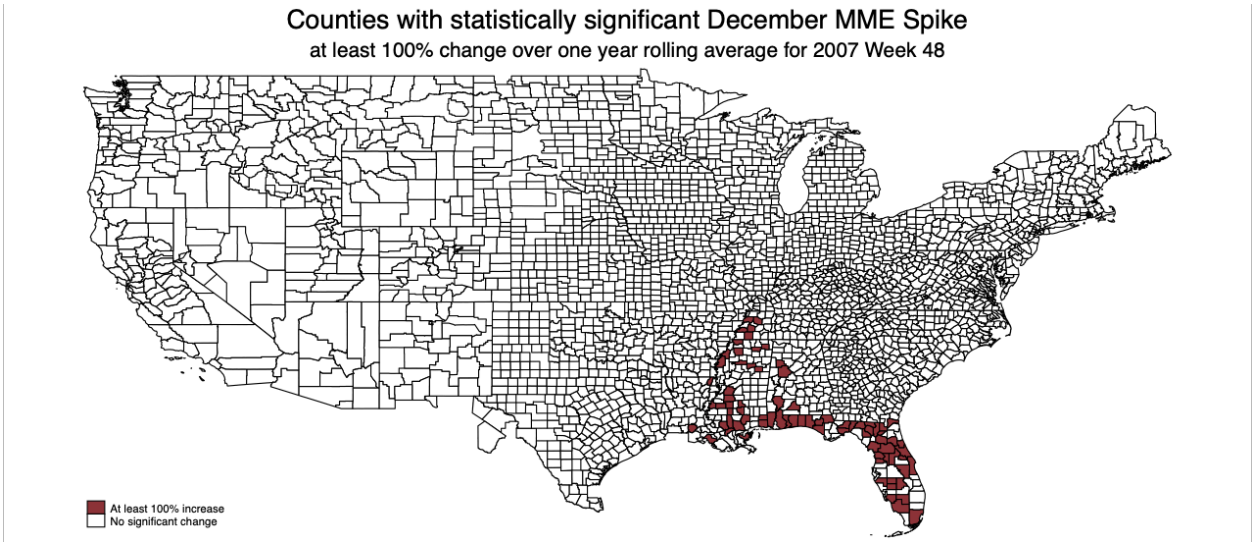


Figure 9: Counties Classified as Having Suspicious Shipments in December 2007, focus on Southeastern U.S.

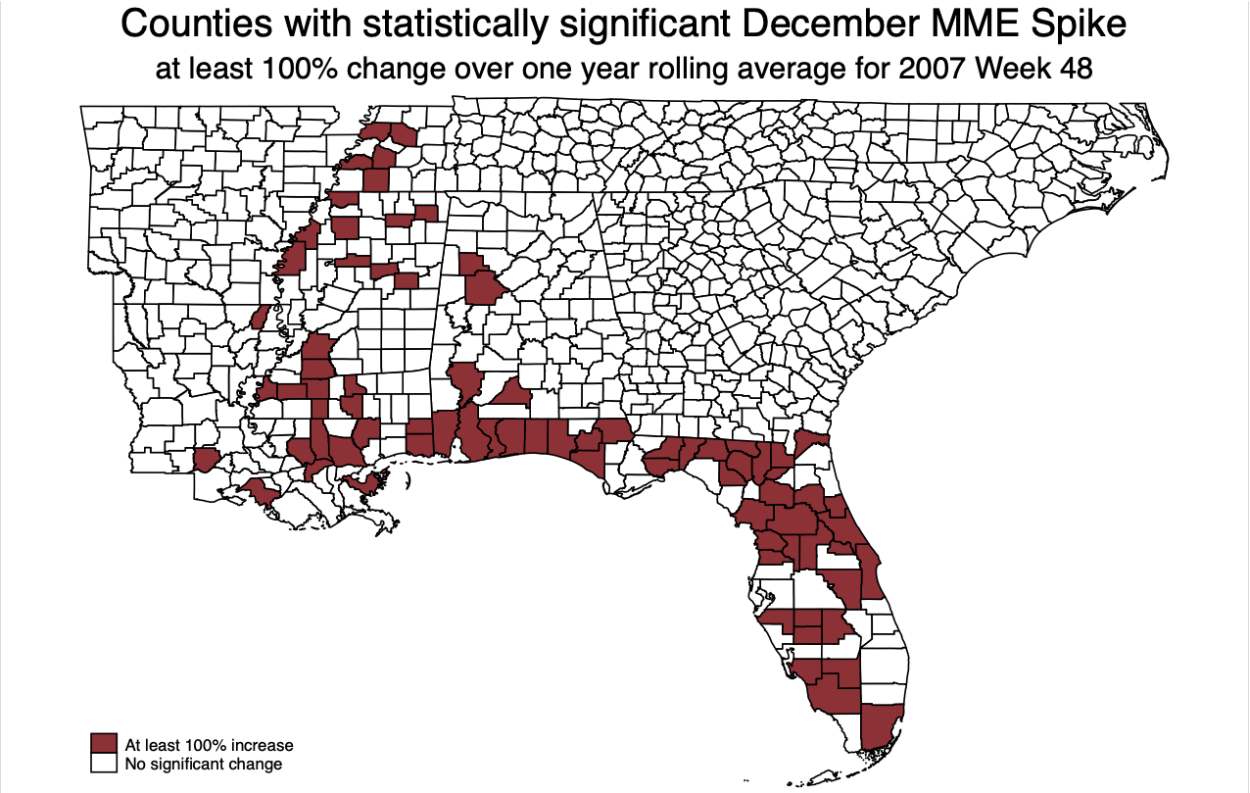
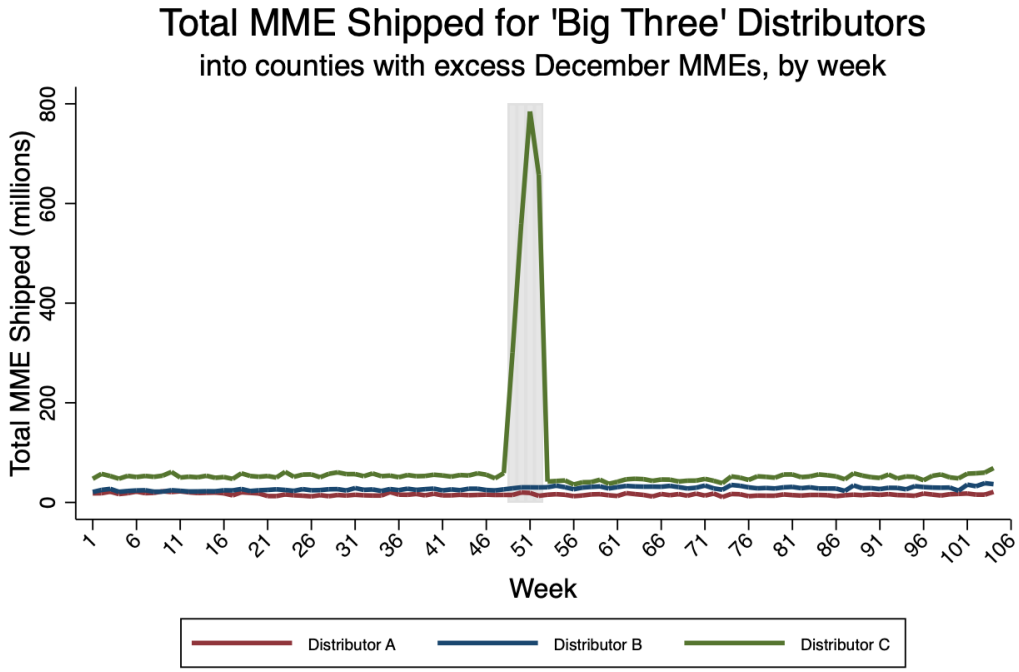
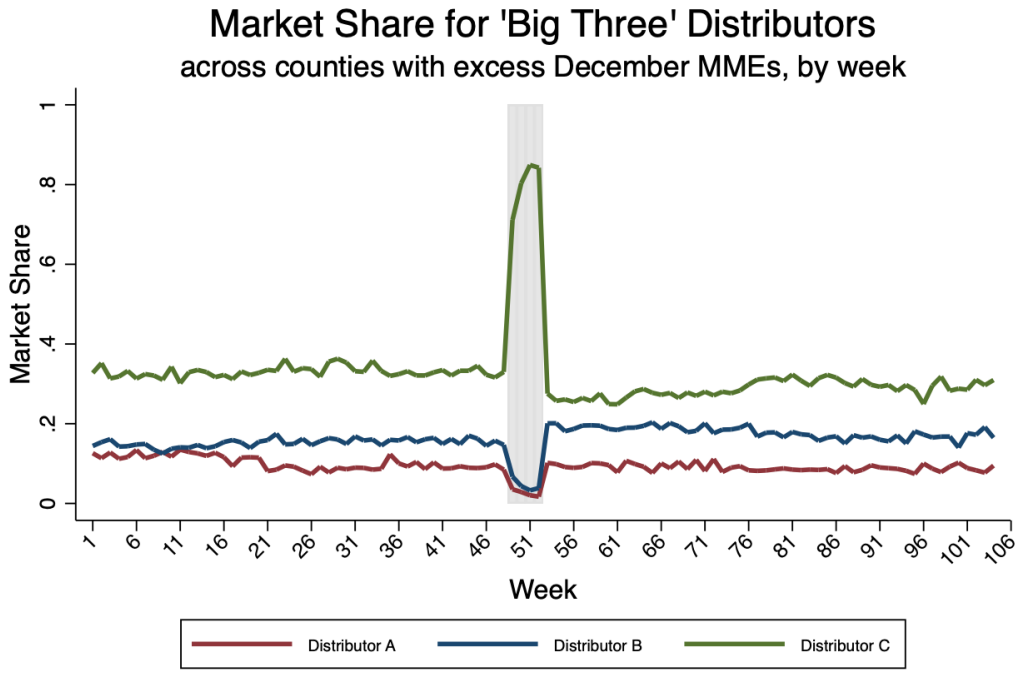


Figure 10: Total Surge MME Shipments and Market Shares by Distributor

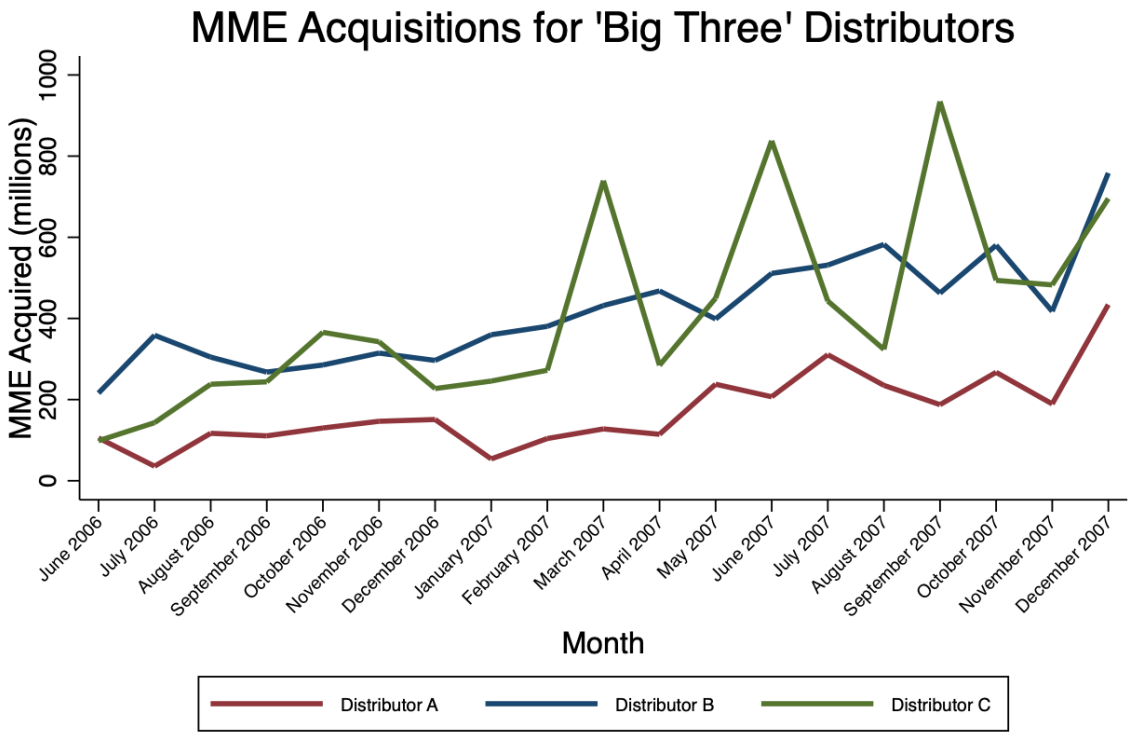


Shipments are millions of MMEs per week for all drugs in transactional ARCOS except OUD formulations of beprenorphine and methadone.



Market shares are percent of shipments of MMEs per week into counties with excess MMEs, for all drugs in transactional ARCOS except OUD formulations of beprenorphine and methadone.

Figure 11: Opioid Purchases from Manufacturers by Distributor C



MMEs are national acquisitions from manufacturers to the three distributors who delivered the greatest amount of opioids into counties with excess December 2007 MMEs. This includes all drugs in transactional ARCOS except methadone. Additionally, seven suspicious transactions from Cantrell Drug Company (which only sold to one distributor) were excluded.

Figure 12: Timeline of Key Events Surrounding December 2007 Opioid Surge

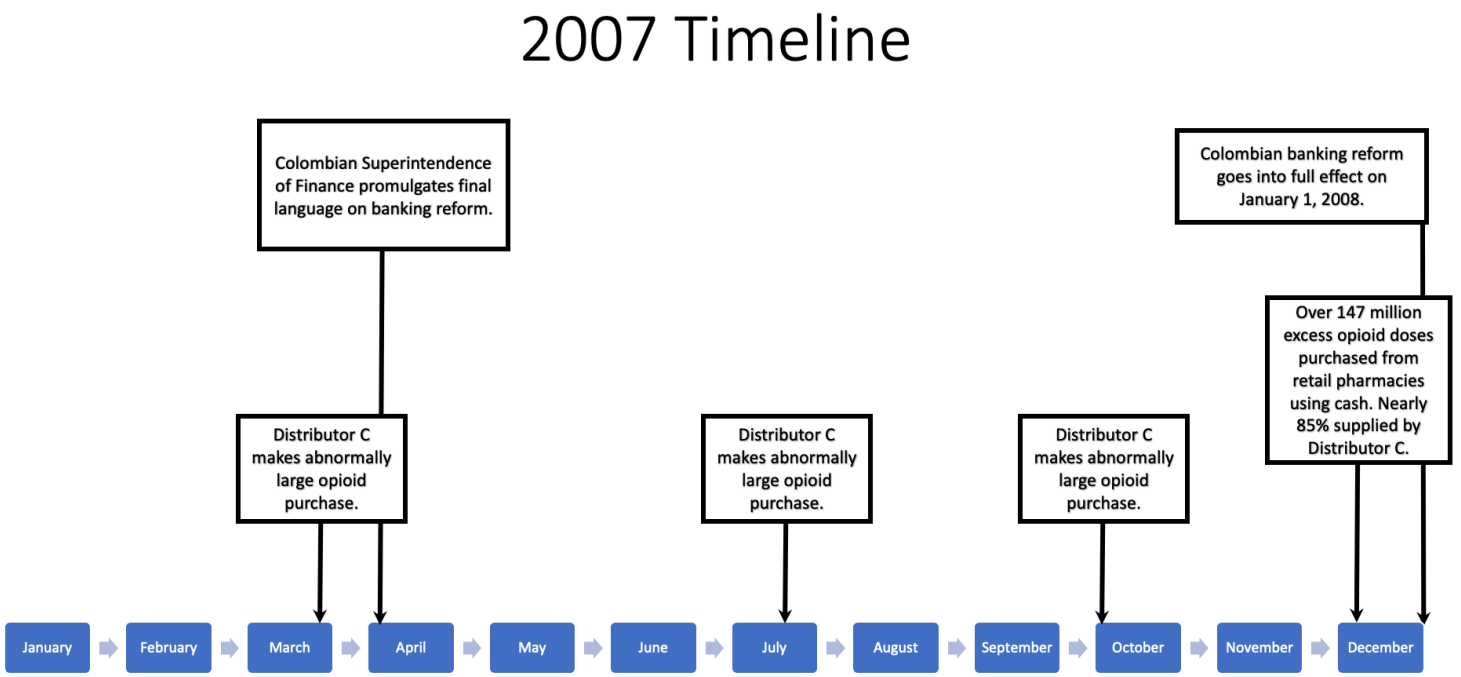
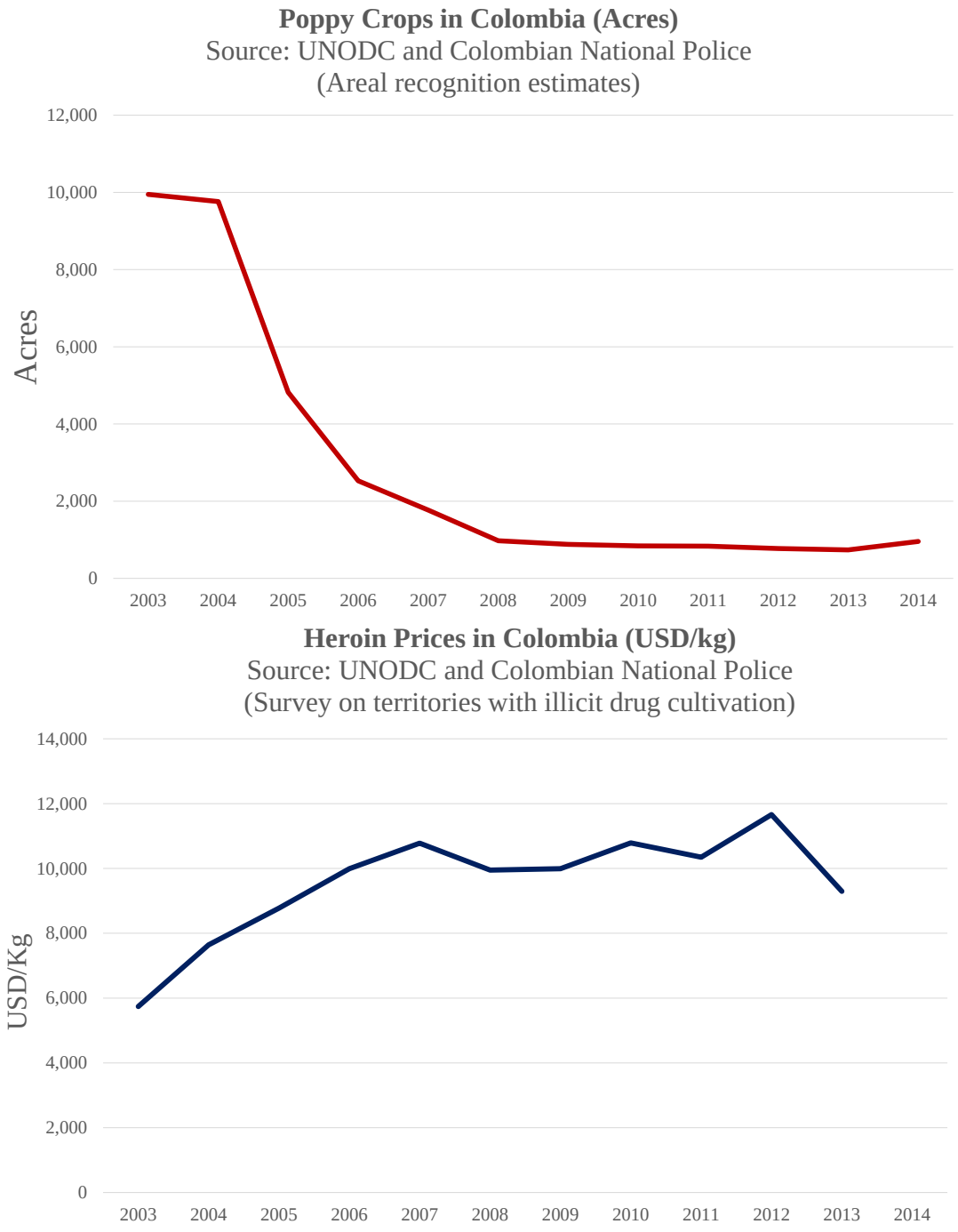
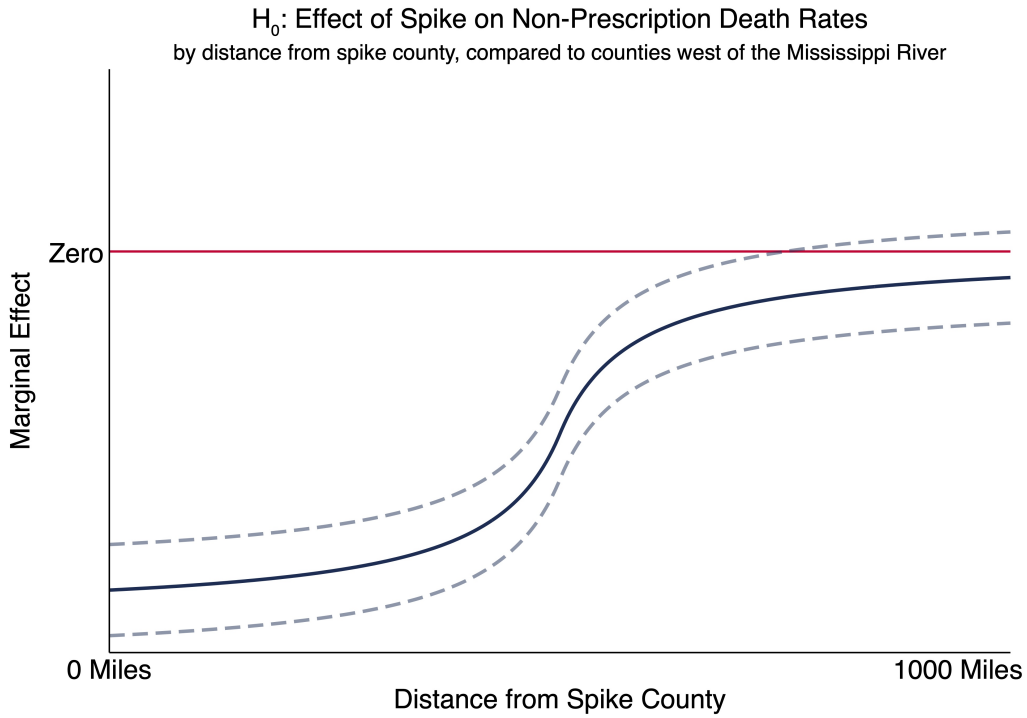


Figure 13: Colombian Poppy Crop Acreage and Heroin prices, 2001-2014



Authors elaboration based on the United Nations Office on Drugs and Crime - Illicit Crop Monitoring Programme reports (2003-2014) for Colombia with information from the Colombian National Police. Reports available at: www.unodc.org. The top panel displays the acreage of poppy cultivation in Colombia, and the bottom panel the average prices at which heroin was sold in territories affected by illicit crop cultivation.

