The Effects of OxyContin Reformulation on Homicides[*][†][‡]

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Abstract

This study examines whether a supply-side intervention on prescription drugs, the introduction of an abuse-deterrent formulation of OxyContin, increased the homicide rate in the United States. If so, could this effect be mitigated? First, leveraging cross-state variation in pre-reformulation OxyContin exposure, difference-in-differences estimates show that OxyContin reformulation led to a transitory increase in homicide rate. This effect is strongest among victims between 15 and 24, which is plausibly due to an increase in illicit drug distribution associated with the rise in post-reformulation demand for illicit opioids. The study then explores the role of medical marijuana laws in moderating post-reformulation homicide rate and finds that medical marijuana legalization is associated with a reduction in post-reformulation homicide rate. This effect is strongest among states where the pre-reformulation OxyContin misuse rates are high.

Keywords: OxyContin Reformulation, Homicide, Medical Marijuana Laws, Prescription Opioids, Illicit Drug Markets

JEL Codes: I12, I18, K32, K42

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1 Introduction

Between 1999 and 2023, the opioid crisis has claimed the lives of an estimated of 807,822 Americans (National Center of Health Statistics, 2024). In 2023, despite the first decline in nearly two decades, the number of overdose deaths involving any opioid remained approximately nine times higher than in 1999. The sources of opioids involved in these overdoses, however, are distinct by period. In the early phase (first wave) of the crisis, they often involved prescription opioids, whereas, after 2010 (second and third wave), illicit opioids (for example, heroin and fentanyl) have become increasingly the underlying causes of opioid overdose deaths (CDC, 2023). This observation highlights the critical role of illicit drug markets in understanding the impact of the opioid crisis. In fact, Maclean et al. (2022) attributes the relatively higher crime rates in more recent waves of the opioid crisis to more significant interaction with black markets by consumers of illicit drugs.

One prescription opioid, OxyContin, is particularly relevant in such interaction. Introduced in 1996 by Purdue Pharma, this medication quickly became the second most prescribed pain management drug in the United States (CDC, 2023), driven by a highly successful marketing campaign (Van Zee, 2009). However, it is also one of the most widely abused prescription opioids, as its active ingredient, Oxycodone, has a high potential for addiction (Cicero et al., 2005). In 2010, as part of the effort to deter widespread nonmedical use of OxyContin, the FDA approved a reformulated version of the drug that significantly reduced its potential for abuse. As a result, dependent users turned to other alternatives, with heroin becoming the most common substitute (Cicero and Ellis, 2015), igniting the heroin epidemic (Evans et al., 2019). This surge in demand for illicit alternatives likely intensified the level of illegal drug market activities, such as drug distribution involving gangs, which are often linked to homicide (Goldstein et al., 1997; Werb et al., 2011), yet there is limited causal evidence (Park, 2021) documenting this effect, and whether this effect could be moderated remains unanswered. This paper leverages cross-state variation in pre-reformulation OxyContin nonmedical use rates from the National Survey of Drug Use and Health (NSDUH), difference-in-differences research designs, and mortality data from the National Vital Statistics System (NVSS) to investigate whether the OxyContin Reformulation increased homicide rates from 2000 to 2017 and whether this effect varies by victim age group. Additionally, this paper examines whether medical marijuana legalization could moderate the rise in homicides associated with this policy shift.

To assess whether the reformulation of OxyContin increased homicide rates, this paper adapts the identification strategy from Alpert et al. (2018), leveraging cross-state variation in pre-reformulation nonmedical exposure to OxyContin as the source of identification. This exposure enables prediction of the reformulation's differential impact on homicide rates across states with high versus low pre-reformulation exposure. This paper implements a two-way fixed effects (TWFE) regression model to capture the differential impact of OxyContin Reformulation on homicide victims, decomposing it into a level and a linear time trend component. Estimates of the preferred specification show that the coefficient associated with the level (or linear time trend) component of the treatment effect is measured at 0.945 (-0.0768) homicide victims per 100,000 individuals and is statistically

significant (insignificant) at the 99% (90%) confidence level[1].