Figure 14: Expectation for the Effect of the Spike on Opioid Mortality



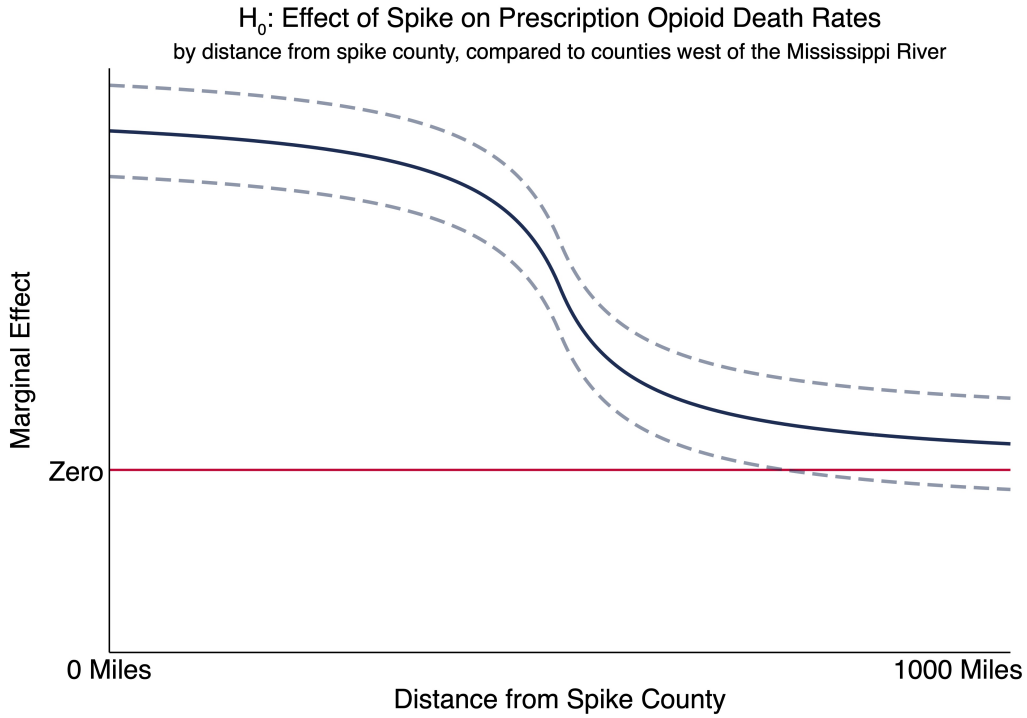
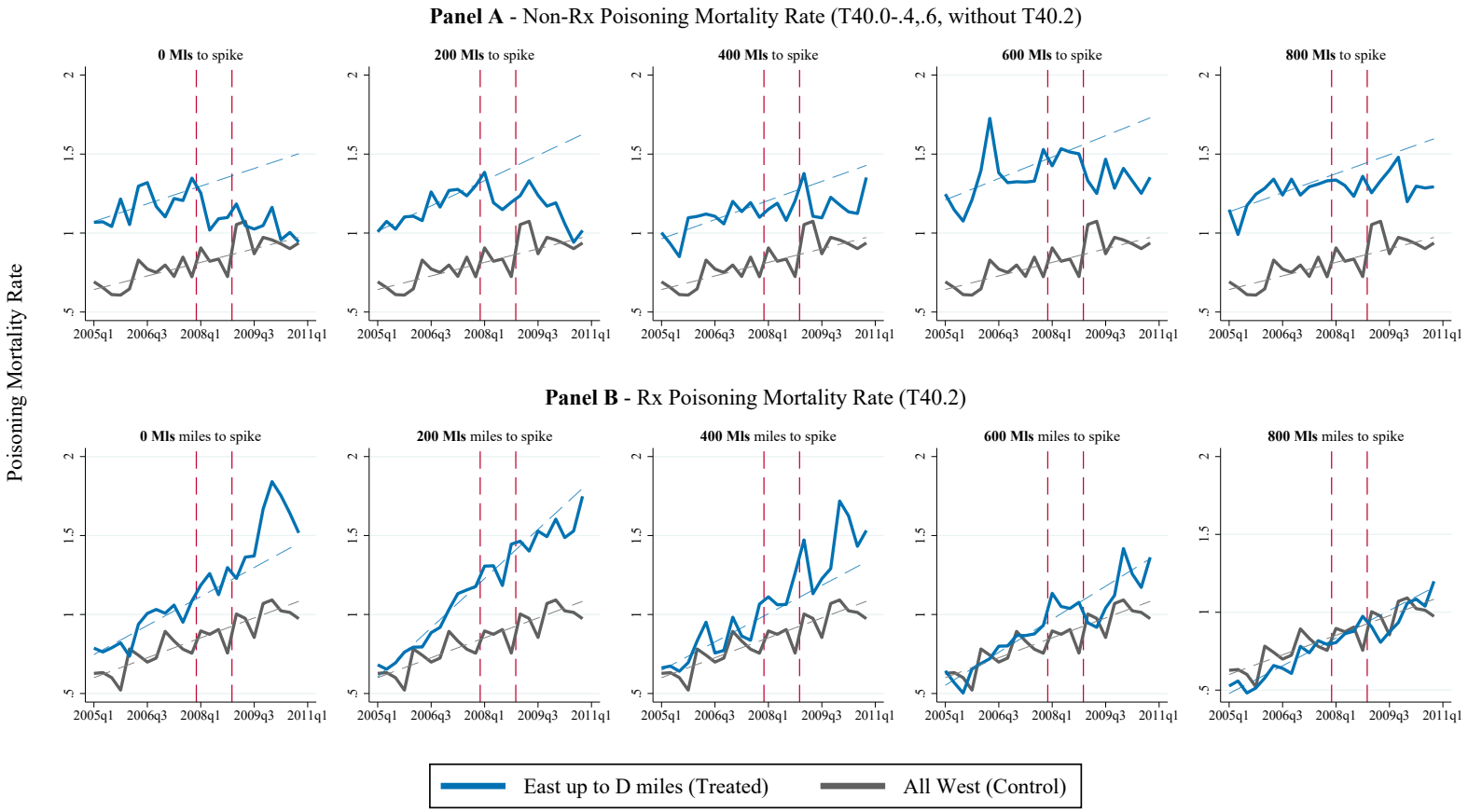
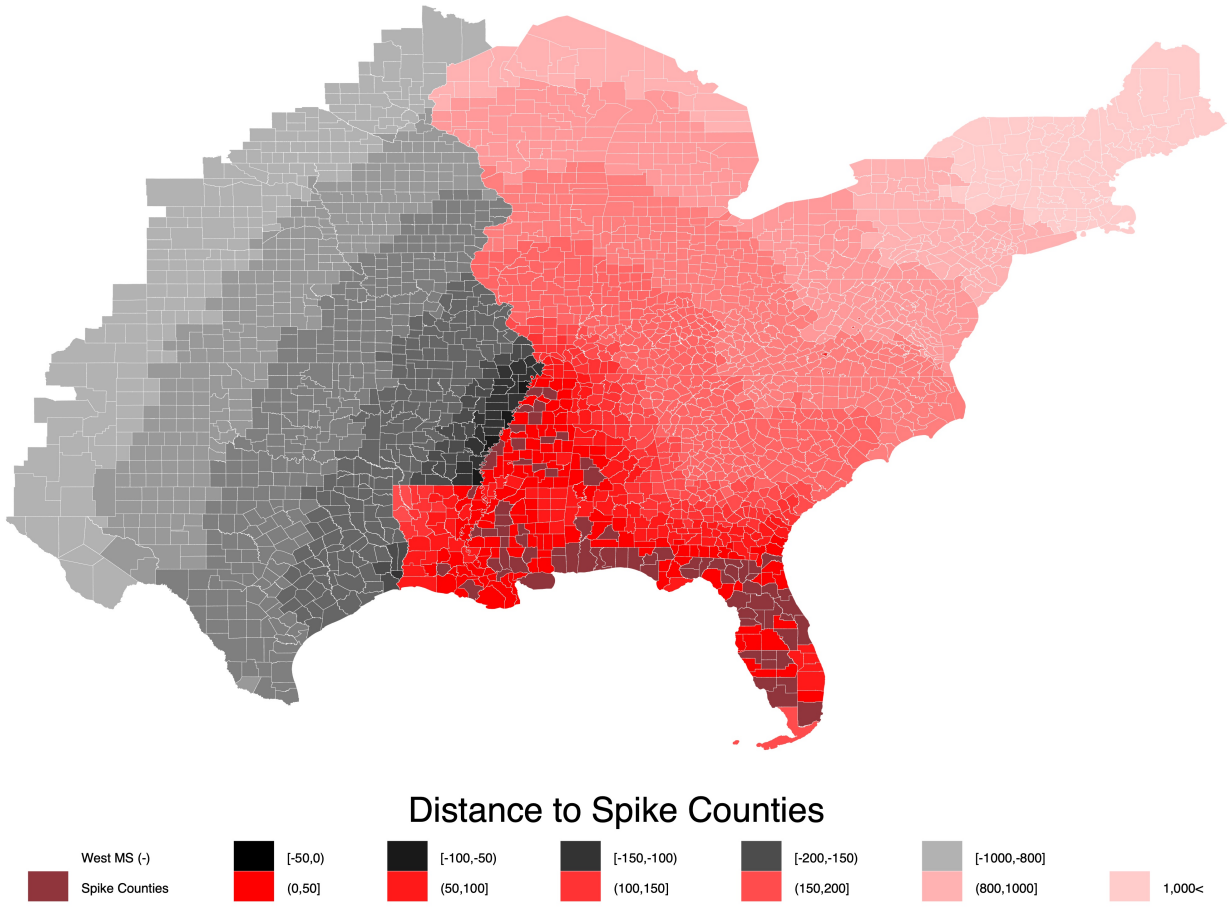


Figure 15: Mortality Series - Do the expectation show in the unprocessed data?



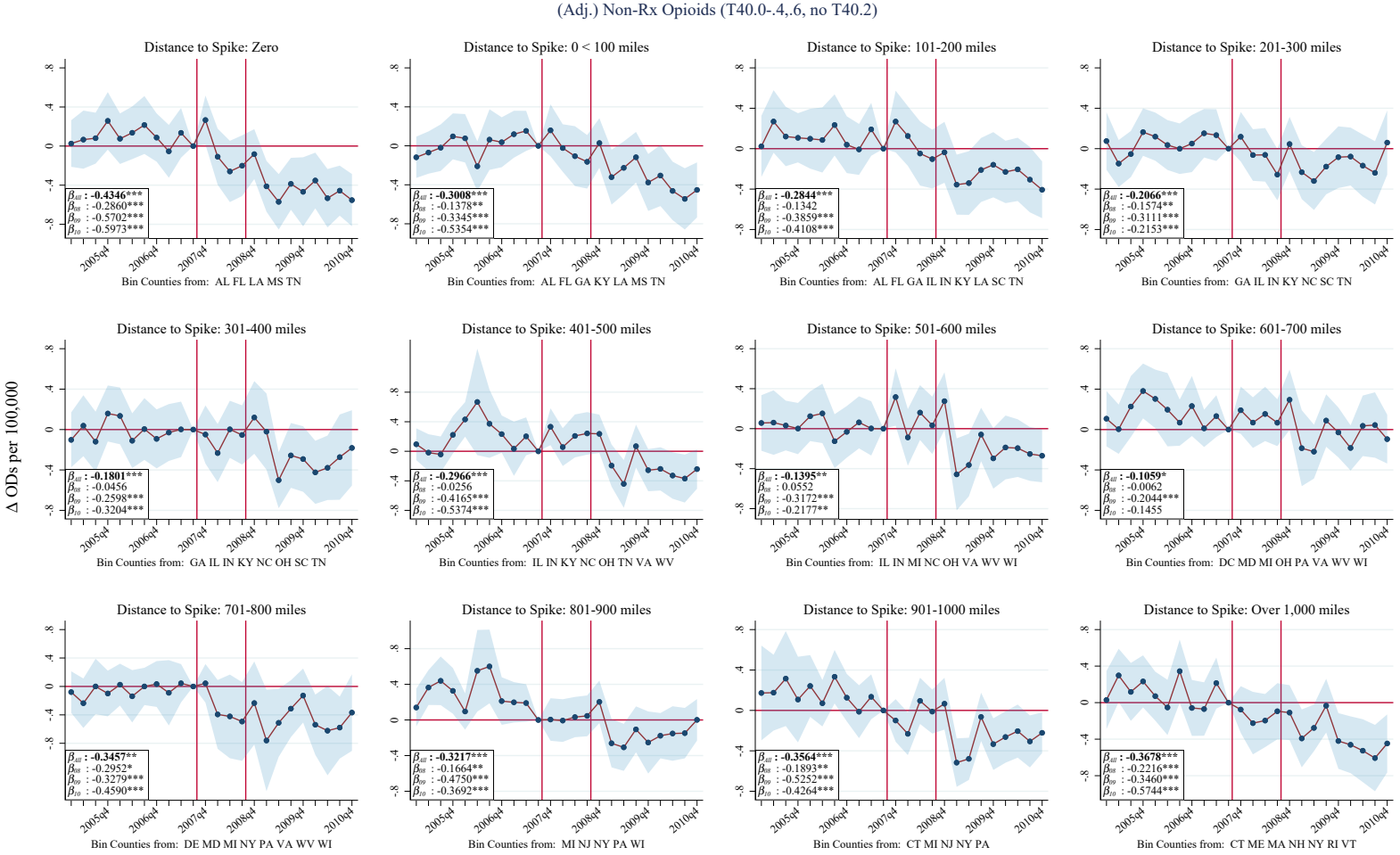
Notes: Opioid mortality series across distance bins for Non prescription opioids in Panel A (including all the MCD classifications in T40.0 to T40.6 without T40.2-Naturally occurring and semi-synthetic opioids and T40.5-Cocaine) and for Prescriptions opioids in Panel B (T40.2-Naturally occurring and semi-synthetic opioids, including oxycodone and hydrocodone). The blue lines portray the series for East-Mississippi river counties plus Louisiana within the specific distance to spike bin. The gray line on the other hand always presents the series for all the counties west of the Mississippi within 1,000 to a spike county which is the group of control counties. The dash lines represent the linear fit for the pre-diversion period.

Figure 16: Treatment and Control



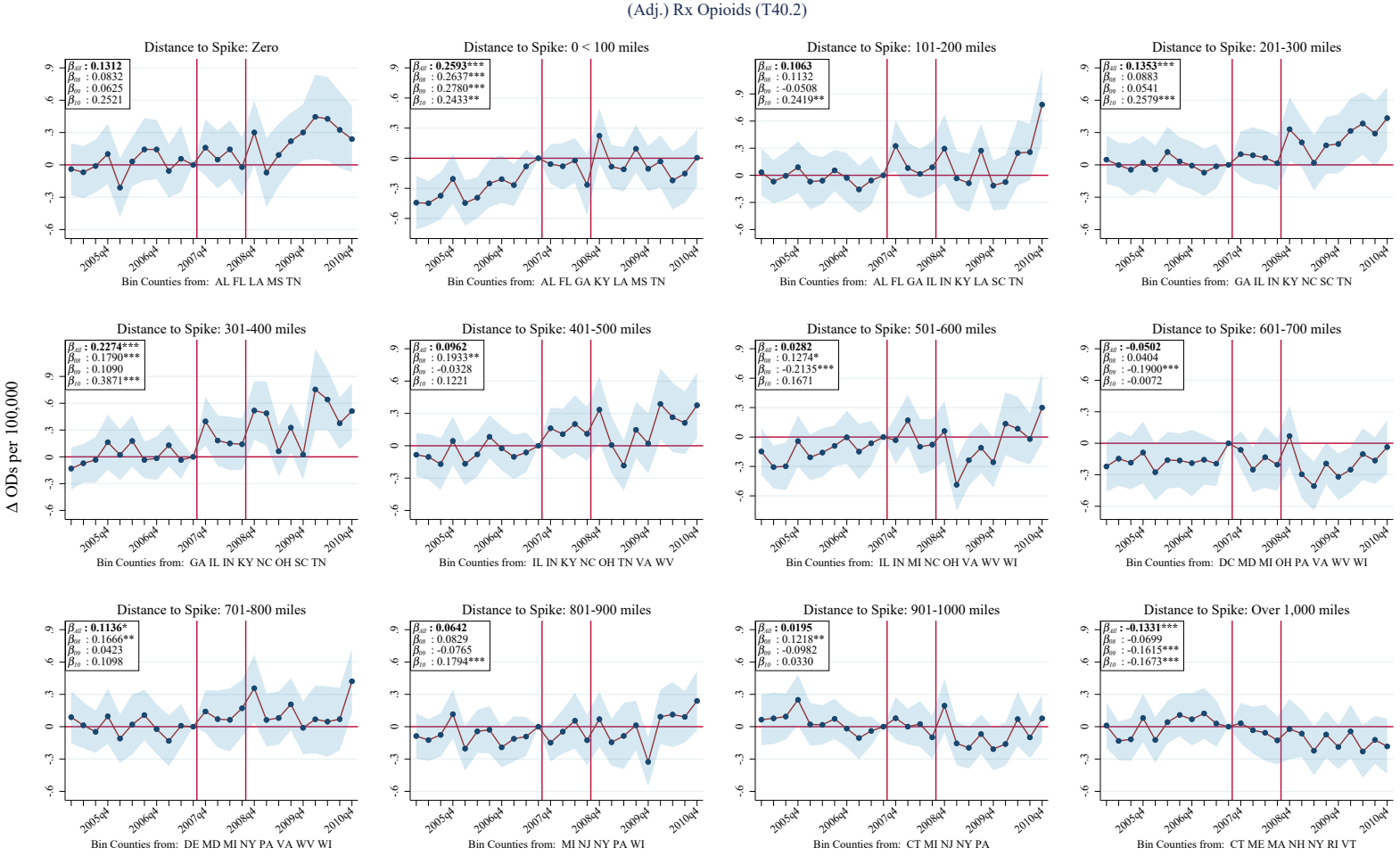
Notes: Numbers in the legends in driving miles to spike counties. We obtain the driving distance to spike counties using Google Distance Matrix API, queried in Jan 2023. There are restrictions in the use of the information source of about 40,000 queries per month. Thus, to obtain the driving distance, we fist calculate the geodetic distance for all additional counties to the identified spike ones for the entire U.S. using population centroids from the Census Bureau. We select the closest 20 on the basis of the geodetic distance for the continental U.S. counties and on these subset we obtain driving distance and time. The graphs shows the distance to the nearest spike county.

Figure 17: Event Study Non-prescription (Non-Rx) Opioid Mortality (Adjusted)



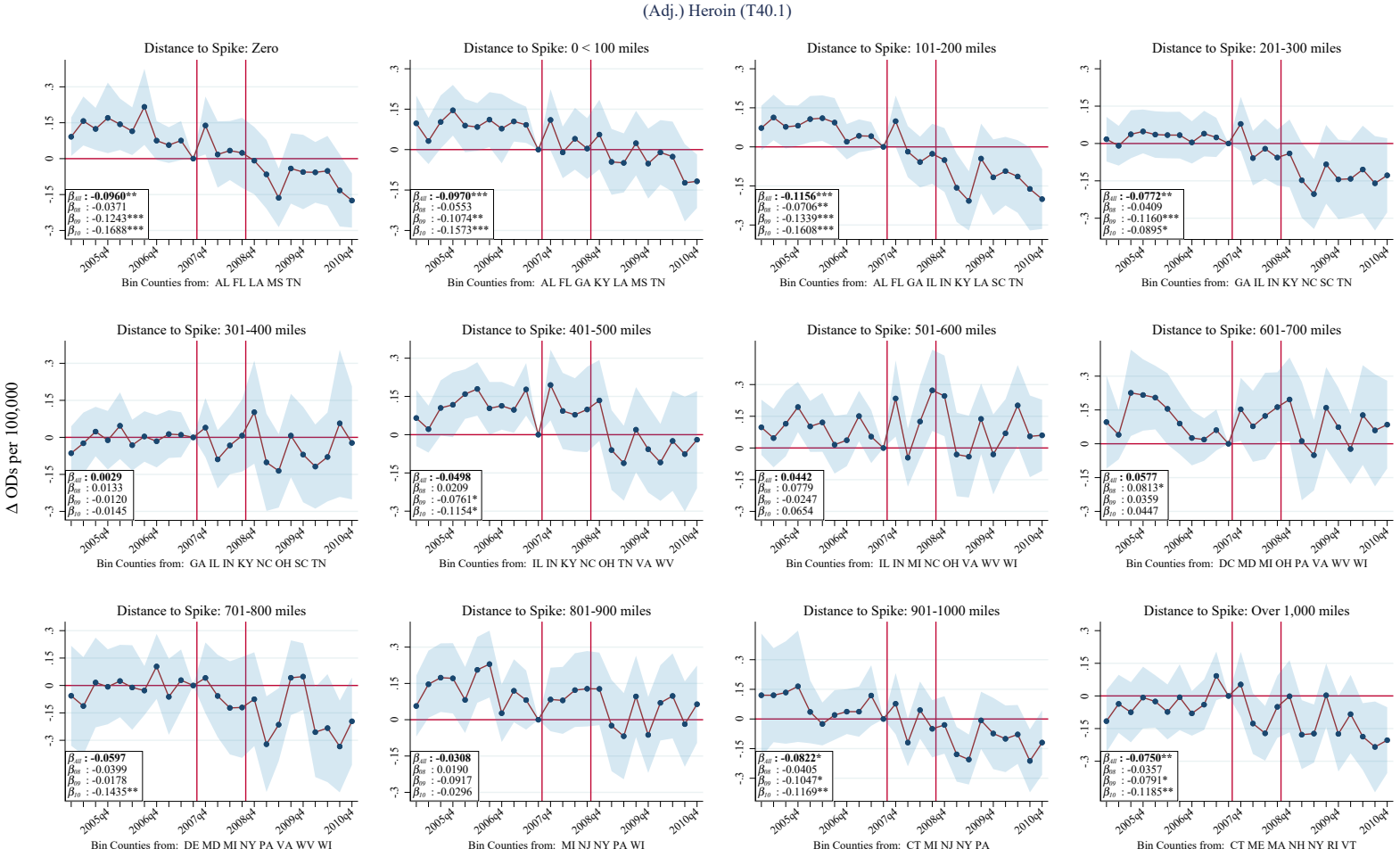
Notes: Each panel presents the set of parameter estimates for $\beta_{d,t}$ from Equation 3 and their 95% confidence intervals for the individual regression on heroin only related mortality. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the period-specific observations and the bin of distance-to-spike counties (d) in miles. The left vertical line indicates the third quarter of 2007, the last quarter prior to the treatment period and the second line in the the third quarter of 2008 is marks as a plausible transition period.

Figure 18: Event Study Natural and Semi-synthetic (Rx) inclusive Mortality



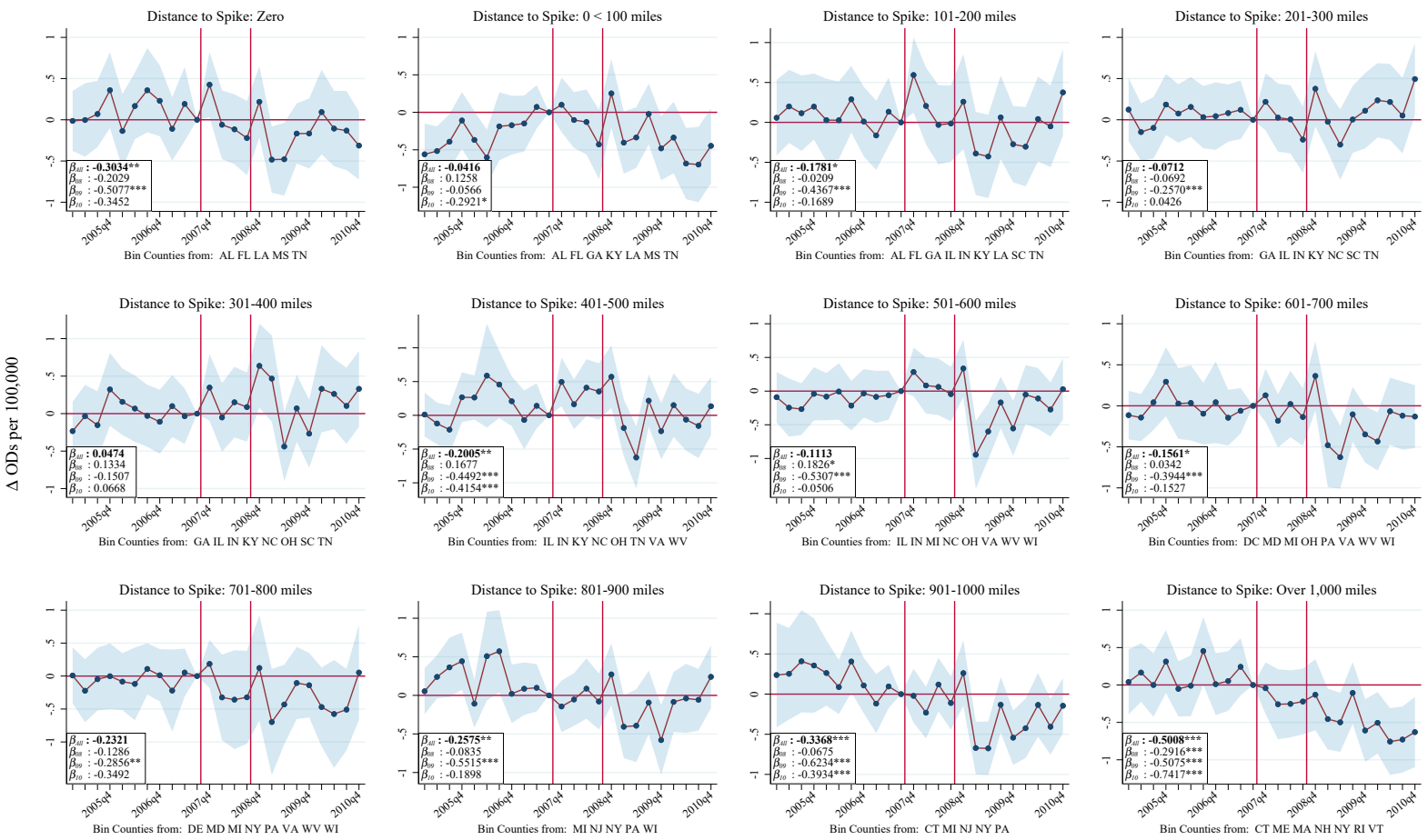
Notes: Each panel presents the set of parameter estimates for $\beta_{d,t}$ from Equation 3 and their 95% confidence intervals for the individual regression on heroin inclusive related mortality. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the period-specific observations and the bin of distance-to-spike counties (d) in miles. The left vertical line indicates the third quarter of 2007, the last quarter prior to the treatment period and the second line in the the third quarter of 2008 is marks as a plausible transition period.