Additionally, this paper implements an event study specification to study the how OxyContin Reformulation impact homicide rates dynamically. The findings suggest that the differential increase in post-reformulation homicide is transitory, approaching zero in the long run. However, the linear predicted treatment effects is estimated at 0.407 at the end of the study period, albeit statistically indistinguishable from zero. To mitigate the concern for this inconsistency, this paper considers 2005 - 2009 age-adjusted cancer mortality rates as a control and allows it to have distinct level and linear time trend parameters. The rationale is that cancer mortality rates could serve as a proxy for the legitimate demand for prescription opioids, reflecting pain management need for severe pain in cancer and palliative care. Estimates of the augmented specification show that the coefficient associated with the level (or linear time trend) component linked to the pre-reformulation OxyCOntin nonmedical exposure is measured at 1.121 (-0.222) homicide victims per 100,000 individuals and is statistically significant (insignificant) at the 99% (90%) confidence level, and the linear predicted treatment effects fell close to zero by year 2015. In contrast, the linear time trend component linked to cancer mortality is measured at 0.00773 homicide victims per 100,000 individuals and is statistically significant at the 99% confidence level. Taken together, these findings suggest that while the OxyContin reformulation initially contributed to a rise in homicide rates, its effect is transitory, as later events such as the influx of illicit fentanyl (Ciccarone, 2019; Powell and Pacula, 2021), nationwide opioid tapering (Busse et al., 2016; Dowell et al., 2016; Guy Jr et al., 2017), and protests against police militarization (Premkumar, 2019) might be playing a moderating role.

To test whether the impact of the OxyContin reformulation on homicide is heterogeneous across age groups, this paper uses a triple difference-in-differences identification strategy modified from Owens (2014). This strategy compares homicide rates across states, before and after the OxyContin Reformulation, and between a chosen age group and the rest of the age distribution. The findings suggest that the increase in homicide rates induced by the reformulation concentrated on younger victims. Estimates from the preferred specification show an 8.152 homicide victim per 100,000 individuals difference between victims aged 15-24 and other age groups. Given that (1) homicide victims due to gang activities are generally younger than those due to the influence of drugs and (2) the likelihood of becoming homicide victims is many times higher for youth gangs members than that of the general population(Morales, 1992; Decker Scott and Van, 1996; Levitt and Venkatesh, 2000), this finding provides suggestive evidence that the increase in post-reformulation homicide victims is primarily due to illicit drug market activities[2] .

This paper hypothesizes that medical marijuana legalization could mitigate post-reformulation homicide, with stronger effects in states with high pre-reformulation OxyContin nonmedical use rates. This hypothesis rests on the asuumption that cross-state variation in pre-reformulation

[1]The point estimate of the coefficient associated with the level component is equivalent to roughly 16% of the average pre-reformulation homicide rate.

[2]Youth gang is another name for street gangs, typically consists of members who are in their adolescence and early 20s.

OxyContin misuse primarily reflects differences in physicians' prescribing behaviors for mild-to-moderate, non-cancer pain management. Medical Marijuana Legalization may reduce homicide by offering a legal alternative to illicit opioids, thereby lowering demand for illicit opioids and associated violence. To support the underlying assumption of the homicide-moderation hypothesis, this paper uses the publicly available National Health Interview Survey (NHIS) data to demonstrate there is positive pre-reformulation association between health insurance coverage and cross-region OxyContin nonmedical use rates among individuals reporting any level of work-limiting pain, a pattern that disappears for those with severe pain. Medical Expenditure Panel Survey (MEPS) show a positive correlation before 2010 between chronic low back pain and OxyContin misuse but not among individuals with cancer diagnoses, further suggesting that misuse misuse was not primarily driven by cancer-related or severe pain management. Lastly, to address variation in the timing of medical marijuana law passage, this paper uses a staggered difference-in-differences approach (Callaway and Sant'Anna, 2021) to estimate the effect of medical marijuana laws on homicide. By grouping states based on their pre-reformulation OxyContin nonmedical use rates and summarizing treatment effects by year, the analysis reveals that treatment effects are negative in the years immediately following OxyContin reformulation, but only in states with above-median pre-reformulation misuse exposure.

These findings of this paper contribute to the growing literature on the unintended consequences of OxyContin Reformulation, such as law enforcement outcomes (Mallatt, 2022; Doleac and Mukherjee, 2022; Deiana and Giua, 2021), labor market outcomes (Park and Powell, 2021), traffic accidents (Betz and Jones, 2022), hepatitis (Powell et al., 2019; Beheshti, 2019), and child maltreatment (Evans et al., 2022). More broadly, they contribute to a growing empirical literature in economics on supply-side policies aiming at curbing the opioid crisis, including OxyContin reformulation (Alpert et al., 2018; Evans et al., 2019; Powell and Pacula, 2021), triplicate prescription programs (Alpert et al., 2022), pain management clinic laws (the "pill mill" laws) (Mathur, 2021; Chisom, 2020; Kaestner and Ziedan, 2023; Mallatt, 2022), must-access prescription drug monitoring programs (PDMP) (Evans et al., 2022; Wang, 2021; Buchmueller and Carey, 2018), and Good Samaritan Laws (Rees et al., 2019). The contribution of this paper is two-fold. First, they provide strengthening evidence that the reformulation of OxyContin led to increase in homicide victims. Such increase is likely transitory, and concentrates on victims between 15-24 year old. Second, the analysis highlights how medical marijuana laws moderated these adverse effects, offering a concrete example of how one supply-side drug policy's unintended consequences can be mitigated by another supply-side policy designed for a different substance. This suggests that indirect interventions could be effective in similar future events, provided that the population affected by such interventions is identified.