Figure 19: Event Study - Heroin inclusive Mortality (Adjusted)



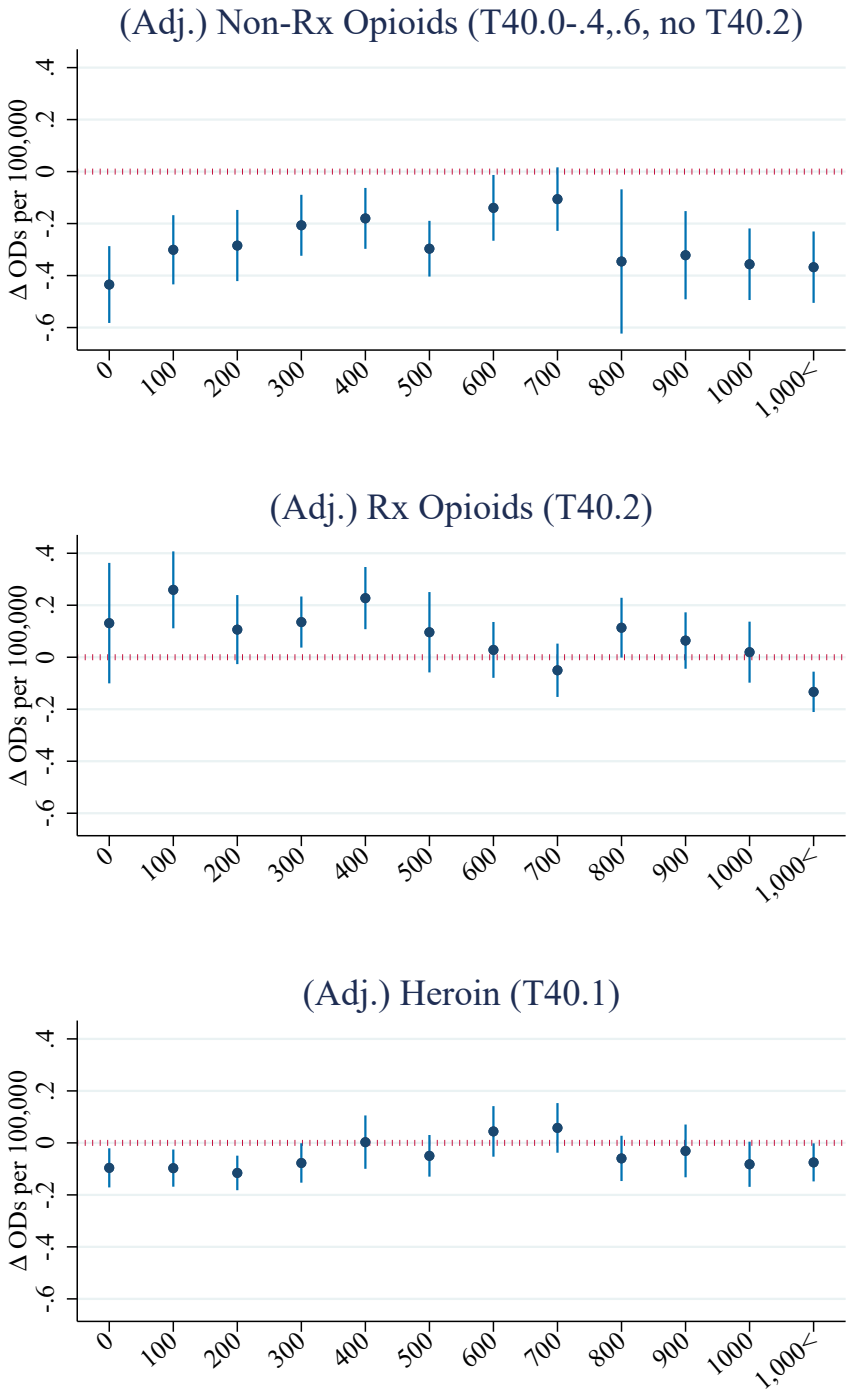
Notes: Each panel presents the set of parameter estimates for $\beta_{d,t}$ from Equation 3 and their 95% confidence intervals for the individual regression on heroin inclusive related mortality. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the period-specific observations and the bin of distance-to-spike counties (d) in miles. The left vertical line indicates the third quarter of 2007, the last quarter prior to the treatment period and the second line in the the third quarter of 2008 is marks as a plausible transition period.

Figure 20: Event Study Any Opioid Mortality



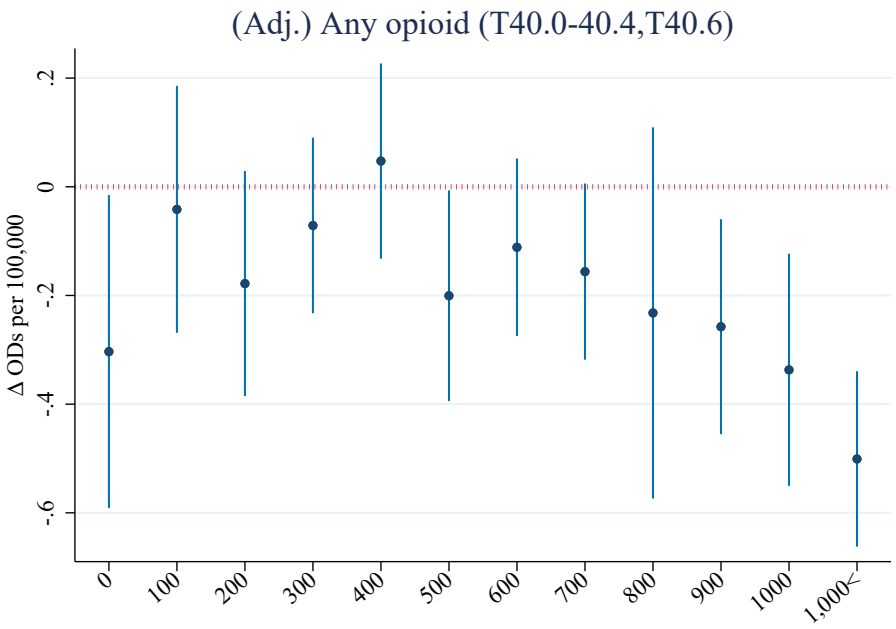
Notes: Each panel presents the set of parameter estimates for $\beta_{d,t}$ from Equation 3 and their 95% confidence intervals for the individual regression on heroin inclusive related mortality. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the period-specific observations and the bin of distance-to-spike counties (d) in miles. The left vertical line indicates the third quarter of 2007, the last quarter prior to the treatment period and the second line in the the third quarter of 2008 is marks as a plausible transition period.

Figure 21: DiD Distance-to-Spike and Opioid Mortality



Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the treated bins of distance-to-spike counties (d) in miles, and the post-treatment period.

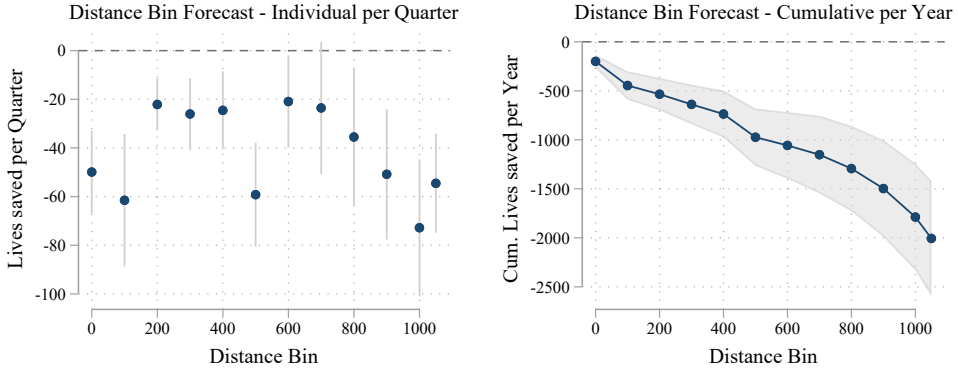
Figure 22: DiD Distance-to-Spike and Mortality Across Any Opioid



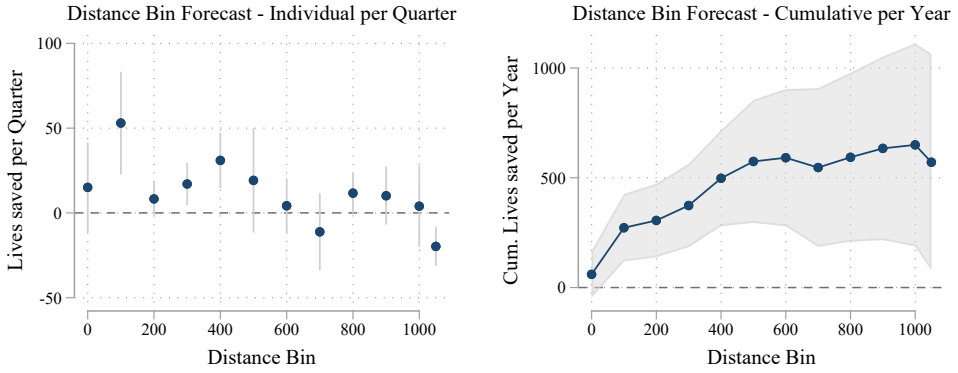
Notes: The graph presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the treated bins of distance-to-spike counties (d) in miles, and the post-treatment period.

Figure 23: Diversion in lives saved and sacrificed

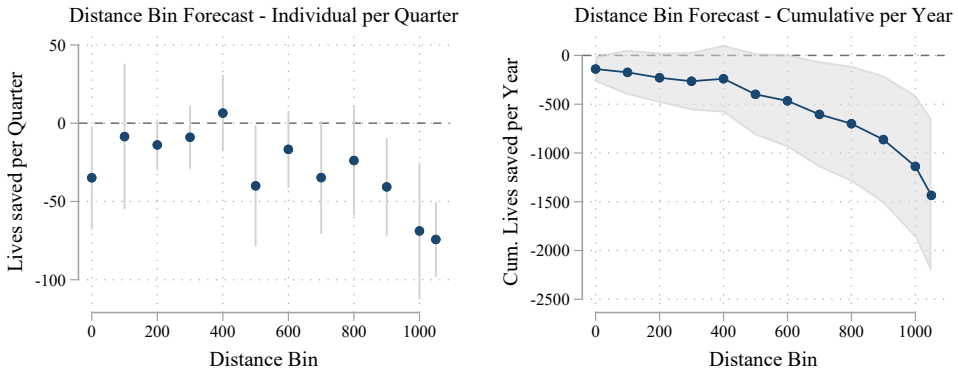
(Adj.) Non-Rx Opioids (T40.0-.4,.6, no T40.2)



(Adj.) Rx Opioids (oxy/hydro) (T40.2)

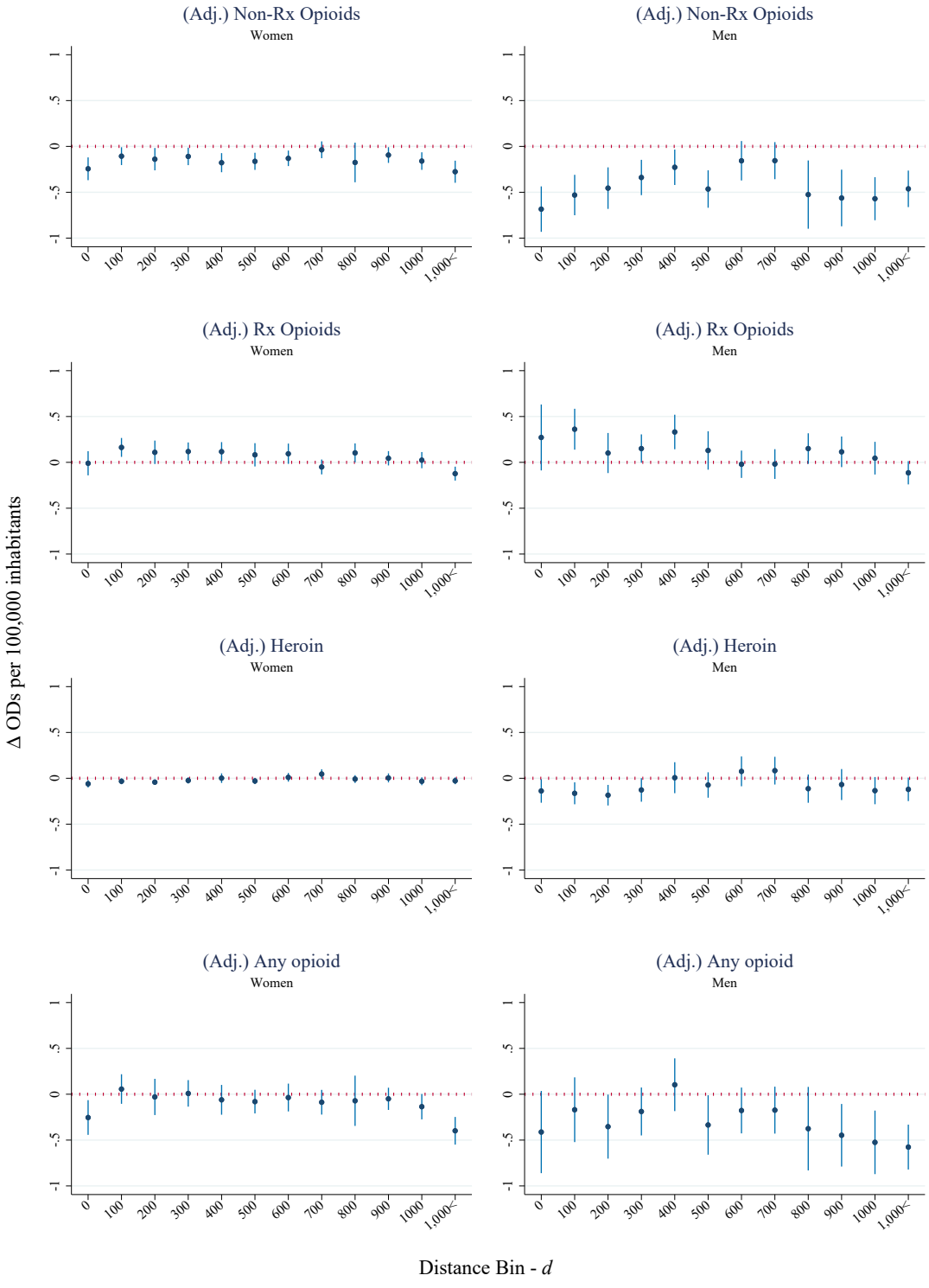


(Adj.) Any Opioid (T40.0-40.4-T40.6)



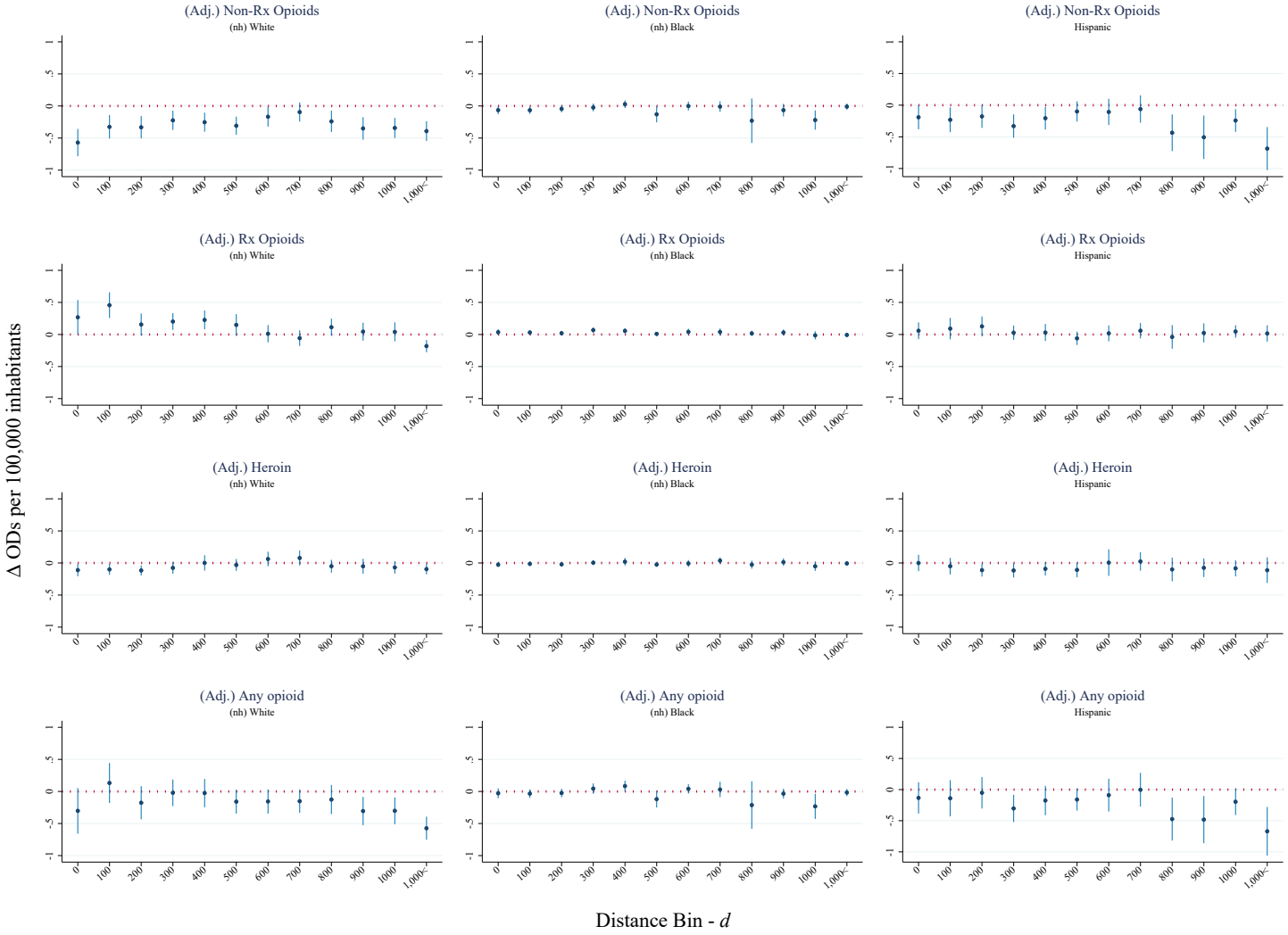
Notes: We perform Back-of-the-Envelope calculations in the following way: The Quarterly benefit/cost in lives of the diversion is estimated as Population (in hundred thousands) times β_d from Equation 2 using quarterly data. To estimate the annual cumulative effect we add over all prior bins and multiply by four, the number of quarters.

Figure 24: Heterogeneity across Genders of Diversion Effects



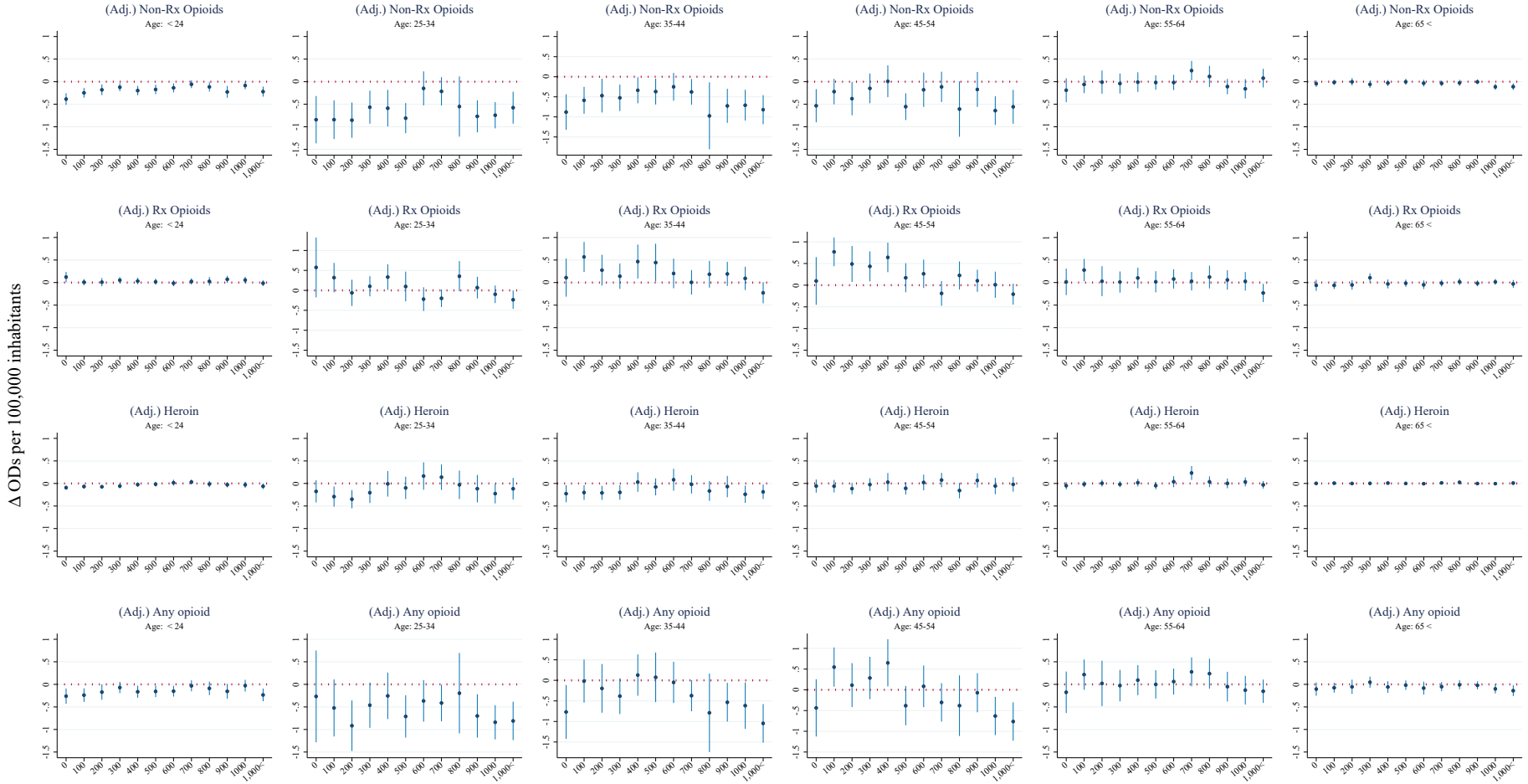
Notes: Estimates of β_d from Equation 2, with their respective 95% confidence interval, for regressions run over sub-populations within counties, women (left) and men (right). Each row of the figure presents a different classification of opioid mortality.

Figure 25: Heterogeneity across Races/Ethnicities of Diversion Effects



Notes: Estimates of β_d from Equation 2, with their respective 95% confidence interval, for regressions run over sub-populations within counties, from left to right: Non-Hispanic White, Non-Hispanic Black and Hispanic. Other Race/Ethnicity results have been omitted. Each row of the figure presents a different classification of opioid mortality.