The rest of this paper is organized as follows. The next section Section 2 provides a brief overview of the background on OxyContin reformulation, the evolution of the illicit drug market, and policies concerning prescription opioids during the study period. Section 3 describes the primary data sources, while Section 4 outlines the empirical strategies used. Section 5 provides

empirical evidence of whether OxyContin reformulation led to an increase in homicide rates and in which age group this effect is concentrated. Section 6 discusses robustness, sensitivity, and falsification tests that support the main results and explores whether medical marijuana laws mitigated post-reformulation homicides. Section 7 concludes the paper.

2 Background

2.1 OxyContin and OxyContin Reformulation

OxyContin, introduced in 1996 by Purdue Pharma, is the brand name of the extended-release formulation of Oxycodone Hydrochloride. Its active ingredient, Oxycodone, is a semisynthetic opioid typically used for the management of pain (Drug Enforcement Administration, Diversion Control Division, Drug & Chemical Evaluation Section, 2023). The long-acting formula of OxyContin claimed to have approximately 12 hours of continuous pain relief, a substantial improvement over previous pain medications [3]. However, the abuse potential of OxyContin became evident as patients discovered that crushing or dissolving the pill released the entire Oxycodone dose instantly instead of continuously [4]. Moreover, Purdue Pharma conducted a highly effective marketing campaign that misrepresented OxyContin's potential for abuse to doctors and patients, resulting in significant market penetration but also widespread nonmedical use[5] (Van Zee, 2009). By 2010, OxyContin's sales exceeded $3 billion, ranking it among the top-selling prescription drugs as well as one of the most commonly prescribed opioid painkillers in the United States (Bartholow, 2011). OxyContin's abuse potential and pervasive use have led experts to link OxyContin to the escalation of the opioid epidemic, with studies indicating its introduction as a critical factor in the rise of overdose deaths since 1996 (Kolodny et al., 2015; Alpert et al., 2022).

In April 2010, in response to the growing concerns over abuse, Purdue Pharma released a reformulated version of OxyContin and subsequently stopped the distribution of the initially formulated version in August of the same year. The reformulated version maintained the therapeutic benefits of the drug for legitimate pain management needs. However, compounded with the high-molecular-weight polyethylene oxide, the pills turn marshmallows when crushed with force and gooey when dissolved (Kibaly et al., 2021), making them difficult to abuse by traditional means, such as snorting or injecting. The reformulation of OxyContin significantly increased the effort needed to abuse the drug (Cicero and Ellis, 2015), successfully reducing the nonmedical use of OxyContin (Cicero et al., 2012). Consequently, it drove users toward alternative illicit opioids, notably heroin (Cicero et al., 2013). Therefore, first and foremost, this shift can be attributed to the pharmacological parallels

[3] An investigation by LA Times (Ryan et al., 2016) concluded that OxyContin lasted shorter than 12 hours for many patients, regardless of dosage and formulation. On the two-pills-a-day scheme, these patients usually found their pain insufficiently managed.

[4] On the 12-hour schedule recommended by Purdue Pharma, many patients developed opioid withdrawal symptoms, including cravings for OxyContin.

[5] GAO (2003) concluded that Purdue Pharma's sales force actively promoted OxyContin to physicians, especially primary care specialists, for treating moderate-to-severe noncancer pain.

between oxycodone and heroin, both being opioid agonists and possessing comparable potency[6] (Kaiko et al., 1981; Curtis et al., 1999). Their analgesic effects stem from the ability to bind to opioid receptors in the brain, effectively blocking the transmission of pain signals [7].

2.2 Evolution of U.S. Illicit Drug Market, 2000 - 2010

The increasing availability of heroin in the United States from 2000 to 2010 further facilitated the transition from nonmedical use of prescription opioids to illicit drug market. In the early 2000s, OxyContin was sometimes referred to as "poor man's heroin." due to its relatively lower cost when covered by health insurance (US Dept of Justice and of America, 2001). However, its street prices were much higher[8]. Consequently, uninsured nonmedical users of OxyContin have been consistently switching to heroin[9], a more affordable alternative[10], well before the reformulation of OxyContin. The increase in demand for heroin was swiftly met by an expansion of international drug trafficking activities in the United States. (of Justice, 2010; Ciccarone, 2019). Heroin trafficking are most prevalent in eastern states, where Mexican DTOs have expanded their distribution networks into areas previously dominated by South American heroin. By 2010, the U.S. heroin supply has shifted from four global sources (Southeast Asia, Southwest Asia, Mexico, and Colombia) to being predominantly supplied by Mexico and Colombia. This shift created a regional divide in prevailing heroin types, with Colombian-sourced heroin dominating the eastern U.S. and Mexican "black tar" heroin becoming the primary form in the western U.S.

Traditionally, a significant portion of the South American heroin smuggled into Florida is transshipped to other states, principally in the northeastern and, to a lesser extent, southeastern United States. Towards the end of 2000s, evidence shows that Mexico-sourced heroin saw significant increases in both purity and quantity, coinciding with the overwhelming dominance of the Southwestern border as the primary entry point for heroin into the United States. Between 2005 and 2009, over 98.5% heroin smuggled into the United States through land were through the Southwestern border. Mexican drug trafficking organizations (DTOs) routinely relied on Southwest Border gangs to secure smuggling operations and maintain control over trafficking routes. These gangs used intimidation, extortion, and violence to enforce control and collect unpaid debts, primarily in Mexico and, to a lesser extent, in U.S. border regions like California and Texas.

Figure 1 presents the 2000 - 2012 average heroin price by census region and by quartiles of

[6] To be more precise, both heroin and oxycodone are pure opioid agonists in the Phenanthrenes family, the prototypical opioid group including (but not limited to) morphine and hydrocodone (Trescot et al., 2008).

[7] There are three main types of opioid receptors in the human body: Mu (μ), Kappa (κ), and Delta (δ). Heroin and oxycodone primarily stimulate μ receptors (the "morphine receptors") to produce analgesia (Trescot et al., 2008)

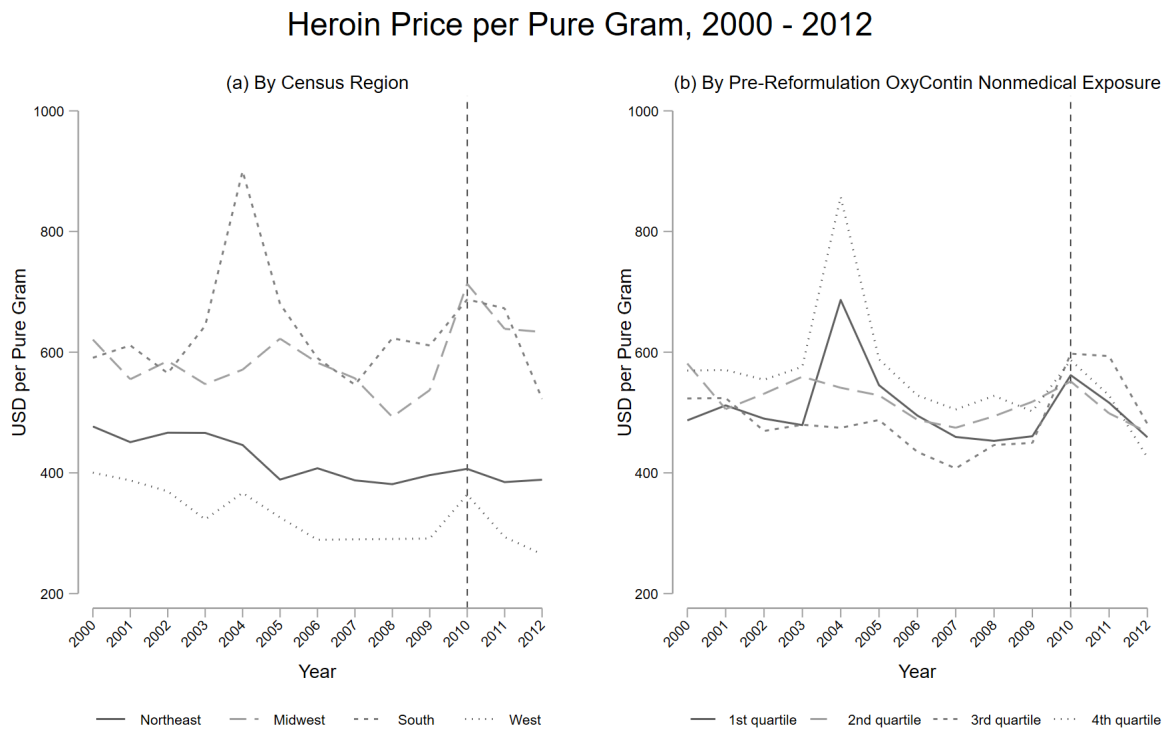
[8] According to the Cincinnati Police Department, the markup could be over 1000%.