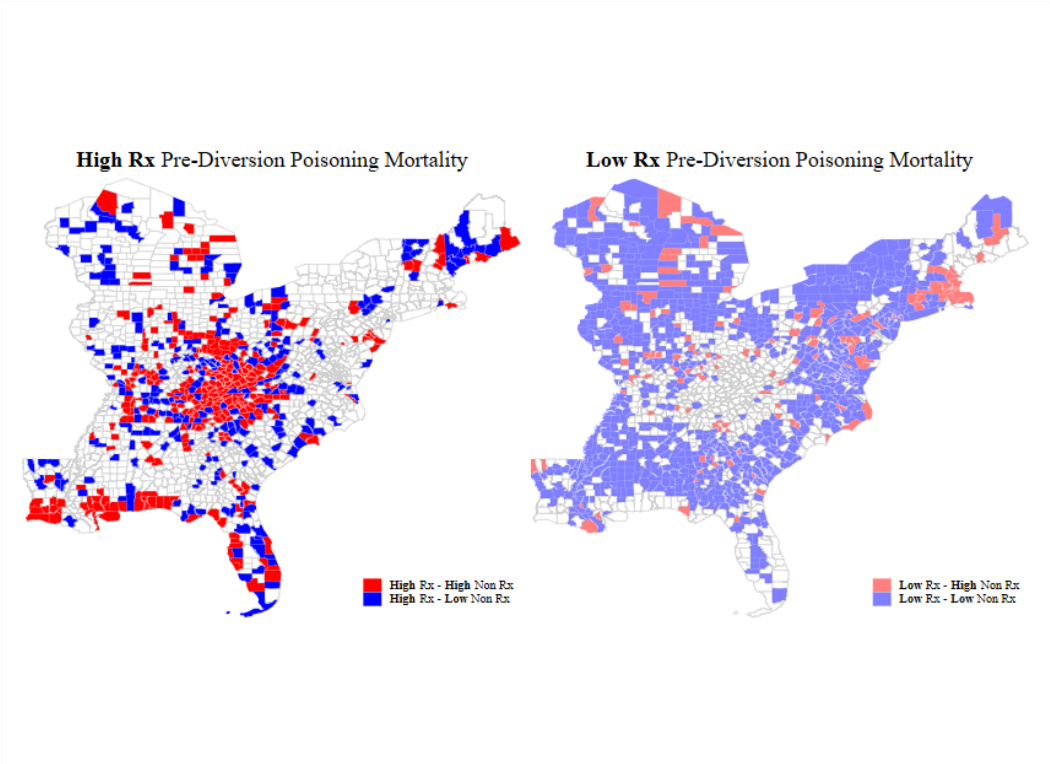
Figure 26: Heterogeneity across Age Groups of Diversion Effects



Notes: Estimates of β_d from Equation 2, with their respective 95% confidence interval, for regressions run over sub-populations within counties, for different age groups, from left to right: Under 24 years of age, from 25 to 34, from 35 to 44, from 45 to 54, from 55 to 65, and over 65. Each row of the figure presents a different classification of opioid mortality.

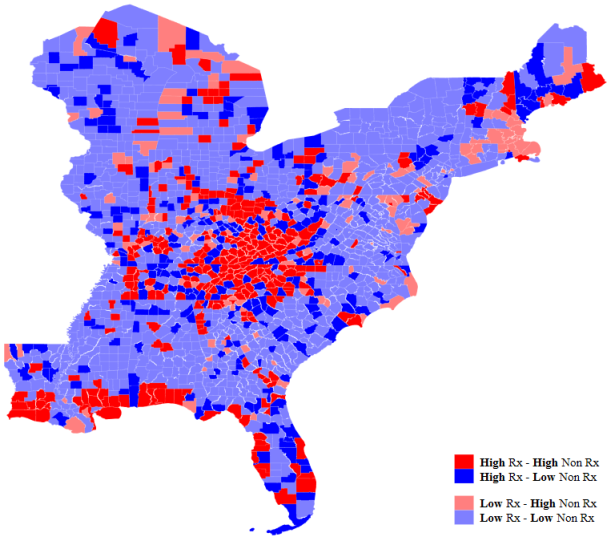
Figure 27: Comparing counties by their pre-diversion prevalence of different opioid mortality

Panel A - Two Separate comparisons



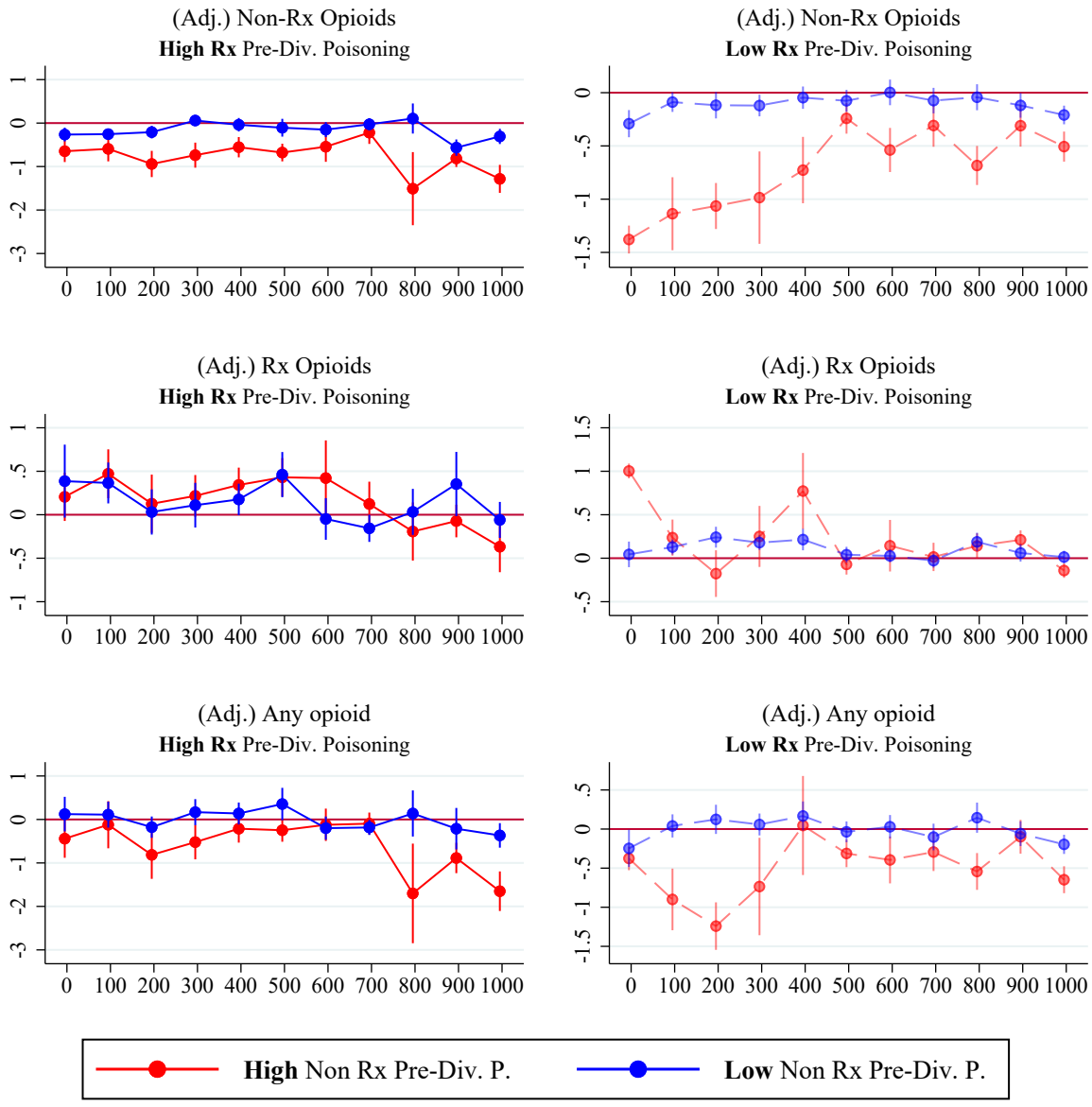
Panel B - All counties classified

Counties by Pre-Diversion Opioid Mortality
High: at the Top 30% of the Poisoning Dist. - Low: Other counties



Notes: Panel A presents the maps on the lines of the comparisons we want to make. We want to compare the diversion effect across counties with different levels of pre-diversion Non-Rx mortality (different levels of DTO driven opioid mortality), conditional on their pre-diversion level of Rx mortality (fixing the level of the pharma-industry driven opioid epidemic). The left panel presents counties with *Low and High Non-Rx* pre-diversion mortality prevalence conditional on *High Rx* pre-diversion prevalence. The right map showcases the same division across Non-Rx pre-diverion mortality conditional on *Low Rx* pre-diversion prevalence. Panel B consolidates the two figures with solid colors for *High Rx* pre-diversion mortality prevalence and tenous colors for *Low Rx*.

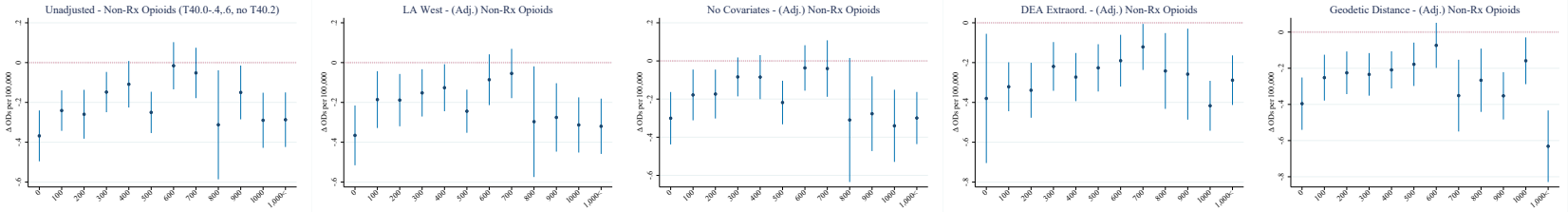
Figure 28: Comparing counties by their pre-diversion exposure to different opioid mortality



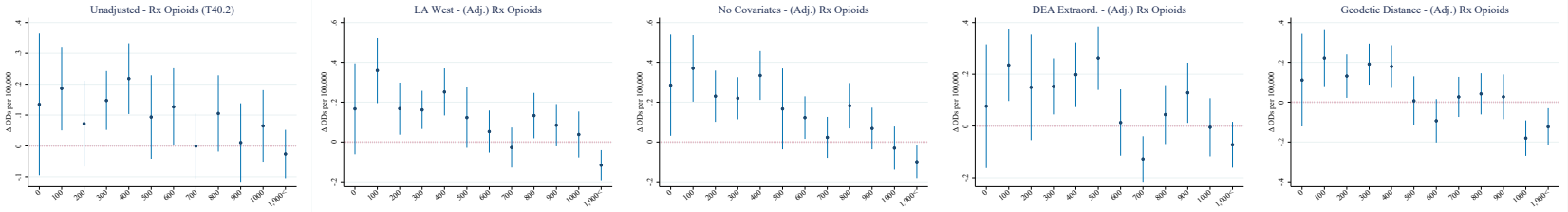
Notes: The figure presents graphically the marginal effects from the diversion on opioid mortality conditioning on pre-diversion Rx and Non-Rx opioid mortality of Table 9. Each graph always compares counties series across their pre-diversion level of Non-Rx mortality prevalence with red for *High* and navy blue for *Low*, the left column graphs show the comparisons conditional on a *High Rx* pre-diversion mortality and the right column for *Low*.

Figure 29: Robustness and Additional Exercises

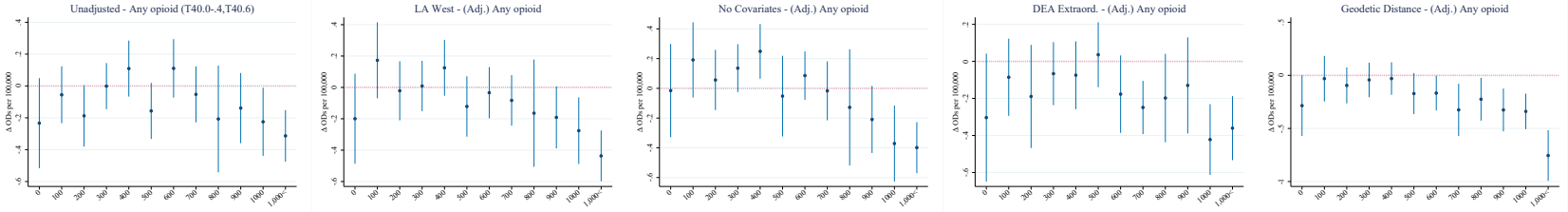
Panel A - Non-Rx Opioid Mortality (T40.0-.4,.6, no T40.2)



Panel B - Rx Opioid Mortality (T40.2)



Panel C - Any Opioid Mortality (T40.0-.4,.6)



Notes: The figure presents results of β_d from Equation 2, with their corresponding 95% confidence intervals, for Non-Rx Opioid Mortality (Panel A), Rx Opioid Mortality (Panel B) and Any Opioid Mortality (Panel C) of the additional exercises we advanced, from left to right: 1) Un-adjusted mortality rates, 2) Considering (non-spike) Louisiana as part of the control, 3) Not considering any covariates different from treatment, 4) Identify spike counties through the DEA Extraordinary Method and 6) Use Geodetic Distances instead of travel distance.

8 Tables

Table 1: Imputed excess doses, MME, and pharmacy invoice costs from spike (for 2x counties)

	Imputed Excess Doses (Millions)	Total Excess MME (Millions)	Wholesale Value Excess MME (Millions)
Alabama	15.71	368.09	$12.51
Florida	102.43	2,400.34	$81.61
Louisiana	11.78	275.96	$9.38
Mississippi	12.28	287.79	$9.78
Tennessee	4.86	113.87	$3.87
All counties with excess	147.05	3,446.04	$117.17

Column 1 reflects imputed excess shipments in millions of doses (assuming 23.4 MME per dose average) for all drugs in transactional ARCOS except OUD formulations of buprenorphine and methadone. Column 2 reflects imputed excess shipments in terms of total MMEs. Column 3 values those excess MME shipments at the average undiscounted invoice price for pharmacies (WAC) per aggregate MME of $0.034 taken from FDA (2018).

Table 2: Treatment and Control - Number of counties in different distance bins

No. Counties in Band - Driving Distance			
Distance (mls)	**Treatment**	**Control**	**Total**
0 - Spike	**78**		**78**
100	245	25	270
200	159	59	218
300	169	89	258
400	179	111	290
500	178	137	315
600	179	132	311
700	158	117	275
800	112	128	240
900	78	90	168
1000	46	70	116
Over 1,000	89	NA	89
No. counties	**1,670**	**958**	**2,628**

Note: Driving distance bins to the closest spike county in miles from Google Distance Matrix API. We obtain the driving distance to spike counties using Google Distance Matrix API, queried in Jan 2023. There are restrictions in the use of the information source of about 40,000 queries per month. Thus, to obtain the driving distance, we fist calculate the geodetic distance for all additional counties to the identified spike ones for the entire U.S. using population centroids from the Census Bureau. We select the closest 20 on the basis of the geodetic distance for the continental U.S. counties and on these subset we obtain driving distance and time. The grouping in each bins uses the distance to the nearest spike county.

Table 3: Pre-Diversion Opioid Mortality rates in bins of treated Distance-to-Spike (Quarterly) Counties

Avg. Quarterly Deaths per 100,000 inh. (2007)						
Dist. (mls)	Heroin	Nat./Semi.(Rx)	Synth.	Methadone	Non-Rx Op.	Any Opioid
0	0.15	1.03	0.30	0.92	1.22	2.24
100	0.19	1.22	0.30	0.94	1.37	2.60
200	0.06	0.86	0.30	0.65	1.00	1.86
300	0.09	0.71	0.32	0.59	0.99	1.70
400	0.17	1.14	0.37	0.88	1.31	2.46
500	0.18	0.83	0.32	0.74	1.50	2.33
600	0.30	0.96	0.33	0.67	1.21	2.18
700	0.33	0.79	0.28	0.52	1.05	1.85
800	0.42	0.76	0.31	0.90	1.81	2.58
900	0.32	0.68	0.28	0.58	1.28	1.96
1000	0.38	0.56	0.14	0.43	0.98	1.54
Over 1,000	0.29	0.71	0.27	0.60	1.58	2.29
Total	**0.25**	**0.85**	**0.29**	**0.69**	**1.27**	**2.12**

Note: Population weighted adjusted mortality means. We adjust quarterly mortality rates following Ruhm (2018). For the estimation we consider only those counties considered treated, in Louisiana and east of the Mississippi. Mortality counts use classification inclusive substances, meaning that from a poli-substance death, we include in our count of a specific substance if the death includes such substance. In part of the analysis ahead, we isolate specific opioids when they are the sole substance included in a particular poisoning.

Table 4: DiD Distance-to-Spike and Opioid Mortality

	(1) Non Rx Opioids T40.0-.1,.3-.4,.6	(2) Rx Opioids T40.2	(3) Heroin T40.1	(4) Any Opioid T40.0-4,.6
0 miles	-0.435***	0.131	-0.0960**	-0.303**
	(0.0753)	(0.118)	(0.0383)	(0.147)
100	-0.301***	0.259***	-0.0970***	-0.0416
	(0.0679)	(0.0754)	(0.0364)	(0.116)
200	-0.284***	0.106	-0.116***	-0.178*
	(0.0698)	(0.0677)	(0.0339)	(0.106)
300	-0.207***	0.135***	-0.0772**	-0.0712
	(0.0598)	(0.0501)	(0.0387)	(0.0824)
400	-0.180***	0.227***	0.00293	0.0474
	(0.0598)	(0.0610)	(0.0524)	(0.0916)
500	-0.297***	0.0962	-0.0498	-0.200**
	(0.0547)	(0.0788)	(0.0408)	(0.0989)
600	-0.140**	0.0282	0.0442	-0.111
	(0.0645)	(0.0548)	(0.0496)	(0.0833)
700	-0.106*	-0.0502	0.0577	-0.156*
	(0.0623)	(0.0523)	(0.0487)	(0.0826)
800	-0.346**	0.114*	-0.0597	-0.232
	(0.141)	(0.0587)	(0.0444)	(0.174)
900	-0.322***	0.0642	-0.0308	-0.257**
	(0.0865)	(0.0554)	(0.0517)	(0.101)
1000	-0.356***	0.0195	-0.0822*	-0.337***
	(0.0702)	(0.0598)	(0.0443)	(0.109)
1,000<	-0.368***	-0.133***	-0.0750**	-0.501***
	(0.0700)	(0.0396)	(0.0374)	(0.0823)
R^2	0.331	0.364	0.417	0.405
N. Clusters	2,628	2,628	2,628	2,628
N	63,072	63,072	63,072	63,072
Baseline	1.268	0.852	0.250	2.120

Note: Estimates for regression coefficients of the bin specific distance-to-spike-counties treatment on adjusted mortality rates per 100,000 inhabitants from Equation 2. Standard errors clustered at the county level in parentheses. Each row reports the distance from counties in each bin, respectively, zero are the spike counties, 100 reports the coefficient for counties under 100 miles to the spike counties' population centroids. Statistical significance reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$.

Table 5: Estimated changes in mortality after the diversion

	Non-Rx Opioid Mortality				**Rx Opioid Mortality**				**Any Opioid Mortality**			
Distance bin (mls) (D)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cum. (A)	Deaths 07 Cum. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cum. (A)	Deaths 07 Cum. (B)	(A) / (B)
0	-49.90***	-199.60***	560	-35.7%	15.07	60.26	471	12.8%	-34.83**	-139.34**	1,031	-13.5%
100	-61.53***	-445.71***	1,683	-26.5%	53.03***	272.37***	1,473	18.5%	-8.50	-173.34	3,157	-5.5%
200	-22.14***	-534.29***	1,995	-26.8%	8.28	305.48***	1,741	17.5%	-13.87*	-228.81*	3,736	-6.1%
300	-26.04***	-638.44***	2,494	-25.6%	17.06***	373.71***	2,101	17.8%	-8.98	-264.73*	4,595	-5.8%
400	-24.53***	-736.58***	3,209	-23.0%	30.99***	497.66***	2,725	18.3%	6.45	-238.92	5,934	-4.0%
500	-59.19***	-973.34***	4,406	-22.1%	19.19	574.42***	3,385	17.0%	-40.00**	-398.92*	7,791	-5.1%
600	-20.92**	-1,057.00***	5,133	-20.6%	4.23	591.34***	3,963	14.9%	-16.69	-465.67*	9,096	-5.1%
700	-23.56*	-1,151.24***	6,070	-19.0%	-11.16	546.70***	4,668	11.7%	-34.72*	-604.54**	10,738	-5.6%
800	-35.49**	-1,293.20***	6,815	-19.0%	11.66*	593.34***	4,981	11.9%	-23.83	-699.86**	11,796	-5.9%
900	-50.82***	-1,496.47***	7,622	-19.6%	10.14	633.91***	5,412	11.7%	-40.68**	-862.56**	13,034	-6.6%
1,000	-72.79***	-1,787.65***	8,422	-21.2%	3.99	649.85***	5,867	11.1%	-68.81***	-1,137.80***	14,289	-8.0%
1,000<	-54.52***	-2,005.74***	9,359	-21.4%	-19.73***	570.92**	6,285	9.1%	-74.25***	-1,434.82***	15,645	-9.2%

Note: We perform Back-of-the-Envelope calculations in the following way: The Quarterly benefit/cost in lives of the diversion is estimated as Population (in hundred thousands) times β_d from Equation 2 which is estimated on quarterly data. To estimate the annual cumulative effect we multiply by four (quarters) and add over all prior bins. Statistical significance reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$, for t-tests on the linear combinations, which can be at the individual quarter per distance bin or annual cumulative across distance bins, up to the indicated distance.

Table 6: Estimated changes in mortality after the diversion, by Gender

	Non-Rx Opioid Mortality				Rx Opioid Mortality				Any Opioid Mortality			
Distance bin (mls) (D)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)
Panel A - Women												
0	-13.97***	-55.87***	183.5	-30.4%	-0.56	-2.26	204.9	-1.1%	-14.53***	-58.13***	388.4	-15.0%
100	-10.90**	-99.48***	555.4	-17.9%	16.72***	64.61**	587.9	11.0%	5.81	-34.87	1,143.3	-3.1%
200	-5.34**	-120.82***	667.1	-18.1%	4.21*	81.44**	705.4	11.5%	-1.13	-39.39	1,372.5	-2.9%
300	-6.81**	-148.06***	847.8	-17.5%	7.38**	110.97***	870.2	12.8%	0.57	-37.09	1,718.0	-2.2%
400	-12.01***	-196.08***	1,112.4	-17.6%	7.89**	142.53***	1,149.7	12.4%	-4.12	-53.56	2,262.1	-2.4%
500	-16.26***	-261.11***	1,496.5	-17.4%	8.23	175.44***	1,396.9	12.6%	-8.03	-85.67	2,893.4	-3.0%
600	-9.80***	-300.32***	1,735.1	-17.3%	7.10*	203.82***	1,627.6	12.5%	-2.71	-96.50	3,362.7	-2.9%
700	-4.18	-317.02***	2,021.8	-15.7%	-5.69	181.04**	1,918.3	9.4%	-9.87	-135.97	3,940.1	-3.5%
800	-9.04	-353.17***	2,262.8	-15.6%	5.36**	202.47**	2,034.1	10.0%	-3.68	-150.70	4,297.0	-3.5%
900	-7.55**	-383.37***	2,495.7	-15.4%	3.54	216.64**	2,196.6	9.9%	-4.01	-166.73	4,692.3	-3.6%
1,000	-16.65***	-449.96***	2,721.8	-16.5%	2.51	226.68**	2,341.8	9.7%	-14.14*	-223.28	5,063.6	-4.4%
1,000<	-20.74***	-532.93***	3,009.7	-17.7%	-9.22***	189.79*	2,526.0	7.5%	-29.97***	-343.14**	5,535.6	-6.2%
Panel B - Men												
	Non-Rx Opioid Mortality				Rx Opioid Mortality				Any Opioid Mortality			
0	-37.51***	-150.04***	376.3	-39.9%	14.90	59.58	266.4	22.4%	-22.61*	-90.46*	642.7	-14.1%
100	-51.70***	-356.82***	1,128.1	-31.6%	35.24***	200.53***	885.2	22.7%	-16.46	-156.29*	1,370.6	-11.4%
200	-16.84***	-424.17***	1,327.9	-31.9%	3.76	215.59***	1,035.8	20.8%	-13.07**	-208.58**	350.4	-59.5%
300	-20.23***	-505.10***	1,646.4	-30.7%	9.00*	251.58***	1,231.1	20.4%	-11.24	-253.52**	513.8	-49.3%
400	-14.70**	-563.89***	2,096.8	-26.9%	21.39***	337.15***	1,575.2	21.4%	6.70	-226.74*	794.5	-28.5%
500	-44.51***	-741.93***	2,909.5	-25.5%	12.41	386.81***	1,988.6	19.5%	-32.10**	-355.12**	1,226.1	-29.0%
600	-11.39	-787.51***	3,398.0	-23.2%	-1.51	380.77***	2,335.3	16.3%	-12.90	-406.74**	835.2	-48.7%
700	-16.71	-854.37***	4,047.9	-21.1%	-2.00	372.78***	2,750.2	13.6%	-18.71	-481.59**	1,064.8	-45.2%
800	-26.09***	-958.75***	4,552.2	-21.1%	7.46*	402.64***	2,947.0	13.7%	-18.63	-556.10**	701.1	-79.3%
900	-42.77***	-1,129.83***	5,125.8	-22.0%	8.74	437.61***	3,215.4	13.6%	-34.03**	-692.22**	842.0	-82.2%
1,000	-55.35***	-1,351.25***	5,700.4	-23.7%	4.43	455.34**	3,524.7	12.9%	-50.92***	-895.90***	883.9	-101.4%
1,000<	-33.15***	-1,483.85***	6,349.5	-23.4%	-8.14*	422.80**	3,759.4	11.2%	-41.29***	-1,061.06***	883.8	-120.1%

Note: The Table presents Back-of-the-Envelope calculations for gender subpopulations. Statistical significance of linear combinations reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$, for t-tests on the linear combinations, which can be at the individual quarter per distance bin or annual cumulative across distance bins, up to the indicated distance.

Table 7: Estimated changes in mortality after the diversion, by Race-Ethnicity Groups

	Non-Rx Opioid Mortality				Rx Opioid Mortality				Any Opioid Mortality			
Distance bin (mls) (D)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul.	(A) / (B)
Panel A - Non-Hispanic White												
0	-37.65***	-150.61***	499.7	-30.1%	17.73**	70.91**	423.0	16.8%	-19.92*	-79.70*	922.7	-8.6%
100	-40.24***	-311.57***	1,511.3	-20.6%	56.62***	297.38***	1,344.1	22.1%	16.38	-14.19	2,855.4	-0.5%
200	-17.70***	-382.37***	1,808.1	-21.1%	8.30*	330.58***	1,598.4	20.7%	-9.40	-51.79	3,406.5	-1.5%
300	-17.96***	-454.21***	2,274.4	-20.0%	16.28***	395.69***	1,933.5	20.5%	-1.68	-58.52	4,208.0	-1.4%
400	-26.00***	-558.20***	2,941.5	-19.0%	23.37***	489.16***	2,533.6	19.3%	-2.63	-69.04	5,475.1	-1.3%
500	-41.21***	-723.03***	3,930.6	-18.4%	19.95*	568.96***	3,169.1	18.0%	-21.26*	-154.07	7,099.7	-2.2%
600	-19.16**	-799.66***	4,570.9	-17.5%	1.36	574.40***	3,696.6	15.5%	-17.80	-225.26	8,267.4	-2.7%
700	-14.96	-859.50***	5,350.9	-16.1%	-9.06	538.15***	4,327.0	12.4%	-24.02	-321.35	9,677.9	-3.3%
800	-19.57***	-937.79***	5,937.8	-15.8%	9.29*	575.30***	4,601.1	12.5%	-10.28	-362.49	10,538.9	-3.4%
900	-39.92***	-1,097.46***	6,599.2	-16.6%	5.07	595.58***	4,982.1	12.0%	-34.85***	-501.88*	11,581.3	-4.3%
1,000	-37.83***	-1,248.76***	7,139.4	-17.5%	4.51	613.61***	5,347.3	11.5%	-33.32***	-635.15**	12,486.8	-5.1%
1,000<	-47.94***	-1,440.50***	7,971.1	-18.1%	-22.13***	525.08**	5,750.1	9.1%	-70.07***	-915.43***	13,721.1	-6.7%
Panel B - Non-Hispanic Black												
0	-2.74**	-10.96**	21.1	-51.9%	1.54	6.14	17.2	35.7%	-1.20	-4.81	38.3	-12.6%
100	-5.68**	-33.66**	85.7	-39.3%	2.72*	17.02**	54.1	31.4%	-2.96	-16.64	139.9	-11.9%
200	-1.54	-39.82**	99.0	-40.2%	0.70	19.84**	65.7	30.2%	-0.84	-19.98	164.7	-12.1%
300	-1.29	-44.98**	129.4	-34.8%	3.75***	34.85***	89.1	39.1%	2.46	-10.14	218.4	-4.6%
400	1.74	-38.00	168.7	-22.5%	3.44***	48.61***	104.4	46.6%	5.19**	10.61	273.1	3.9%
500	-10.74**	-80.97***	324.5	-25.0%	0.82	51.90***	122.8	42.2%	-9.92*	-29.07	447.3	-6.5%
600	-0.03	-81.09***	389.0	-20.8%	2.81*	63.12***	159.4	39.6%	2.78	-17.97	548.5	-3.3%
700	-0.92	-84.75**	517.2	-16.4%	3.94	78.90***	218.7	36.1%	3.03	-5.86	735.9	-0.8%
800	-10.84	-128.13**	663.7	-19.3%	0.81	82.15***	254.5	32.3%	-10.03	-45.98	918.2	-5.0%
900	-4.37	-145.62**	751.5	-19.4%	2.06	90.41***	284.2	31.8%	-2.31	-55.22	1,035.7	-5.3%
1,000	-15.60***	-208.01***	874.6	-23.8%	-0.94	86.64**	323.5	26.8%	-16.54**	-121.38	1,198.1	-10.1%
1,000<	-0.63	-210.52***	906.6	-23.2%	-0.46	84.81**	330.0	25.7%	-1.08	-125.71	1,236.6	-10.2%
Panel C - Hispanic												
0	-4.46**	-17.83**	34.4	-51.9%	1.36	5.44	30.5	17.8%	-3.10	-12.39	64.9	-19.1%
100	-4.48**	-35.77**	78.7	-45.5%	1.78	12.56	71.6	17.5%	-2.70	-23.20	150.3	-15.4%
200	-0.64*	-38.31**	80.1	-47.8%	0.45	14.38	72.9	19.7%	-0.18	-23.93	153.0	-15.6%
300	-2.53***	-48.41**	82.6	-58.6%	0.22	15.24	74.4	20.5%	-2.31***	-33.17	157.1	-21.1%
400	-1.24**	-53.37***	88.0	-60.6%	0.18	15.98	79.4	20.1%	-1.06	-37.39	167.5	-22.3%
500	-2.19	-62.14**	136.5	-45.5%	-1.32	10.69	84.8	12.6%	-3.51*	-51.45*	221.3	-23.3%
600	-0.90	-65.75**	154.6	-42.5%	0.15	11.31	95.5	11.8%	-0.75	-54.44	250.1	-21.8%
700	-0.75	-68.73**	175.7	-39.1%	0.72	14.18	108.7	13.0%	-0.03	-54.55	284.5	-19.2%
800	-1.56***	-74.95**	183.4	-40.9%	-0.14	13.63	110.4	12.3%	-1.69***	-61.33	293.7	-20.9%
900	-6.73***	-101.88***	233.2	-43.7%	0.33	14.93	128.6	11.6%	-6.41**	-86.95**	361.8	-24.0%
1,000	-9.72***	-140.76***	363.4	-38.7%	1.86	22.36	174.4	12.8%	-7.86*	-118.41**	537.8	-22.0%
1,000<	-6.79***	-167.91***	431.2	-38.9%	0.16	22.99	182.5	12.6%	-6.63***	-144.93**	613.8	-23.6%

Note: The Table presents Back-of-the-Envelope calculations for race and ethnicity subpopulations. Statistical significance of linear combinations reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$, for t-tests on the linear combinations, which can be at the individual quarter per distance bin or annual cumulative across distance bins, up to the indicated distance.

Table 8: Estimated changes in mortality after the diversion, by Age Groups

	Non-Rx Opioid Mortality				Rx Opioid Mortality				Any Opioid Mortality			
Distance bin (mls) (D)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul.	(A) / (B)
Panel A - Age Group Under 24												
0	-14.00***	-56.00***	83.6	-67.0%	4.50**	17.99**	43.4	41.5%	-9.50***	-38.02***	126.9	-29.9%
100	-16.44***	-121.76***	272.1	-44.8%	0.59	20.33	166.9	12.2%	-15.85***	-101.43***	438.9	-23.1%
200	-4.73***	-140.68***	321.5	-43.8%	0.25	21.31	201.8	10.6%	-4.49**	-119.37***	523.3	-22.8%
300	-5.21***	-161.51***	391.7	-41.2%	2.24	30.28	239.3	12.7%	-2.96	-131.22***	631.0	-20.8%
400	-8.90***	-197.12***	501.1	-39.3%	1.52	36.35	300.0	12.1%	-7.39**	-160.77***	801.0	-20.1%
500	-11.52***	-243.20***	679.6	-35.8%	1.14	40.92	364.9	11.2%	-10.38**	-202.28***	1044.4	-19.4%
600	-7.08***	-271.50***	799.5	-34.0%	-0.75	37.92	411.1	9.2%	-7.82**	-233.58***	1210.6	-19.3%
700	-4.19	-288.27***	925.4	-31.2%	1.84	45.28	483.0	9.4%	-2.35	-242.99***	1408.4	-17.3%
800	-3.84**	-303.64***	1014.7	-29.9%	0.93	48.98	517.6	9.5%	-2.92	-254.66***	1532.2	-16.6%
900	-11.68***	-350.38***	1144.1	-30.6%	3.74*	63.94	563.6	11.3%	-7.94*	-286.43***	1707.7	-16.8%
1,000	-5.57**	-372.67***	1214.8	-30.7%	3.64	78.51	603.6	13.0%	-1.93	-294.16***	1818.4	-16.2%
1,000<	-10.45***	-414.47***	1321.4	-31.4%	-0.66	75.88	637.0	11.9%	-11.11***	-338.59***	1958.4	-17.3%
Panel B - Age Group 25 to 34												
0	-11.42***	-45.67***	135.4	-33.7%	7.81	31.24	94.2	33.2%	-3.61	-14.43	229.7	-6.3%
100	-21.47***	-131.55***	425.5	-30.9%	8.15*	63.84**	318.6	20.0%	-13.32	-67.70	744.1	-9.1%
200	-8.56***	-165.79***	504.9	-32.8%	-0.63	61.32**	366.1	16.8%	-9.19***	-104.47**	871.0	-12.0%
300	-9.43***	-203.51***	633.6	-32.1%	1.72	68.20**	427.7	15.9%	-7.71*	-135.31**	1061.3	-12.7%
400	-10.19***	-244.26***	820.8	-29.8%	5.78**	91.33**	535.9	17.0%	-4.41	-152.93**	1356.7	-11.3%
500	-21.22***	-329.14***	1106.2	-29.8%	2.56	101.55**	673.2	15.1%	-18.66***	-227.58***	1779.4	-12.8%
600	-2.78	-340.26***	1265.7	-26.9%	-4.10	85.14*	790.3	10.8%	-6.88	-255.12***	2056.0	-12.4%
700	-5.99	-364.21***	1468.8	-24.8%	-5.55*	62.96	923.6	6.8%	-11.53**	-301.25***	2392.4	-12.6%
800	-6.48	-390.14***	1627.1	-24.0%	4.18*	79.70	979.3	8.1%	-2.30	-310.45***	2606.3	-11.9%
900	-14.28***	-447.27***	1827.8	-24.5%	1.29	84.85	1071.2	7.9%	-12.99***	-362.42***	2899.0	-12.5%
1,000	-20.44***	-529.03***	1998.9	-26.5%	-2.66	74.19	1163.2	6.4%	-23.10***	-454.84***	3162.1	-14.4%
1,000<	-10.01***	-569.06***	2216.0	-25.7%	-4.05**	57.99	1239.4	4.7%	-14.06***	-511.08***	3455.4	-14.8%
Panel C - Age Group 35 to 44												
0	-13.36***	-53.44***	147.4	-36.3%	1.67	6.69	127.6	5.2%	-11.69**	-46.75**	275.0	-17.0%
100	-16.28***	-118.56***	406.2	-29.2%	15.77***	69.79***	367.3	19.0%	-0.51	-48.77	773.4	-6.3%
200	-5.00**	-138.54***	485.1	-28.6%	2.92	81.48***	437.7	18.6%	-2.07	-57.06	922.7	-6.2%
300	-9.48***	-176.46***	614.8	-28.7%	2.56	91.71***	547.8	16.7%	-6.92*	-84.75	1162.6	-7.3%
400	-6.38**	-201.97***	791.9	-25.5%	8.80**	126.91***	720.9	17.6%	2.42	-75.06	1512.8	-5.0%
500	-10.35**	-243.38***	1121.3	-21.7%	12.44**	176.69***	910.5	19.4%	2.09	-66.69	2031.7	-3.3%
600	-5.20	-264.18***	1322.3	-20.0%	4.18	193.42***	1073.7	18.0%	-1.02	-70.75	2396.0	-3.0%
700	-11.95**	-311.99***	1550.7	-20.1%	0.16	194.05***	1233.4	15.7%	-11.80*	-117.94	2784.1	-4.2%
800	-14.07**	-368.26***	1768.4	-20.8%	2.66	204.69***	1317.7	15.5%	-11.41	-163.57	3086.1	-5.3%
900	-16.14***	-432.82***	1985.4	-21.8%	4.28	221.81***	1432.0	15.5%	-11.86**	-211.01*	3417.4	-6.2%
1,000	-21.33***	-518.12***	2206.4	-23.5%	2.81	233.07***	1550.0	15.0%	-18.51**	-285.05**	3756.4	-7.6%
1,000<	-17.57***	-588.42***	2472.8	-23.8%	-4.86*	213.61**	1652.3	12.9%	-22.44***	-374.80**	4125.1	-9.1%

Note: The Table presents Back-of-the-Envelope calculations for age group subpopulations. Statistical significance of linear combinations reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$, for t-tests on the linear combinations, which can be at the individual quarter per distance bin or annual cumulative across distance bins, up to the indicated distance.

Table 8: Estimated changes in mortality after the diversion, by Age Groups (cont.)

	Non-Rx Opioid Mortality				Rx Opioid Mortality				Any Opioid Mortality			
Distance bin (mls) (D)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul. (B)	(A) / (B)	Quarter Eff. per bin D	Annual Eff. Cumul. (A)	Deaths 07 Cumul.	(A) / (B)
Panel D - Age Group 45 to 54												
0	-8.47***	-33.90***	148.0	-22.9%	1.55	6.21	131.1	4.7%	-6.92	-27.68	279.1	-9.9%
100	-6.37	-59.38**	421.1	-14.1%	22.26***	95.24***	404.0	23.6%	15.89**	35.86	558.2	6.4%
200	-4.06**	-75.63***	499.1	-15.2%	5.28**	116.35***	484.2	24.0%	1.22	40.73	1104.2	3.7%
300	-2.62	-86.11**	624.1	-13.8%	7.70**	147.14***	587.1	25.1%	5.08	61.03	1262.4	4.8%
400	0.18	-85.39**	797.2	-10.7%	12.28***	196.25***	786.5	25.0%	12.46**	110.86*	1490.3	7.4%
500	-15.77***	-148.45***	1118.2	-13.3%	4.89	215.79***	989.1	21.8%	-10.88	67.34	1862.8	3.6%
600	-3.95	-164.26***	1306.0	-12.6%	5.84	239.14***	1176.8	20.3%	1.88	74.88	2386.4	3.1%
700	-3.88	-179.78**	1588.0	-11.3%	-6.40	213.55***	1429.2	14.9%	-10.28	33.77	2761.9	1.2%
800	-9.52*	-217.85***	1812.1	-12.0%	3.53	227.68***	1533.2	14.8%	-5.99	9.82	3296.3	0.3%
900	-4.12	-234.32***	2004.4	-11.7%	2.43	237.41***	1663.2	14.3%	-1.68	3.09	3624.4	0.1%
1,000	-18.99***	-310.29***	2253.6	-13.8%	0.33	238.73***	1801.4	13.3%	-18.66***	-71.57	3946.7	-1.8%
1,000<	-12.82***	-361.58***	2522.9	-14.3%	-4.76*	219.67**	1938.7	11.3%	-17.59***	-141.91	4334.1	-3.3%
Panel E - Age Group 55 to 64												
0	-2.52	-10.09	39.8	-25.4%	0.19	0.78	55.3	1.4%	-2.33	-9.31	95.1	-9.8%
100	-1.40	-15.68	130.9	-12.0%	6.31**	26.02*	166.6	15.6%	4.91	10.34	297.5	3.5%
200	-0.08	-15.98	150.8	-10.6%	0.26	27.05	195.8	13.8%	0.18	11.07	346.6	3.2%
300	-0.54	-18.16	187.8	-9.7%	0.17	27.73	237.3	11.7%	-0.37	9.57	425.1	2.3%
400	-0.14	-18.72	243.2	-7.7%	1.53	33.85	305.3	11.1%	1.39	15.13	548.5	2.8%
500	-0.39	-20.29	313.2	-6.5%	0.37	35.35	361.8	9.8%	-0.02	15.05	675.0	2.2%
600	-0.28	-21.41	361.3	-5.9%	1.31	40.60	409.9	9.9%	1.03	19.19	771.3	2.5%
700	6.24**	3.55	447.0	0.8%	0.77	43.67	475.1	9.2%	7.01*	47.23	922.1	5.1%
800	1.39	9.11	496.2	1.8%	1.48	49.60	502.3	9.9%	2.87	58.71	998.5	5.9%
900	-1.93	1.38	555.8	0.2%	1.04	53.77	545.9	9.8%	-0.89	55.15	1101.8	5.0%
1,000	-3.47	-12.52	630.4	-2.0%	0.62	56.24	603.9	9.3%	-2.86	43.73	1234.3	3.5%
1,000<	1.37	-7.06	690.3	-1.0%	-4.02**	40.17	659.7	6.1%	-2.65	33.12	1350.0	2.5%
Panel F - Age Group Over 65												
0	-0.79	-3.15	5.6	-56.4%	-1.08	-4.32	19.7	-21.9%	-1.87	-7.47	25.3	-29.5%
100	-0.42	-4.85	27.8	-17.4%	-1.75	-11.31	48.8	-23.2%	-2.17	-16.15*	76.6	-21.1%
200	-0.02	-4.95	33.5	-14.7%	-0.48	-13.23	54.7	-24.2%	-0.51	-18.18*	88.3	-20.6%
300	-0.82	-8.24	42.3	-19.5%	1.49**	-7.26	61.1	-11.9%	0.67	-15.50	103.4	-15.0%
400	-0.47	-10.13	55.0	-18.4%	-0.51	-9.29	75.4	-12.3%	-0.98	-19.42	130.3	-14.9%
500	-0.08	-10.46	67.6	-15.5%	-0.35	-10.70	85.1	-12.6%	-0.44	-21.16	152.6	-13.9%
600	-0.62	-12.96	78.2	-16.6%	-0.90	-14.30	100.1	-14.3%	-1.52	-27.26	178.3	-15.3%
700	-1.06	-17.20	89.8	-19.1%	-0.40	-15.90	123.2	-12.9%	-1.46	-33.10	213.1	-15.5%
800	-0.38	-18.73	96.6	-19.4%	0.25	-14.91	130.1	-11.5%	-0.13	-33.64	226.7	-14.8%
900	-0.10	-19.14	104.0	-18.4%	-0.37	-16.39	135.0	-12.1%	-0.47	-35.52	239.0	-14.9%
1,000	-2.98***	-31.05*	118.1	-26.3%	0.40	-14.79	143.5	-10.3%	-2.58*	-45.84	261.6	-17.5%
1,000<	-2.22***	-39.94**	135.8	-29.4%	-0.59	-17.14	157.2	-10.9%	-2.81**	-57.08*	293.0	-19.5%

Note: The Table presents Back-of-the-Envelope calculations for age group subpopulations. Statistical significance of linear combinations reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$, for t-tests on the linear combinations, which can be at the individual quarter per distance bin or annual cumulative across distance bins, up to the indicated distance.

Table 9: What counties are driving the results?

Pre-Diversion Poisoning Mortality across Rx and Non-Rx subgroups

Panel A - Effect over Non-Prescription Opioids

	Main	**High-Rx**		**Low-Rx**	
	Results	High Non-Rx	Low Non-Rx	High Non-Rx	Low Non-Rx
0 miles	-0.435***	-0.648***	-0.259***	-1.389***	-0.291***
	(0.0753)	(0.151)	(0.0961)	(0.0804)	(0.0778)
100	-0.301***	-0.593***	-0.250***	-1.138***	-0.0863
	(0.0679)	(0.175)	(0.0767)	(0.207)	(0.0559)
200	-0.284***	-0.941***	-0.209**	-1.062***	-0.117
	(0.0698)	(0.183)	(0.0876)	(0.131)	(0.0756)
300	-0.207***	-0.738***	0.0578	-0.988***	-0.120*
	(0.0598)	(0.175)	(0.0717)	(0.265)	(0.0616)
400	-0.180***	-0.555***	-0.0404	-0.735***	-0.0465
	(0.0598)	(0.142)	(0.0940)	(0.189)	(0.0639)
500	-0.297***	-0.678***	-0.109	-0.272***	-0.0779
	(0.0547)	(0.123)	(0.125)	(0.0766)	(0.0627)
600	-0.140**	-0.544**	-0.152	-0.553***	0.00300
	(0.0645)	(0.211)	(0.104)	(0.119)	(0.0729)
700	-0.106*	-0.220	-0.0299	-0.320***	-0.0740
	(0.0623)	(0.158)	(0.0859)	(0.118)	(0.0731)
800	-0.346**	-1.509***	0.103	-0.670***	-0.0426
	(0.141)	(0.511)	(0.210)	(0.111)	(0.0741)
900	-0.322***	-0.814***	-0.558***	-0.300**	-0.121*
	(0.0865)	(0.119)	(0.115)	(0.122)	(0.0705)
1000	-0.356***	-1.125***	-0.0152	-0.697***	-0.240***
	(0.0702)	(0.0535)	(0.135)	(0.143)	(0.0598)
1,000<	-0.368***	-1.294***	-0.425***	-0.421***	-0.114
	(0.0700)	(0.208)	(0.105)	(0.0997)	(0.0853)
R^2	0.331	0.384	0.210	0.326	0.203
N. Clust.	2,628	1,282	1,245	1,092	1,883
N	63,072	30,768	29,880	26,208	45,192
Basel.	1.268	2.424	1.218	1.776	0.825

Panel B - Effect over Prescription Opioids (Rx)

	Main	**High-Rx**		**Low-Rx**	
	Results	High Non-Rx	Low Non-Rx	High Non-Rx	Low Non-Rx
0	0.131	0.206	0.392	1.002***	0.0442
	(0.118)	(0.169)	(0.255)	(0.0510)	(0.0892)
100	0.259***	0.472***	0.371***	0.237*	0.127**
	(0.0754)	(0.171)	(0.143)	(0.126)	(0.0524)
200	0.106	0.126	0.0324	-0.177	0.241***
	(0.0677)	(0.204)	(0.159)	(0.162)	(0.0730)
300	0.135***	0.217	0.109	0.250	0.179***
	(0.0501)	(0.146)	(0.156)	(0.214)	(0.0509)
400	0.227***	0.343***	0.174	0.771***	0.214***
	(0.0610)	(0.121)	(0.110)	(0.266)	(0.0751)
500	0.0962	0.430***	0.459***	-0.0757	0.0416
	(0.0788)	(0.134)	(0.158)	(0.0716)	(0.0550)
600	0.0282	0.421	-0.0493	0.141	0.0268
	(0.0548)	(0.263)	(0.146)	(0.181)	(0.0452)
700	-0.0502	0.123	-0.158*	0.0129	-0.0278
	(0.0523)	(0.156)	(0.0948)	(0.0989)	(0.0491)
800	0.114*	-0.192	0.0312	0.144	0.188***
	(0.0587)	(0.203)	(0.161)	(0.0877)	(0.0640)
900	0.0642	-0.0722	0.361	0.213***	0.0614
	(0.0554)	(0.114)	(0.224)	(0.0662)	(0.0605)
1000	0.0195	-1.140***	0.274	-0.172	0.0300
	(0.0598)	(0.0468)	(0.201)	(0.115)	(0.0499)
1,000<	-0.133***	-0.317*	-0.195	-0.128***	-0.0378
	(0.0396)	(0.181)	(0.131)	(0.0449)	(0.0488)
R^2	0.364	0.371	0.296	0.292	0.259
N. Clust	2,628	1,282	1,245	1,092	1,883
N	63,072	30,768	29,880	26,208	45,192
Basel.	0.852	1.784	1.378	0.534	0.534

Note: The Table presents regression results for the classification of counties according to their pre-diversion opiod mortality prevalence for both Non-Rx and Rx. Standard errors clustered at the county level in parentheses. Statistical significance reported at: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$.

Table 10: Robustness and Additional Exercises

	(1) Main	(2) Unadjusted	(3) LA West	(4) No Covars	(5) DEA Extr.	(6) Geod. Dist.	(1) Main	(2) Unadjusted	(3) LA West	(4) No Covars	(5) DEA Extr.	(6) Geod. Dist.	(1) Main	(2) Unadjusted	(3) LA West	(4) No Covars	(5) DEA Extr.	(6) Geod. Dist.
	Panel A - Non-Rx Opioids (T40.0-.4,.6, no T40.2)						**Panel B - Rx Opioids** (T40.2)						**Panel C - Any Opioids**					
0 miles	-0.435***	-0.368***	-0.366***	-0.300***	-0.380**	-0.396***	0.131	0.135	0.166	0.285**	0.0768	0.111	-0.303**	-0.233	-0.199	-0.0150	-0.303*	-0.285*
	(0.0753)	(0.0651)	(0.0766)	(0.0701)	(0.166)	(0.0738)	(0.118)	(0.117)	(0.116)	(0.130)	(0.122)	(0.119)	(0.147)	(0.144)	(0.146)	(0.160)	(0.176)	(0.146)
100	-0.301***	-0.241***	-0.186**	-0.178***	-0.321***	-0.252***	0.259***	0.186***	0.359***	0.370***	0.236***	0.221***	-0.0416	-0.0553	0.173	0.191	-0.0856	-0.0308
	(0.0679)	(0.0519)	(0.0728)	(0.0679)	(0.0627)	(0.0646)	(0.0754)	(0.0691)	(0.0834)	(0.0852)	(0.0708)	(0.0718)	(0.116)	(0.0911)	(0.124)	(0.129)	(0.106)	(0.109)
200	-0.284***	-0.260***	-0.189***	-0.174***	-0.339***	-0.225***	0.106	0.0722	0.167**	0.230***	0.150	0.131**	-0.178*	-0.187*	-0.0214	0.0562	-0.189	-0.0943
	(0.0698)	(0.0626)	(0.0670)	(0.0654)	(0.0704)	(0.0601)	(0.0677)	(0.0709)	(0.0666)	(0.0655)	(0.104)	(0.0557)	(0.106)	(0.0986)	(0.0962)	(0.103)	(0.142)	(0.0863)
300	-0.207***	-0.148***	-0.152**	-0.0838	-0.219***	-0.234***	0.135***	0.147***	0.161***	0.220***	0.153***	0.191***	-0.0712	-0.000905	0.00894	0.136*	-0.0662	-0.0428
	(0.0598)	(0.0516)	(0.0605)	(0.0520)	(0.0624)	(0.0600)	(0.0501)	(0.0486)	(0.0489)	(0.0538)	(0.0551)	(0.0527)	(0.0824)	(0.0738)	(0.0818)	(0.0821)	(0.0868)	(0.0830)
400	-0.180***	-0.109*	-0.126**	-0.0848	-0.273***	-0.209***	0.227***	0.218***	0.251***	0.334***	0.198***	0.179***	0.0474	0.109	0.125	0.249***	-0.0745	-0.0300
	(0.0598)	(0.0596)	(0.0602)	(0.0588)	(0.0617)	(0.0524)	(0.0610)	(0.0585)	(0.0601)	(0.0625)	(0.0637)	(0.0548)	(0.0916)	(0.0897)	(0.0910)	(0.0939)	(0.0932)	(0.0781)
500	-0.297***	-0.250***	-0.244***	-0.218***	-0.226***	-0.178***	0.0962	0.0935	0.123	0.166	0.262***	0.00655	-0.200**	-0.157*	-0.121	-0.0522	0.0360	-0.172*
	(0.0547)	(0.0529)	(0.0553)	(0.0583)	(0.0606)	(0.0612)	(0.0788)	(0.0689)	(0.0775)	(0.104)	(0.0627)	(0.0626)	(0.0989)	(0.0898)	(0.0980)	(0.138)	(0.0893)	(0.0986)
600	-0.140**	-0.0159	-0.0861	-0.0367	-0.190***	-0.0734	0.0282	0.127**	0.0523	0.122**	0.0137	-0.0935*	-0.111	0.111	-0.0338	0.0856	-0.177*	-0.167**
	(0.0645)	(0.0604)	(0.0651)	(0.0608)	(0.0663)	(0.0636)	(0.0548)	(0.0637)	(0.0539)	(0.0544)	(0.0653)	(0.0555)	(0.0833)	(0.0935)	(0.0832)	(0.0829)	(0.107)	(0.0832)
700	-0.106*	-0.0519	-0.0548	-0.0399	-0.121**	-0.351***	-0.0502	-0.000668	-0.0280	0.0230	-0.127***	0.0261	-0.156*	-0.0526	-0.0827	-0.0169	-0.249***	-0.325***
	(0.0623)	(0.0645)	(0.0632)	(0.0755)	(0.0590)	(0.101)	(0.0523)	(0.0541)	(0.0513)	(0.0525)	(0.0449)	(0.0513)	(0.0826)	(0.0896)	(0.0823)	(0.101)	(0.0733)	(0.126)
800	-0.346**	-0.313**	-0.297**	-0.310*	-0.242**	-0.266***	0.114*	0.105*	0.133**	0.182***	0.0443	0.0416	-0.232	-0.207	-0.164	-0.128	-0.198	-0.225**
	(0.141)	(0.140)	(0.142)	(0.166)	(0.0971)	(0.0893)	(0.0587)	(0.0630)	(0.0581)	(0.0581)	(0.0580)	(0.0526)	(0.174)	(0.171)	(0.174)	(0.199)	(0.122)	(0.103)
900	-0.322***	-0.150**	-0.275***	-0.277***	-0.258**	-0.352***	0.0642	0.0110	0.0843	0.0676	0.129**	0.0267	-0.257**	-0.139	-0.191*	-0.209*	-0.130	-0.326***
	(0.0865)	(0.0689)	(0.0876)	(0.0999)	(0.117)	(0.0667)	(0.0554)	(0.0649)	(0.0542)	(0.0533)	(0.0592)	(0.0572)	(0.101)	(0.112)	(0.101)	(0.115)	(0.132)	(0.103)
1,000	-0.356***	-0.290***	-0.313***	-0.340***	-0.417***	-0.159**	0.0195	0.0648	0.0375	-0.0308	-0.00485	-0.181***	-0.337***	-0.225**	-0.276**	-0.371***	-0.422***	-0.339***
	(0.0702)	(0.0706)	(0.0707)	(0.0965)	(0.0639)	(0.0659)	(0.0598)	(0.0591)	(0.0589)	(0.0552)	(0.0573)	(0.0454)	(0.109)	(0.109)	(0.108)	(0.130)	(0.0974)	(0.0853)
1,000<	-0.368***	-0.287***	-0.320***	-0.299***	-0.288***	-0.631***	-0.133***	-0.0262	-0.117***	-0.0996**	-0.0722	-0.124***	-0.501***	-0.313***	-0.437***	-0.399***	-0.360***	-0.755***
	(0.0700)	(0.0699)	(0.0708)	(0.0697)	(0.0635)	(0.101)	(0.0396)	(0.0400)	(0.0385)	(0.0418)	(0.0452)	(0.0475)	(0.0823)	(0.0824)	(0.0826)	(0.0874)	(0.0881)	(0.122)
R^2	0.331	0.314	0.330	0.328	0.331	0.330	0.364	0.338	0.365	0.362	0.366	0.361	0.405	0.396	0.405	0.402	0.406	0.404
N. Clus.	2,628	2,628	2,628	2,628	2,628	2,765	2,628	2,628	2,628	2,628	2,628	2,765	2,628	2,628	2,628	2,628	2,628	2,765
N	63,072	63,072	63,072	63,072	62,592	66,360	63,072	63,072	63,072	63,072	62,592	66,360	63,072	63,072	63,072	63,072	62,592	66,360
Basel.	1.268	0.923	1.268	1.268	1.268	1.268	0.852	0.603	0.852	0.852	0.852	0.852	2.120	1.526	2.120	2.120	2.120	2.120

Note: The Table presents regression results for Heroin (Panel A), Rx (Panel B) and Non-Rx (Panel C) regressions. The Main results are accompanied by each one of the exercises: 1) Unadjusted mortality rates, 2) Considering (non-spike) Louisiana as part of the control, 3) Using the start of the Post period as 2008Q1, 4) Identify spike counties through the DEA Extraordinary Method and 6) Use Geodetic Distances instead of travel distance. Standard errors clustered at the county level in parentheses. Statistical significance reported at: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$.

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A Appendix

A.1 Evidence for December 2007 Diversion Event

A.1.1 Release of Transaction-Level ARCOS Data

In response to the rapid spread of opioid use disorders and rising opioid mortality throughout the United States, more than 2000 cases were filed in state and federal courts by health systems, cities, counties, and states to seek civil damages against the major participants in the pharmaceutical industry that supplied opioids. The main targets were the opioid manufacturers (e.g., Endo, Insys, Mallinckrodt, and Perdue among others), the major wholesale distributors (AmeriSourceBergen, Cardinal Health, and McKesson), and major pharmacy groups (e.g., CVS, Eckerd, Walgreen, etc.). The range of defendants in the several thousand cases mirrored the distribution system for pharmaceuticals in the U.S.: pharmaceutical companies manufacture doses of FDA-approved drugs; doses destined for retail pharmacies are delivered to wholesale distributors (or directly to large pharmacy chains who manage their own warehouses) for storage until needed by the local pharmacies; when a local (non-warehousing) pharmacy runs low on inventory it contacts the distributor and orders drugs to replenish their stocks; the drugs are delivered to the local pharmacy and then sold to individual customers who arrive at the pharmacy with a legitimate prescription from a licensed prescriber (usually, a physician); if the distributor happens to be out of stock when the local pharmacy calls, the pharmacy will call another distributor until it has sources the product it needs. For controlled substances like opioids, this entire chain from manufacture to local pharmacy is tracked by the Drug Enforcement Agency (DEA) using an electronic system called the Automation of Reports and Consolidated Orders System (ARCOS).

In December 2017 more than 2000 cases were consolidated by the overseeing United States Judicial Panel on Multi-District Litigation (MDL 2017) into a single venue, the Northern District of Ohio Federal Court under the oversight of Federal Judge Dan A. Polster. Judge Polster was tasked with coordinating the many pretrial motions, identifying a manageable set of bellwether venues, and setting a rational schedule. The multi-district litigation (MDL) was called the National Prescription Opiate Litigation. Throughout the course of the litigation, Judge Polster ordered various documents (deposition, emails, etc.) be released publically. One particularly contentious request for public release was for the raw ARCOS dataset. Since the DEA began requiring manufacturers, distributors, and pharmacies (among other entities) to report on the detailed flow of controlled substances through the pharmaceutical sector as part of the Controlled Substances Act in 1970 industry participants have fought to keep the data strictly confidential. The DEA has released aggregations of the data at coarse geographic (3-digit ZIP code or state), time (quarterly), and drug (generic name) levels but has never been willing to make the detailed transaction-level ARCOS available.

Plaintiffs in the MDL requested and were granted access to the transaction-level ARCOS data from the DEA for 2006 – 2014 (inclusive). The plaintiffs requested ARCOS unedited data in the native format for the following drugs: buprenorphine, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanal, meperidine, methadone, morphine, powdered opium, oxycodone, oxymorphone and tapendadol. Data requested included seller name, seller major business activity, seller street address, buyer name, buyer major business activity, buyer street address,

specific drug identifiers (drug name and NDC code), packages in shipment, units per package, grams of base controlled substance per shipment, MME equivalents, and other key data. The DEA initially resisted all requests for these data, asserting that it would violate confidentiality agreements, release sensitive commercial information (e.g., customer lists for manufacturers) and pose a security risk for local entities that could be identified as having large volumes of opioids on hand. However, in mid- July 2019, Judge Polster ordered that the entire database be released in response to a motion by the Washington Post and HD Media (of Charleston, WV). The raw data was released to the general public by the Northern District of Ohio courts[15].

A.1.2 Identifying Unprecedented Surges of Opioids into Several States

We extract all ARCOS data elements for the entire 2006-2014 time period (though our mortality models focus on the 2005-2010 time period using different data). We keep all records associated with transactions for finished (non-bulk) opioids where the endpoint was to a retail pharmacy (brick and mortar or online); we exclude shipments of opioids where the final disposition was to a hospital, practitioner or mid-level provider, central fill pharmacy, ambulance service, nursing home, or military outlet (including the VA). We geocode all pharmacies in the data and track shipments of all opioids to each pharmacy. Opioids are measured as both grams and morphine milligram equivalent (MME) units in each shipment. Converting the amount of each shipment into MME units allows for adding shipment amounts of different drugs together in a meaningful way[16]. We exclude shipments of buprenorphine that are approved for the treatment of opioid use disorder based on the product National Drug Code[17]. Observations are aggregated by total MME and then MME per generic drug name to the county (in which each pharmacy was located) and week level for the entire January 2006 through December 2014 time period for the purposes of identifying the spike event.

With the raw aggregated data in hand we examine flows of opioids into each state by month. Our first pass assessment graphs the total MME (of all drugs) summed across all counties by month and state for the following tracked opioids: oxycodone, oxymorphone, hydrocodone, hydromorphone, codeine, dihydrocodeine, fentanyl, levorphanol, meperidine, morphine, opium, buprenorphine for pain, and methadone for pain. There is an anomaly immediately obvious for the state of Florida, where total MMEs flowing into retail pharmacies for December 2007 are strikingly higher than in other months observable in the data (see Figure 2). We do not observe anything like a similar spike in total opioid shipments for other comparably large states (California, New York, and Texas; see Figure 3). However, on further investigation, it is clear that the unexplained and sudden excess opioid shipments in December 2007 occurred in three other states: Alabama, Louisiana, and Mississippi (see Figure 4). This pattern appears in no other states[18]. We further

[15]The raw data is very large - over 180 GB in total - and is available for download at: file.opioidanalytics.com

[16]The *Washington Post* constructed its own aggregations of ARCOS data to support its reporting and has made this data available to the public. However, the Post chose to count the number of pills of hydrocodone, hydromorphone, oxycodone, and oxymorphone only, without any adjustment for dosage strength (within drug class) or molecule strength (across drug classes). Thus, for detailed research purposes, the *Washington Post* data is quite limited. See Washington Post (2023) for a description of the data.

[17]A list of excluded buprenorphine formulations is available upon request.

[18]While not apparent on the initial graphs of state-wide total MMEs, several counties in far western Tennessee are

examine the flow of opioids by specific drugs into each state. Figure 5 presents the flow of total MME by tracked drug into Florida, where the spike event in December 2007 is apparent across all substances. Note that while the spike appears for all opioids, the magnitude of the spike is much larger for oxycodone (at this time primarily Oxycontin®, manufactured by Perdue Pharmaceuticals), the most commonly used prescription opioid at the time (Evans et al. 2019). The patterns apparent in Florida are generally representative of the patterns apparent in Alabama, Louisiana, and Mississippi.

A.1.3 Were the Excess Opioids Purchased by Insured Customers?

One question that springs immediately to the fore is: "Who is purchasing these excess doses?" To address this question, we turn to three sources of data. Lozano-Rojas et al. (2022) examine the impact of cannabis laws on the use of opioid medications in a large commercial claims database on over 20 million enrollees on average per year nationwide. The appendix to their work presents time series flows of MMEs by month into each state. Bradford et al. (2023) examine the impact of cannabis laws on opioid use in, among other settings, a Medicare Advantage (MA) claims database from one of the largest third-party sponsors of MA plans. The appendix to their paper also contains a monthly time series of the total flows of opioids (in terms of MMEs) to each state. We reproduce the graphs of paid claims for opioid prescriptions from commercial claims and MA plans in Florida from these two sources in Figure 6. We see no evidence of the unusual spike in payments for opioids in Florida to match the surge in shipments in December 2007. We also extract data on Medicaid payments for opioids by state over 2006 to 2010 from the State Drug Utilization Data (SDUD). We extract data for each of the opioid drugs listed above separately. Since SDUD data is reported quarterly we cannot generate a monthly series directly comparable to the commercial and MA series. Also, oxymorphone is reimbursed by Florida Medicaid very infrequently before 2010, so we do not generate that graph. Nonetheless, Figure 7 demonstrates that the rapid influx of opioids into Florida in December 2007 is not reflected in Medicaid prescriptions at the quarterly level[19]. Taken together, the fact that the December 2007 surge of opioids into Florida retail pharmacies does not appear in commercial insurance, Medicare, or Medicaid paid claims means that the excess doses must have been paid by cash transactions as no remaining payor source could absorb the volume of pills that surged into the state.

A.1.4 Identifying Specific Counties Involved in the Surge

The next step in our exploration of this unusual surge in opioid doses is to identify which specific counties are involved. The spike is visually apparent at the state level, but a sub-state assessment has several advantages. First, it may be that only some specific geographies in the affected states are involved, and that could provide information that to suggest a reason for the surge. Second, while the spike is obvious at the state level for Alabama, Florida, Louisiana, and Mississippi, it is possible that similar spikes happened in counties in other states in December 2007 but those surges

also involved.

[19]The lack of evidence for a Medicaid spending spike is not a function of the quarterly aggregation. When we aggregate the ARCOS data to the quarter level the spike in opioids into Florida in the 4^{th} quarter 2007 is still obvious.

are not obvious at the state level. Third, we want to establish a methodology for identifying counties that is systematic, grounded in standard practice for identifying suspicious opioid shipments, and free of any bias associated with us believing that there was a December 2007 spike in four states based merely on visual inspection.

As mentioned above, the transaction level ARCOS data was publicly released as part of a large federal MDL. Discovery in that MDL generated tens of thousands of pages of evidence including depositions by industry participants. One deposition was taken of a DEA agent who regularly examined ARCOS data to identify individual pharmacies with suspicious patterns of opioid acquisition or sales. As reported by the Washington Post: *"The DEA is purposefully vague in how it defines what is a suspicious amount of opioids ordered by a buyer. But in a recent lawsuit, a former DEA agent described five methodologies: Maximum Monthly, Trailing 6 Month Threshold; 2x Trailing 12 Month average; Extraordinary Order Method – 3x Trailing 12 Month Average; Maximum 8,000 Dosage Units Monthly; Maximum Daily Dosage Units."* (Washington Post 2021). Two of these methods are straightforwardly adapted to the task of identifying whether any counties have a suspicious amount of opioids shipped to all pharmacies (collectively) in any given week. Our primary analysis identifies a county as having a suspicious surge in opioid shipments by comparing each December 2007 week to the average shipment volume for the 52 weeks preceding Week 49 that year (The first week of December was the 49^{th} week in 2007)[20].

We first construct a data set for every county in the U.S. in 2007 with one observation per week. We then run 2,980 separate regressions, one for each county in the continental U.S., with the following form:

$$MME_{ct} = \beta_0 + \beta_1 Dec_{c,t} + \beta_2 t + \epsilon_{c,t} \tag{A1.4}$$

where $MME_{c,t}$ is the total opioid MME received by all retail pharmacies in county c in week t, $Dec_{c,t}$ is an indicator variable for whether the week is in December of 2007, and t is a continuous calendar time (week) variable. Once all 2,980 regressions are run, each county in the United States is characterized as being a "spike county" if two conditions are met: 1) the coefficient on β_1 is statistically significant at the 5% level or better, and 2) there are at least two weeks in December 2007 where the total MME shipments into the county are 200% or more of baseline (the average weekly shipments for the 52 weeks preceding Week 49).

Figure 8 shows the 78 U.S. counties that meet these two criteria; these counties are indicated in red. Figure 9 zooms in on the Southeastern region of the U.S.[21]. There are several important facts to note. First, without any criteria other than the two listed above, we see that with the exception of three parishes in Louisiana all of the suspicious "spike" counties are east of the Mississippi River and located in Alabama, Florida, Louisiana, Mississippi, and (with the benefit of a county-level

[20]We do not directly apply the DEA standard of checking every county-week's shipment against the rolling 52-week average because some counties had such enormous increases in the first week of the spike that it artificially inflates the rolling 52-week lag average for the second week. Given the size of the spike, we measure each December county-week against the 52-week average immediately prior to the spike event.

[21]When we use the DEA "Extraordinary Order" criterion, we identified 30 counties with more than 300% of the trailing 52-week average opioid MME deliveries. The higher threshold identifies fewer counties, but they have the same pattern as the baseline criteria and do not change the conclusions of subsequent analyses. Results from the secondary analysis are available on request.

analysis) far western Tennessee. Second, the non-Florida counties are all located along navigable waterways (the Mississippi, Pearl, Pascagoula, Black Warrior, and Tombigbee Rivers) or Interstates 55 and 65. The significance of the fact that no counties west of the Mississippi River are identified as spike counties is discussed below.

A.1.5 Determining the Size of the December 2007 Surge

Once the set of counties that had suspicious surges of opioid shipments into retail pharmacies in December 2007 are identified, we estimate the magnitude of the event. The first step in this process is to identify which county-week observations are suspicious under the criteria outlined above. To do this we calculate the shipment volume into each identified "spike" county during each week in December 2007 (Weeks 49 through 52) and compare that to the average shipment volume for that county for the 52 weeks prior to Week 49 of 2007. If a December week is at least 200% of that county's baseline then we designate that as a "spike week." All counties identified as having suspicious shipment volumes had at least two spike weeks, and many had three[22]. No county has spike volumes for all weeks in December 2007.

As is evident from Figures 2 through 4 shipments of opioids trend steadily up in all states during the 2007-2012 time period. Thus, in order to more accurately reflect the magnitude increases in MMEs shipped during the spike weeks, we calculate excess MMEs shipped during the surge as the difference between the actual MMEs shipped during spike weeks and the average weekly shipments to those same counties during September, October, and November 2007 (the three months prior to December). We calculate the excess number of doses using the average ratio of 23.43452 MME/dose in the ARCOS data[23]. Finally, to arrive at a dollar estimate on the value of excess shipments, we assign a wholesale price of $0.034 per MME taken from Food and Drug Administration (2018)[24].

The estimated excess MME, doses, and wholesale value for the December 2007 surge appear in Table 1. We find that the volume of excess shipments of opioids ranges from 113.87 million MME (about 4,86 million doses) in Tennessee to 2.4 billion MME (about 102.43 million doses) in Florida. Altogether, we estimate that the suspicious surge in opioid shipments to select counties in these five states amounts to an excess of more than 3.4 *billion* MMEs, or over 147 million av-

[22]The spike event appears to have lasted between 10 and 14 days, with some variation around the first day. In some counties those 10-14 days spanned three calendar weeks and in some counties the spike days spanned only two calendar weeks.

[23]While in principle we can use the number of doses reported in the raw ARCOS data, it turns out that the MME/dose data is missing for 7,333,276 observations out of a total of 35,931,593 transactions in 2007. Rather than base the excess dose calculation on a different set of observations than we use to calculate excess MME, we use the average non-missing MME per dose ratio to impute the number of excess doses from the volume of excess MME. The MME per dose = 23.43452 using non-missing observations.

[24]The FDA uses IQVIA National Sales Perspective (NSP) data to calculate the mean Wholesale Acquisition Cost (WAC) for all opioids purchased by U.S. retail pharmacies from 1992 to 2016, adjusted to constant 2016 dollars using the CPI-U. We use the 2007 average WAC of $40.034 for our calculations. The WAC is the price that a manufacturer charges a wholesaler when they take possession of a drug. It is a list price and does not reflect discounts or rebates that may be applied to particular units of the drug depending on who is the ultimate purchaser. WAC is used as a benchmark for the reimbursement of drugs by public and private payers, particularly many state Medicaid agencies. It is important to note that the WAC is not necessarily reflective of the price that a particular purchaser actually pays for a drug, as the actual price can be influenced by various factors such as negotiation and rebates.

erage doses. Pharmacies would have had to spend approximately $117.17 million to acquire those doses from manufacturers, which would then be sold to patients who came into the pharmacies with prescriptions. Recall that since we find no evidence of this spike in opioids in commercial, Medicare, or Medicaid claims we conclude that they were purchased from the pharmacies in cash transactions; retail cash prices for drugs are much higher than WAC. Thus, the number of dollars required to actually purchase this volume of drugs with cash is a multiple of the $117.17 million estimated wholesale (pharmacy) cost.

A.1.6 How Feasible is the Spike?

How feasible this is from a production standpoint? Each opioid tablet must be dispensed as a consequence of a prescription actually written by a provider with a DEA license to prescribe controlled substances (almost always a physician). How many physicians must be involved in this scheme in order to produce enough prescriptions to allow dispensing 147 million excess opioid doses? Consider the situation in Florida in the mid-2000s. Rigg *et al.* document the experiences of individuals suffering from serious OUDs who frequented Florida pill mills during the time period surrounding the spike event (Rigg et al. 2010). Rigg and coauthors recruited a sample of 54 individuals from south Florida whose responses to a larger quantitative survey indicated that they frequented pill mills and were heavily involved with diversion efforts to shift the opioids they obtained to the illicit market. The authors report findings of structured interviews with these participants that illuminate how the diversion market functioned. With respect to how many pills were obtained per prescription, respondents frequently report such things as:

- "[I said to the physician] "How about this – you give me 200 Roxi's [Roxicodone] and 100 Oxy [Oxycontin] 80's"
- "They are prescribing like 180 to 200 Roxi's a month along with Xanax. They are just legal drug dealers is all they are. . . "
- "Listen, I want 240 Roxi's, I want 190 Oxy's, and I want 90 Xanax" and he gives it to me."
- "You could be ridiculous and say ... I mean, I could get 200 of each, Roxi's and Oxy's at the same time, which makes no sense, and Xanny bars (Xanax) at the same time."

Ultimately, most respondents report getting prescriptions for 200-300 pills each (especially high-dose Oxycontin and Roxicodone).

Further, according to a 2011 indictment of 32 people involved in a single Florida pain clinic (pill mill), patients commonly received 3 – 4 separate prescriptions per visit. That same federal indictment reports that the arrested (and ultimately convicted) physicians were seeing up to 500 patients per day. Thus, if we assume for the sake of illustration that corrupt pill mill physicians were operating at the maximum reported capacity (300 pills per prescription, 4 prescriptions per visit, 500 patients per day per physician) then the entire spike event (across all counties in each of the five states) would have only required 490,000 individual prescriptions, which could have been written in 245 physician days. In other words, if these 13 physicians from *one pill mill* in *one Florida county* (Broward) had attempted to write all the prescriptions necessary to support the spike event in all states using their maximum production effort, they could have done so in 13.6

days. The spike event itself lasts between 10 – 14 days. Of course, many more physicians would have been involved than that - at least one would be required per state. The primary lesson from accounts and legal documents at the time is that, as remarkable as it may seem, it would have been trivially easy for as few as two or three dozen corrupt physicians to provide sufficient prescriptions to allow the purchase of all 147 million excess doses associated with the December 2007 spike event.

A.1.7 How prescription drugs get from manufacturer to patient

Before considering whether any actor in each of these levels of production was the primary facilitator of the spike in shipments, it is worth reviewing how shipments of drugs actually make their way through the supply chain and end up in the hand of a customer with a valid prescription[25].

The first stage of the process is manufacturing. Manufacturers of opioid drugs may either make the active pharmaceutical ingredient (API) themselves or purchase it from a third party that manufactures bulk API[26]. Manufacturers like Perdue, Teva, and Mallinckrodt produce a variety of final-form opioid products under a quota system that is managed by the U.S. Drug Enforcement Agency. Self-administered opioids are produced in pill or liquid form and packaged into doses of various strengths under processes approved and supervised by the U.S. Food and Drug Administration. Some opioids are formulated as single-molecule pills (e.g. the brand-name Oxycontin or a generic oxycodone), some opioids are multi-molecule pills (e.g., branded Vicodin or a generic hydrocodone-acetaminophen combination), and some opioids come in liquid form (e.g., branded Dilaudid oral liquid or generic promethazine with codeine). Manufacturers produce final form products and stockpile them in their own warehouses.

Once drugs are produced by the manufacturers they are delivered to pharmacies for distribution to patients with valid prescriptions. The process of delivering opioids from manufacturers to pharmacies takes one of two primary routes. The most common route is that intermediary wholesale distributors buy pallets of finished drugs (including opioids) from the manufacturers and stockpile the doses at warehouses scattered around the United States ready to fill pharmacy demand[27]. When a local pharmacy runs low on some drug, it contacts its usual distributor and orders a new batch of the drugs which are then delivered to the pharmacy using secure drivers, often within 12 hours and almost always within 24 hours. Rapid delivery of product is the reason that wholesalers have dispersed warehouses across the U.S. This permits drugs to be stored securely until they are needed by pharmacies while assuring that patients can get their needed pharmaceuticals within a day even if their local pharmacy is temporarily out. If it happens that the product is out of stock at the closest warehouse of the distributor when a local pharmacy needs it (and the distributor cannot quickly ship from another of its warehouses) then the local pharmacy will call another distributor

[25] In what follows it is useful to remember that each step in the process – from production to local pharmacy – is tracked and visible in the transactional ARCOS data that we use in this analysis.

[26] Some do both. Johnson and Johnson is the parent company of an agricultural concern in Australia that grows a substantial portion of the opium poppies that are used as raw ingredients to manufacture prescription opioids on the world market. Johnson and Johnson uses some portion of the poppy crop to provide raw ingredients for its own use and sells the remaining crop to other API or finished-product manufacturers.

[27] The pharmacy wholesale sector in the U.S. is dominated by three large distributors: AmerisourceBergen, Cardinal Health, and McKesson Corporation.

until it finds the product it needs in a timely fashion.

The second common route bypasses wholesale distributors. Some pharmacies, such as Walgreen, have their own dedicated warehouse system. They take possession from manufacturers directly, distribute products among their own network of regional warehouses, and then ship directly to local Walgreen pharmacies as needed. From the customer's standpoint, there is no effective distinction between a chain pharmacy that manages its own distribution warehouse system and a pharmacy that purchases drugs from a wholesale distributor. In either case, the patient presents a prescription to the local pharmacist and the pharmacist either fills the prescription if they have product on hand, or delays fulfillment by 12-24 hours if the product must be delivered from a regional warehouse.

Given the magnitude of the surge, which mostly occurred over a discrete 10-14 day period in December 2007 in these spike counties, it is important to establish how so many excess doses of opioids came to be available to support these cash transactions. Did any of the three levels in the supply chain outlined above disproportionately enable the excess flow of opioids? We examine the data to assess whether there are any systematic changes in market shares for each of these levels of the market.

A.1.8 Changes in local pharmacy demand during spike

Once we identify the counties involved in the surge in opioid shipments in December of 2007 (Figure 9) we then calculate the total shipments received to each pharmacy in those counties for every week in 2007 and each pharmacy's average market share for opioid shipments in two time periods: weeks from January - November of 2007 and weeks during the December spike event. Shipments of opioids across multiple sites of chain-owned pharmacies (e.g., CVS, WalMart, or Walgreen) are combined. For example, if a county has six CVS outlets their shipments are aggregated together before market shares are calculated. We do observe changes to market shares across the January-November and the December spike periods, but there is no systematic pattern. For example, in Florida, the top five pharmacies by market share before the spike are: Walgreen (26%), CVS (12.9%), Publix (4.6%), WalMart (3.2%), and Winn Dixie (3%). During the spike the market share leaders are: CVS (34.3%), Walgreen (13.9%), Kash N Karry (3.7%), K-Mart (2.3%), and Publix (1.9%). In Alabama, the pre-spike market share leaders are: CVS (16.3%), Walgreen (6%), Village Pharmacy (4.4%), Winn Dixie (4.2%), and Harco (3.9%). During the spike event the market share leaders in Alabama are: CVS (40%), Winn Dixie (11.3%), Natural Rx (8.4%), Bruno's (6.6%), and Lloyd's (4%). Louisiana, Mississippi, and Tennessee counties show a similar lack of pattern. Dominant market pharmacies prior to the spike remain dominant during the spike; moderate market share pharmacies move around but since the market shares for pharmacies ranked 6^{th} through 20^{th} generally range from .5% to 3% small, economically irrelevant, changes in market share can induce large ranking movements for individual pharmacies. Ultimately, we conclude that no player in the retail pharmacy sector disproportionately benefits from the spike, in terms of systematically capturing a large portion of the sales.

A.1.9 Changes in manufacturer demand during spike

We repeat the exercise above for manufacturers to assess whether there were significant changes in manufacturer market share. For this, we track the flow of opioids (in total MME) into the spike counties for each week in 2007. (That is, we do not include flows of opioids from manufacturers into non-spike counties in the analysis) We calculate manufacturer market shares in those counties for January - November (collectively) and for the spike weeks in December. As with the pharmacy markets, while there is some churn among the top prescription suppliers across the non-spike and spike periods, the changes are not systematic. For example, in Florida the top five manufacturers from January through November are: Actavis (27.2%), Specgx (20.3%), Purdue (7.0%), Par (5.9%), and Mylan (5.3%)[28]. During the December 2007 spike event the top five Florida manufacturers are: Specgx (22.1%), Actavis (21.4%), Purdue (8.3%), Indivior (6.5%), and Par (6.3%). Similarly, in Alabama the top five manufacturers from January through November are: Par (28.0%), Specgx (18.4%), Actavis (7.6%), Invidior (6.5%), and Sandoz (6.3%). During the December 2007 spike event the top five manufacturers selling opioids in Alabama are: Specgx (24.0%), Par (22.3%), Invidior (7.1%), Cebert (6.4%), and Hikma (6.2%). There are similar patterns in Louisiana, Mississippi, and Tennessee spike counties where the ranking among the top-10 manufacturers shifts but the companies comprising the top ranks do not change. Fundamentally, there is little apparent evidence of movement or disproportionate gains in shipments from any manufacturer associated with the excess MME shipments during December 2007.

A.1.10 Changes in distributor (wholesaler) supply during spike

Unlike the situation for the pharmacy and manufacturer levels of the supply chain for opioids, where we find no clear patterns in who supplied opioids during the spike events, we do find a striking change in market shares among the major wholesale distributors. As with the pharmacy and manufacturer levels, we track changes in shipments from wholesalers into the spike counties (only). As mentioned above there are generally two types of distributors (wholesalers): independent distributors that purchase drugs from manufacturers and sell to local pharmacies, and warehousing pharmacies that take direct shipments of large quantities of drugs from manufacturers, warehouse the drugs at company-specific locations and distribute to company-owned pharmacies. The latter group - including firms such as Walgreen (18.3% of shipments during the baseline), Wal-Mart (4.1% of baseline shipments), and Smith Drug Company (3.4% of shipments during baseline) - are excluded from the distributor analysis since they are tied exclusively to company-owned local pharmacies and the analysis above indicates that there is no pattern in pharmacy market share shifts during the spike event. So, to assess whether any distributor plays a disproportionate role in the spike we focus on the independent wholesalers, in particular the "big three": AmerisourceBergen, Cardinal Health, and McKesson. In what follows, they will be referred to as Distributor A, Distributor B, and Distributor C - though those designations are not in alphabetical order.

As before, we calculate total flows of opioid MME and market share in all spike counties (irrespective of state) for each week of 2007 and 2008 for the big three distributors. Two striking patterns are immediately obvious. As shown in the top panel of Figure 10 the total amount of opioids flowing into these spike counties from each of the Big Three distributors is very stable

[28] Specgx is a subsidiary of Mallinckrodt that has primary responsibility for opioid manufacturing.

for nearly all of 2007 and for all of 2008. Of course, for two weeks in December 2007 the total flow of opioids spike up. But, what is striking is that the increase is almost entirely supplied by a single wholesaler - Distributor C. The lower panel in 10 shows that Distributor C market share goes from a stable one-third of opioid shipments outside the spike event to almost 85% share during the spike event. Distributor C shipped an average of 98 million MME per week from January through November into the spike counties; shipments into the affected counties from Distributor C rose to 1.098 billion MME during the spike weeks in December. Then, after the spike event was over, Distributor C returned essentially to baseline.

How did Distributor C support such a dramatic change in its opioid sales volume and market shares during the spike? Recall from Section A.1.7 above the process that pharmacies follow when they run out of a particular drug and need to fill a customer's prescription: the pharmacy will call its usual distributor to order a delivery; if the distributor does not have any of the specific drug (by dosage and formulation) then the pharmacy will call another distributor until they can quickly source the product they need. However, this process breaks down in the spike counties during the several weeks in December 2007. Distributors A and B appear to run out of opioids to supply the pharmacies. Only Distributor C has sufficient product on hand to supply pharmacies in the spike counties during this event.

To understand how Distributor C came to have enough opioids on hand when the other two did not, we track its acquisition of opioids from manufacturers from June 2006 through the end of December 2007. According to the *ARCOS Registrant Handbook*, the transaction code field indicates when a reporting registrant either acquires, dispenses, or transfers between sites any tracked opioid. Transaction code "P" designates acquisition of an opioid by one ARCOS registrant from another, the transfer of an opioid from one physical location to another, or the establishment of the initial stock for a new ARCOS registrant. When distributors ship opioids between their own warehouses to manage the logistical process of supplying pharmacies, those transactions are also in the ARCOS. Since we are not interested in how distributors managed their inventory but rather how they acquired opioids from the manufacturers we only measure sales (transaction code = "S") where the buyer has the business activity "DISTRIBUTOR" and the reporter (seller) has the business activity "MANUFACTURER." While this will miss instances when, for example, Distributor A purchases opioids from Distributor B to fill its demand, the process captures flows between manufacturers and initial distributors and thus provide a first glimpse into how Distributor C has enough opioids on hand for the spike in December 2007. Figure 11 plots monthly shipments from manufacturers to the Big Three distributors. Note that Distributors A and B have relatively unremarkable acquisition profiles that gradually increase over time. However, Distributor C has at least three outlier purchase events, the first occurring in the last week of March 2007. These acquisitions are not only notable because of their raw magnitude, but they also stand out as the only months with statistically significant day indicators from a regression on doses received each day by Distributor C[29].

[29]It may also be noteworthy that the statistically significant excess manufacturer purchases by Distributor C all involve shipment initially to only two warehouses: one near Columbus, OH and one near Nashville, TN. The reason to note this will become apparent in the next section.

A.1.11 Historical Context for the Illicit Drug Market in 2007

During 1990s and early 2000s, the U.S. illicit drug market, at least for cocaine and heroin, was dominated by two groups of drug DTOs, those headquartered in Mexico and those headquartered in Colombia. According to Ciccarone et al. (2009), the Mexican DTOs were able to gain a foothold in the western heroin market due to the weakening of the Colombian DTOs in the 1990s, which had previously dominated the entire US market. The Mexican DTOs were able to leverage their proximity to the productive poppy fields in Mexico and the established smuggling routes across the southern U.S. border to become major players in the heroin trade. The Colombian DTOs more easily defended their hold on the eastern U.S. market, where they had established supply and distribution networks and were able to offset declines in Colombian-produced heroin via connections with suppliers in Southeast Asia. Throughout this period of disruption, the Mexican and Colombian DTOs sought to minimize competition since "competition" for drug sales territories usually involved violence. By the 1990s the DTOs arrived at a detente where the Mexican DTOs controlled the illicit heroin market west of the Mississippi River and the Colombian DTOs controlled the heroin market in Louisiana and east of the Mississippi. **?**Castillo et al. (2020); Ciccarone et al. (2009)

Both groups sourced raw materials (coca leaves and opium poppy latex) primarily from farms in their respective home territories. Mexican, Colombian, and U.S. authorities waged a decades-long battle against the DTOs that was multi-pronged in nature. Authorities attempted to eradicate the agricultural source of raw materials, interdict finished drugs before they could be sold in the U.S., and cut off access to international banking systems that allowed the DTOs to launder profits. U.S. and Colombian authorities cooperated in opium poppy eradication projects that sought to destroy the agricultural base for opium latex production in Colombia itself. Bureau of International Narcotics and Law Enforcement Affairs (2002) For example, the U.S. and Colombian authorities established the Colombian National Police's (CNP) Anti-Narcotics Directorate (DIRAN) in 1997 to implement and coordinate eradication and interdiction operations against illegal drug crops and drug traffickers in Colombia. Bureau of International Narcotics and Law Enforcement Affairs (2000) The U.S. provided training and equipment to DIRAN, and U.S. drug enforcement officials worked closely with their Colombian counterparts to identify and target drug trafficking organizations operating in the country. Similarly, the U.S. and Colombian authorities collaborated in the establishment of the Andean Regional Initiative (ARI) in 2001 to facilitate U.S. support for anti-narcotics efforts in Colombia, as well as in other Andean countries like Bolivia and Peru. Bureau of International Narcotics and Law Enforcement Affairs (2002) Through the ARI, the U.S. provided funding for anti-narcotics programs, including crop substitution programs for farmers who had previously grown illegal drug crops. According to the U.S. Department of State, between 1996 and 2001, the amount of land dedicated to opium poppy cultivation in Colombia decreased by over 90%. This was largely due to the Colombian government's eradication efforts, which were supported by the U.S. through programs like the DIRAN and the ARI. As illustrated in 13 these efforts to eliminate opium poppy crops and opium latex production depressed Colombian production.

A second front in the drug war, and perhaps the more significant one for this research, was waged on the Colombian DTOs' capacity to launder profits from the drug trade. During the 1990s and early 2000s, Colombia was a major hub for illegal money laundering activities in the Western hemisphere. DTOs used various methods to launder their money and avoid detection by law en-

forcement authorities. Kar and Cartwright-Smith (2009); Kar and Spanjers (2015); Reuter (2012); Thoumi and Anzola (2010; 2012) One common method was for DTOs to buy or create businesses that have predominately cash transactions, such as restaurants, hotels, casinos, or foreign currency exchange companies, and use those to launder drug money. DTOs would mix illicit cash with legitimate revenue from the business and deposit the cash into Colombian bank accounts. This method was particularly difficult for authorities to detect, as the businesses appeared to be legitimate and the money appeared to be from legal sources. The DTOs then set up front companies and shell corporations in countries known to be tax havens and transfered the laundered cash from Colombia to those offshore businesses. United Nations Office on Drugs and Crime (2002) The shell companies would often have no real business operations and would exist solely to move money, making them difficult for authorities to trace.

The Colombian government, with the assistance of international organizations such as the United Nations, made significant strides in the early 2000s to combat money laundering activities in the country. In April of 2007, the Superintendence of Finance of Colombia announced the final language for regulations requiring all financial institutions under its authority to bring monitoring and financial processing procedures to international standards by January 1, 2008 Colombian Government (2007). This regulatory change aimed to increase transparency and combat money laundering and other financial crimes, which had been a longstanding challenge for Colombia's banking sector. One of the key impacts of this regulatory change was that it made migrating large amounts of U.S. currency out of Colombia using the domestic and international banking system much more difficult. This regulation automatized reporting of suspicious activities, tightened the scope of the regulator across all financial institutions, and over foreign currency transactions and foreign exchange houses in particular, which before the reform produced more than half of the reports of suspicious activitiesUIAF (2011); Caballero et al. (2016). As mentioned above, drug traffickers and other criminal organizations were able to use the financial system to launder their profits and move large amounts of cash across borders prior to the implementation of these regulations Bureau of International Narcotics and Law Enforcement Affairs (2019). However, the new regulations made it much harder for these organizations to move their money undetected. According to the U.S. Department of State, the implementation of these regulations helped to disrupt the flow of drug money from Colombia to the U.S. As a result, many drug traffickers were forced to find new ways to move their cash and achieve positive returns on investment from it.

We emphasize the following fact: these new Colombian anti-money laundering regulations were set to take full effect (and did take full effect) on January 1, 2008 – three weeks before 147 million excess doses of opioids were purchased with cash in 78 Southeastern U.S. counties, *all* of which are located in the Colombian DTOs' heroin sales territory.

A.1.12 What the Evidence Suggests

In summary, we observe the following broad facts, some of which are illustrated in Figure 12.

- A large, unprecedented, spike in (apparent) cash purchases of just over 147 million opioid doses took place in December 2007.
- The excess shipments were concentrated in counties that were: 1) east of the Mississippi River or in Louisiana, and 2) largely along navigable waterways.

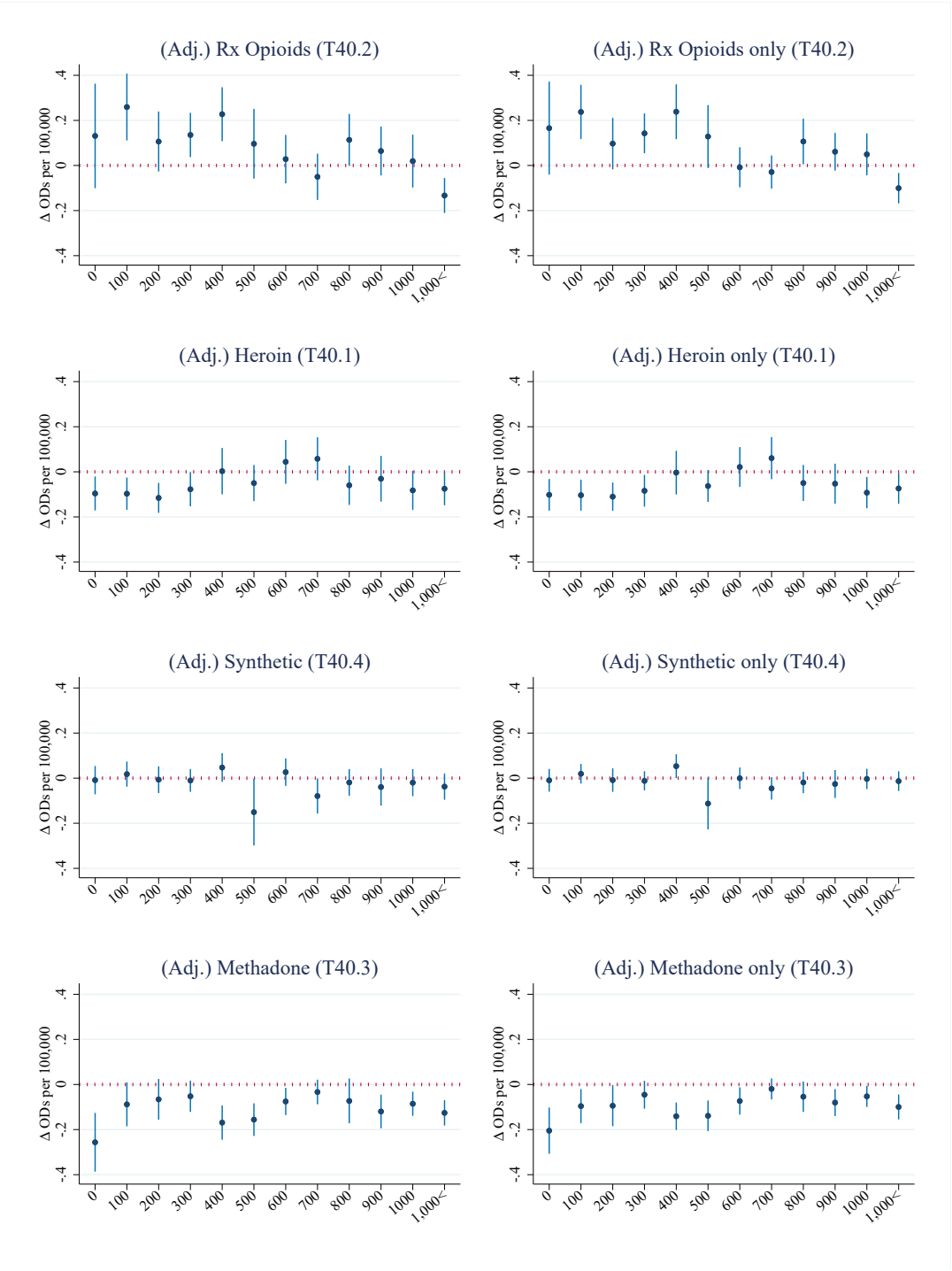
- Colombian DTOs controlled the heroin market east of the Mississippi River and Louisiana at this time.
- Only one US pharmaceutical distributor pre-positioned itself to fill this demand, and so supplied in excess of 80% of the spike demand.
- The timing of the start of inventory accumulation by this distributor coincided with the release of the final language for the Colombian Ministry of Finance about reforms that would make money laundering very difficult.
- The actual cash purchase of excess opioids from Southeastern US pharmacies came just before the new Colombian banking regulations took effect.

This evidence is consistent with the following narrative. In 2007 the Colombian DTOs faced a shortage of opioids to sell in the eastern U.S. illicit drug market. At the same time, they faced a looming threat to their ability to launder large amounts of cash through the Colombian banking sector. They responded by moving cash to, or leaving cash in, U.S. counties which were easily accessible via navigable waterways (where the DTOs had long-standing smuggling infrastructure) and purchased around 147 million doses of prescription opioids over a 2-week period in December 2007. The wholesale value of the purchases would have been around $117 million; the cost to purchase that many doses in cash from retail pharmacies would have been a multiple of that number. This sudden spike in purchases had the effect of directing 84% of the wholesale demand to Distributor C, whose acquisition of opioids stood out as an aberration, in terms of magnitude and timing, compared to Distributors A and B. Given the evidence that these purchases were made in cash – bypassing any monitoring that would have occurred if third-party payers were involved and taking place in states without mandatory PDMPs – and that the spike in purchases/shipments occurred no more than three weeks before the Colombian anti-money laundering banking rules went into effect, we believe these prescription opioids were diverted to the illicit market to replace depleted Colombian heroin supplies. The purchases happened along waterways and roadways commonly used by Colombian drug smugglers, facilitating the smuggling of physical cash into the U.S. to bankroll the purchases.

The importance of the accumulated evidence and most likely conclusions are twofold. First, the December 2007 spike in opioid shipments into 78 select Southeastern U.S. counties represents Colombian drug DTOs combating the twin challenges of reduced heroin production and sharply increasing money laundering costs by purchasing prescription opioids that could be resold in the illicit opiate market they controlled. Second, sales of those diverted opioids would have occurred only east of the Mississippi River; locations west of the Mississippi River (under Mexican DTO control) would have been unaffected. Thus, we present strong evidence of a shock to the illicit market east of the Mississippi that made heroin harder to obtain and prescription opioids easier to obtain, which would have altered the substance mix in illicit markets. But, only illicit markets east of the Mississippi river were affected. This sets up the possibility of assessing the impact of this large, real-world, shock to illicit markets that replaced non-prescription (illicitly manufactured) opioids which are more risky (high variance in dosage strength) products, with a less risky (low dosage variance) product (prescription opioids). The data-generating process aligns with a near-ideal difference-in-differences framework.

A.2 Treatment Effects over Individual Categories of Opioid Mortality

Figure A2.1: DiD Distance-to-Spike and Opioid Mortality - Individual Opioid Categories



Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Mortality series have been adjusted following the procedure recommended by Ruhm (2018). Each coefficient parameter captures the interaction between each of the bins of distance-to-spike counties (d) in miles, and the post-treatment period.

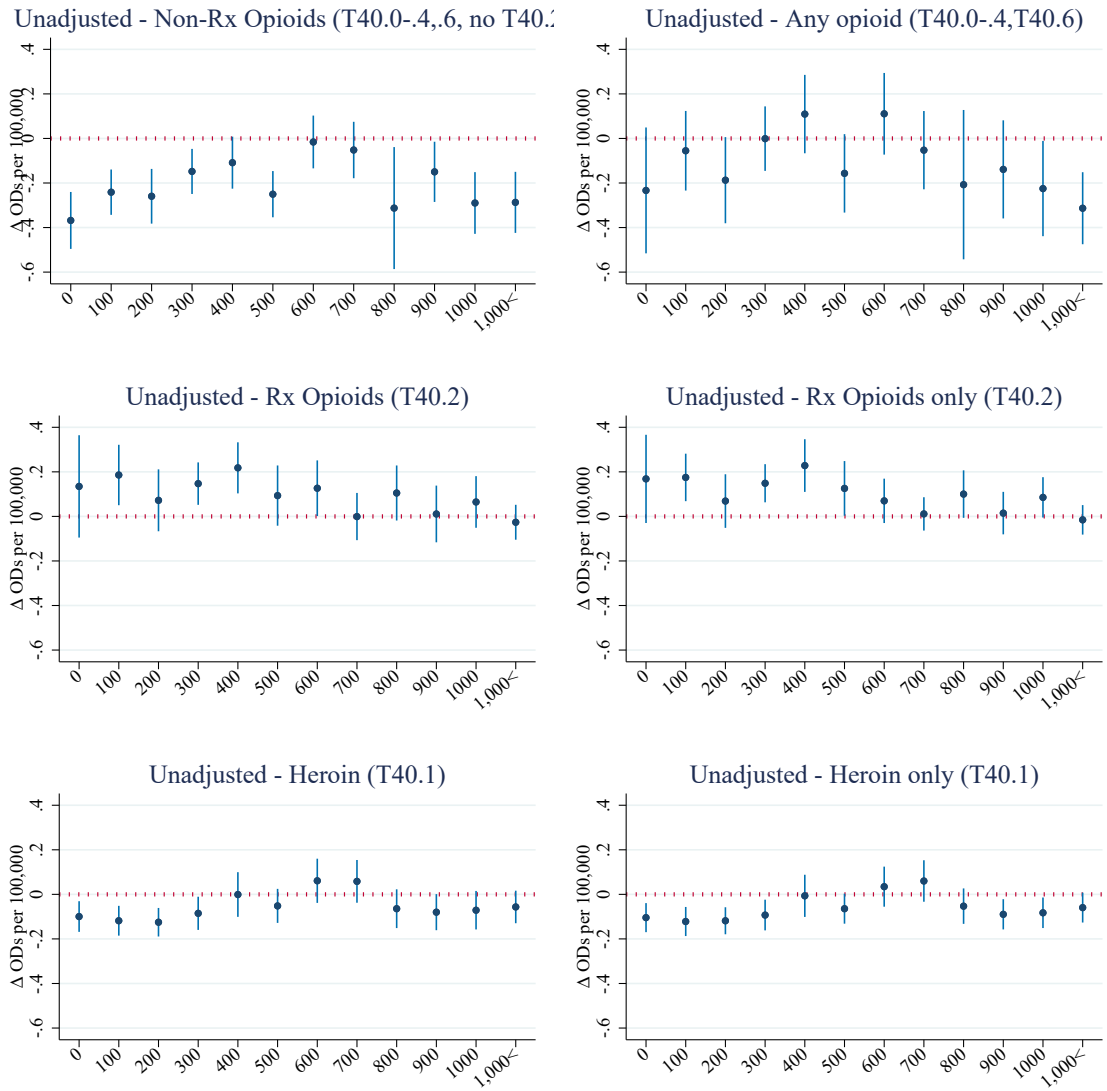
Table A2.1: DiD - Distance-to-Spike and Individual Opioid Substance Mortality

	(1) Rx Op. only T40.2	(2) Heroin only T40.1	(3) Synthetic T40.4	(4) Synth. only T40.4	(5) Methadone T40.3	(6) Meth. only T40.3	(7) Nat/Syn/Her T40.1/2/4
0 miles	0.166	-0.102***	-0.00875	-0.00946	-0.256***	-0.205***	0.0139
	(0.105)	(0.0358)	(0.0320)	(0.0257)	(0.0664)	(0.0522)	(0.132)
100	0.238***	-0.104***	0.0179	0.0194	-0.0881*	-0.0959**	0.179**
	(0.0613)	(0.0351)	(0.0284)	(0.0223)	(0.0496)	(0.0385)	(0.0896)
200	0.0972*	-0.110***	-0.00674	-0.00860	-0.0658	-0.0941**	-0.00306
	(0.0582)	(0.0320)	(0.0302)	(0.0265)	(0.0461)	(0.0463)	(0.0842)
300	0.143***	-0.0841**	-0.0101	-0.0119	-0.0522	-0.0454	0.0461
	(0.0450)	(0.0359)	(0.0257)	(0.0217)	(0.0353)	(0.0315)	(0.0663)
400	0.238***	-0.00356	0.0473	0.0532**	-0.169***	-0.141***	0.260***
	(0.0621)	(0.0494)	(0.0326)	(0.0269)	(0.0387)	(0.0312)	(0.0847)
500	0.128*	-0.0631*	-0.151**	-0.112*	-0.156***	-0.139***	-0.0944
	(0.0712)	(0.0358)	(0.0755)	(0.0586)	(0.0369)	(0.0345)	(0.155)
600	-0.00802	0.0215	0.0267	-0.000412	-0.0752**	-0.0733**	0.0516
	(0.0453)	(0.0450)	(0.0311)	(0.0244)	(0.0308)	(0.0309)	(0.0777)
700	-0.0290	0.0608	-0.0793**	-0.0454*	-0.0331	-0.0194	-0.0480
	(0.0375)	(0.0476)	(0.0397)	(0.0254)	(0.0278)	(0.0238)	(0.0753)
800	0.107**	-0.0494	-0.0191	-0.0190	-0.0729	-0.0542	0.0437
	(0.0515)	(0.0408)	(0.0300)	(0.0244)	(0.0506)	(0.0343)	(0.0864)
900	0.0610	-0.0526	-0.0394	-0.0258	-0.120***	-0.0801***	-0.0270
	(0.0425)	(0.0452)	(0.0421)	(0.0316)	(0.0380)	(0.0306)	(0.0821)
1000	0.0493	-0.0925***	-0.0197	-0.00330	-0.0854***	-0.0526**	-0.0778
	(0.0474)	(0.0354)	(0.0306)	(0.0229)	(0.0273)	(0.0237)	(0.0936)
1,000<	-0.101***	-0.0738**	-0.0375	-0.0132	-0.126***	-0.0995***	-0.212***
	(0.0344)	(0.0343)	(0.0296)	(0.0222)	(0.0287)	(0.0281)	(0.0572)
R^2	0.327	0.402	0.152	0.121	0.276	0.233	0.375
N. Clusters	2628	2628	2628	2628	2628	2628	2628
N	63072	63072	63072	63072	63072	63072	63072
Baseline	0.647	0.210	0.286	0.208	0.688	0.539	1.307

Note: Estimates for regression coefficients of the bin specific distance-to-spike-counties treatment on un-adjusted mortality rates per 100,000 inhabitants from Equation 2. Standard errors clustered at the county level in parentheses. Each row reports the distance from counties in each bin, respectively, zero are the spike counties, 50 reports the coefficient for counties under 50 miles to the spike counties' population centroids. Statistical significance reported at the following levels: $^{*}p < 0.10$, $^{**}p < 0.05$, $^{*}p < 0.01$.

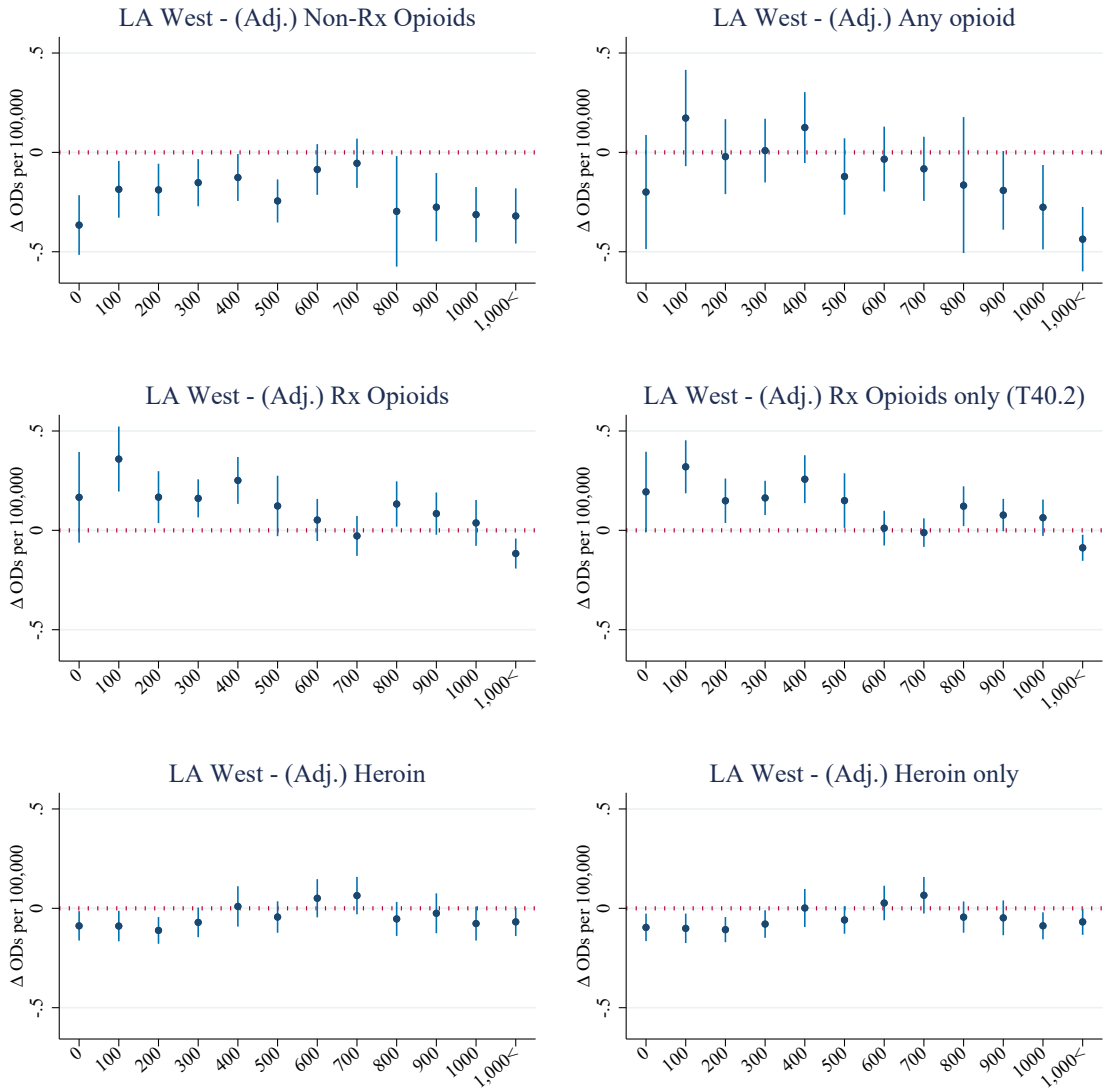
A.3 Robustness Exercises

Figure A3.1: Robustness DiD Distance-to-Spike and Opioid Mortality - Un-adjusted Mortality



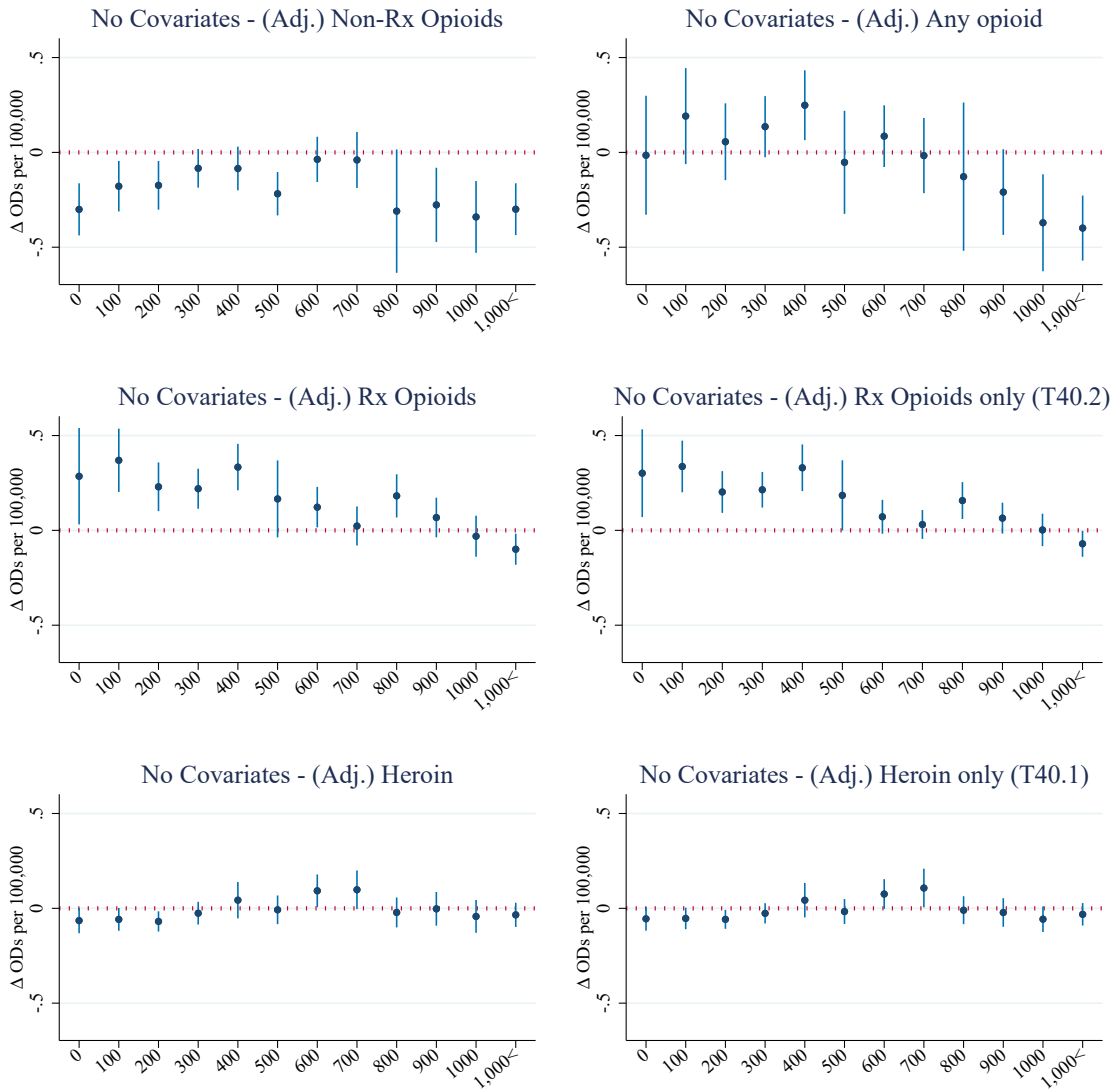
Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Each coefficient parameter captures the interaction between each of the bins of distance-to-spike counties (d) in miles, and the post-treatment period. In this exercise the mortality outcome variables were not adjusted following the correction suggested by Ruhm (2018).

Figure A3.2: Robustness DiD Distance-to-Spike and Opioid Mortality - Louisiana as Control in the West



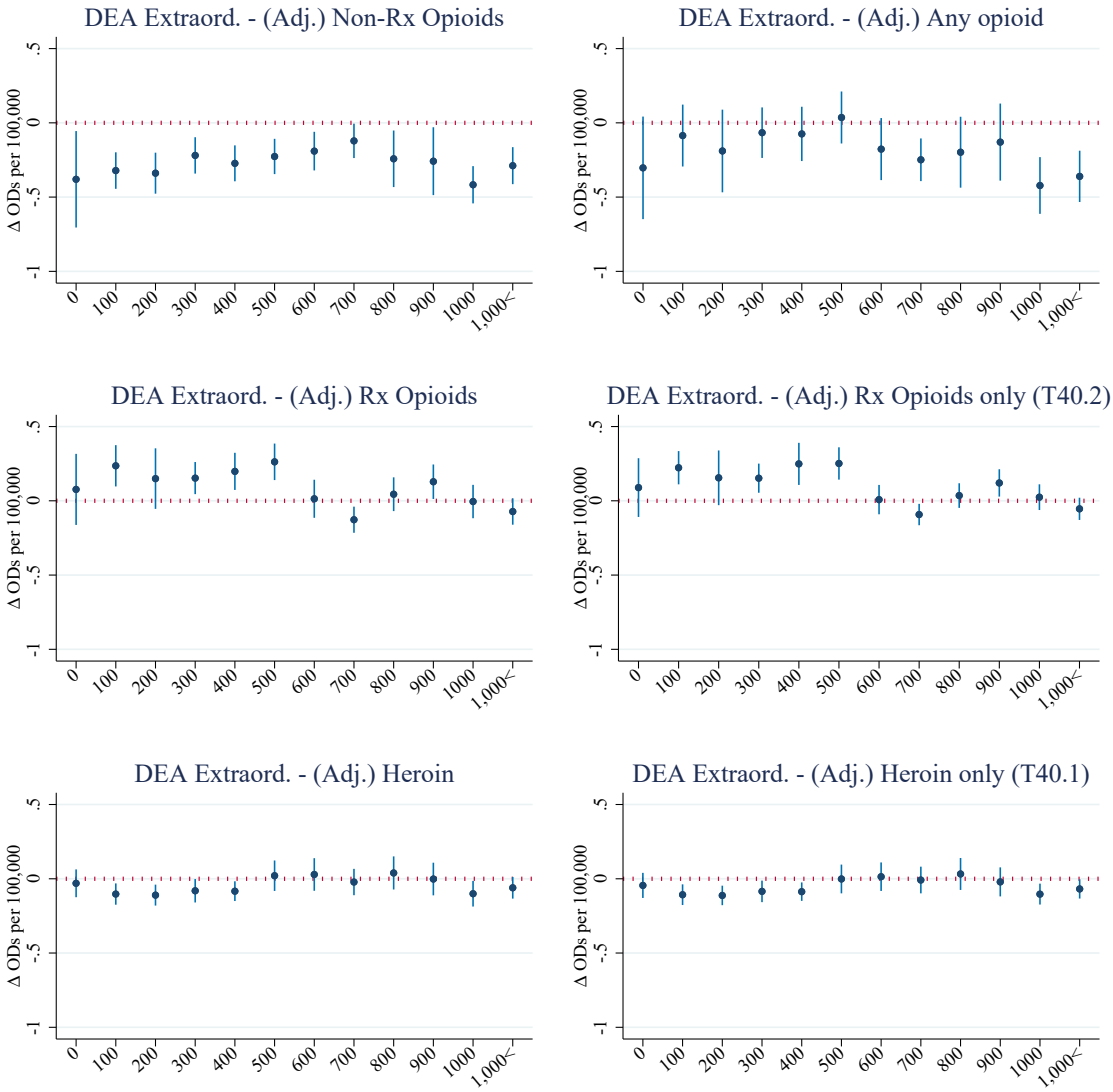
Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Each coefficient parameter captures the interaction between each of the bins of distance-to-spike counties (d) in miles, and the post-treatment period. In this exercise the state of Louisiana is part of the control units, with the exception of the spike counties in the state.

Figure A3.3: Robustness DiD Distance-to-Spike and Opioid Mortality - No Covariates considered



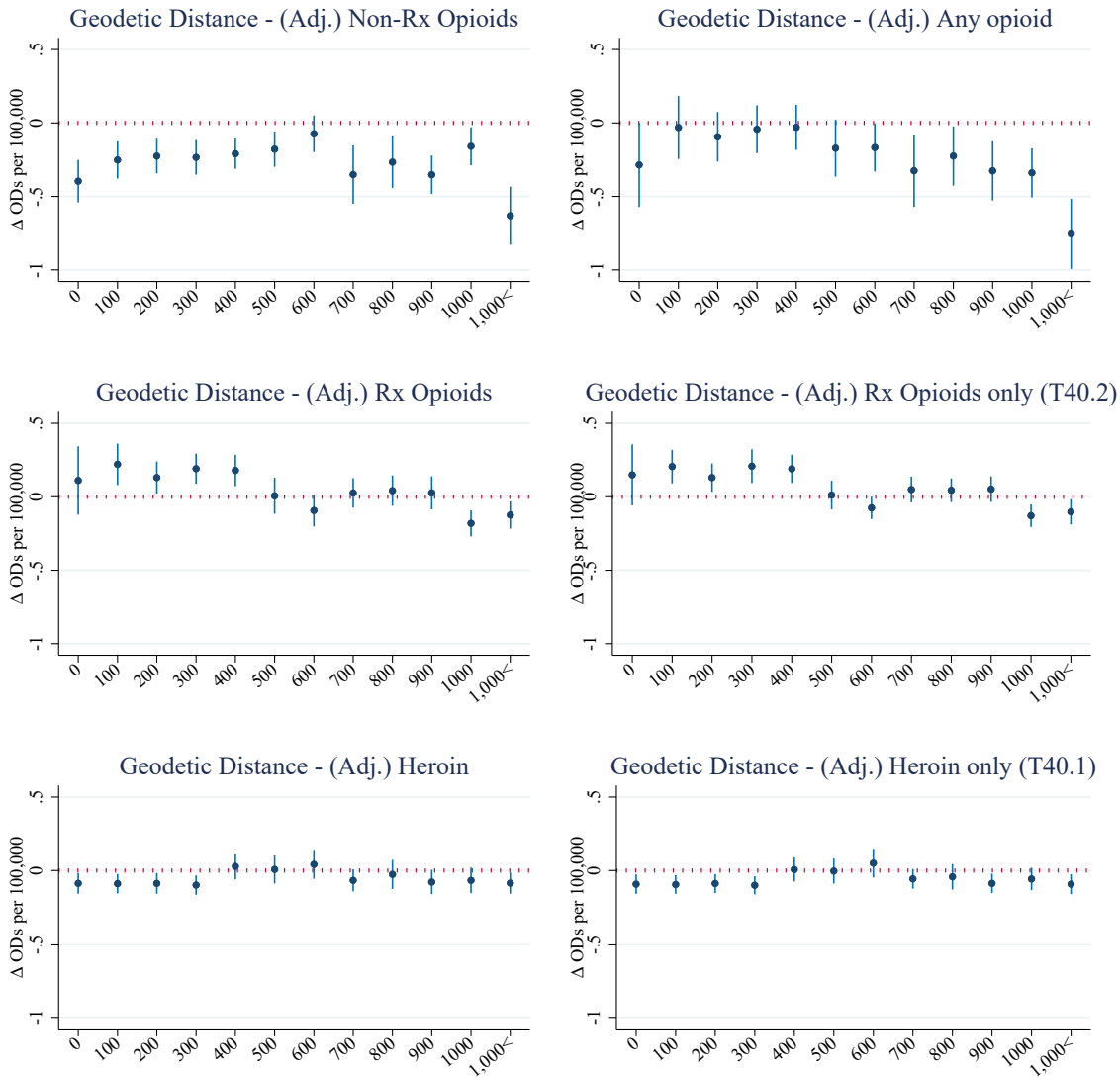
Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Each coefficient parameter captures the interaction between each of the bins of distance-to-spike counties (d) in miles, and the post-treatment period. In this exercise we have not included any covariates from time-changing county characteristics nor state policies.

Figure A3.4: Robustness DiD Distance-to-Spike and Opioid Mortality - Spikes from DEA Extraordinary Methods



Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Each coefficient parameter captures the interaction between each of the bins of distance-to-spike counties (d) in miles, and the post-treatment period. In this exercise to identify spike counties we use the DEA Extraordinary methods which imply a 200% increase in distribution of opioids in comparison to the 12 month moving average.

Figure A3.5: Robustness DiD Distance-to-Spike and Opioid Mortality - Geodetic Distance



Notes: Each panel presents the set of parameter estimates for β_d from Equation 2 and their 95% confidence intervals. Each coefficient parameter captures the interaction between each of the bins of distance-to-spike counties (d) in miles, and the post-treatment period, which we set in 2008. In this exercise, for the exposure to the spike variable, we use geodetic distance (equivalent to the state line over the surface of the Earth), instead of driving distance.