[9] A typical progression from OxyContin prescription to heroin use, according to LA Times (Ryan et al., 2016), is the following. Patients prescribed OxyContin under Purdue Pharma's 12-hour recommendation often found the drug's effects wearing off prematurely. This led physicians to either prescribe it more frequently or at higher dosages and patients to deviate from the recommendation to satisfy their pain management needs. However, insurance companies frequently denied claims for additional prescriptions, leaving patients with limited options and pushing some towards heroin as an alternative.

[10] Typical nonmedical users of OxyContin could sustain their habit at a cost of one-third to one-half that of prescription opioids by switching to heroin (of Justice, 2010)

Pre-Reformulation OxyContin Nonmedical Use rates. Panel (a) shows considerable regional disparities in cross-region evolution of heroin prices. Panel (a) highlights significant regional disparities in the evolution of heroin prices, with Southern states—and to a lesser extent, Midwestern states—experiencing a price surge around 2005. Notably, panel (b) reveals that this price hike occurred in states within both the top and bottom quartiles of OxyContin exposure, suggesting that supply-side factors in the illicit drug market may have contributed. Despite these regional differences, heroin prices generally show a noticeable increase from 2009 to 2010, followed by a sharp decline to pre-reformulation levels after 2010. Taken together, these findings provide suggestive evidence that the OxyContin reformulation might coincide with escalated illicit drug market activity during its implementation year and such association likely dissipated over time.

Figure 1: Average Heroin Street Prices: by Census Region and Misuse



Sources: Alpert et al. (2018)

Notes: This figure presents average heroin street price (adjusted for purity) by census region (Panel (a)) and by pre-reformulation OxyContin nonmedical exposure quartiles (Panel (b)) between 2000 and 2012 (inclusive). The heroin price data is taken from the replication package of Alpert et al. (2018). The misuse data is 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

2.3 Evolution of Policies Regarding Prescription Opioids

Recent research suggests that between mid-1990s and 2010, the drastic increase in prescription opioid use and overdoses was primarily due to an increase in the use of opioids to treat chronic non-cancer pain (Boudreau et al., 2009; Von Korff et al., 2008), likely driven by a combination of aggres-

sive pharmaceutical marketing similar to that of OxyContin (Van Zee, 2009) and social/regulatory policy advocating for the liberal use of opioid analgesics (Veterans Health Administration, 2000; Joint Commission on Accreditation of Health Care Organizations, 2001). Between 1991 and 2011, the estimated total number of opioid prescriptions in the United States increased from 76 million to 219 million (Compton et al., 2015). Between 2000 and 2010, the estimated prescription opioid users among adult Americans jumped roughly 60 percentage points, whereas major disability and health status metrics either declined or stayed unchanged among the users (Sites et al., 2014). The cross-state evaluation shows that variation in underlying health status cannot sufficiently explain variation in opioid prescription behaviors (Paulozzi et al., 2014). Although the amount of opioids prescribed in the United States peaked in 2010 and subsequently declined each year through 2015, it remained nearly three times higher than in 1999. Substantial variations in prescribing patterns at the county level highlight inconsistent clinical practices and a lack of consensus on appropriate opioid use(Guy Jr et al., 2017). For example, patients routinely received opioid prescriptions from procedures as standard as wisdom tooth extraction, estimated to have been performed over 3.5 million times in 2004 (Harbaugh et al., 2018).

As the nation became increasingly aware of the ongoing opioid crisis, an array of restrictive supply-side policies aiming at reducing access to prescription opioids have been implemented at the national and state level, including OxyContin reformulation in 2010, pain management clinic laws (the "pill mill" laws), must-access prescription drug monitoring programs (PDMP), the rescheduling of Tramadol in 2014 (Gupta et al., 2023), and CDC Guideline for Prescribing Opioids for Chronic Pain in 2016 (Busse et al., 2016; Dowell et al., 2016), resulting consistent decrease in prescription opioids consumption (Guy Jr et al., 2017). In addition, in recent years, Medicaid programs have been pursuing strategies for alternative, non-opioid solutions for managing chronic pain (Traylor, 2019). The post-2010 change of wind likely gears physicians toward the more conservative side of prescribing opioid painkillers. Recent studies have found that patients already on prescription opioids are routinely denied treatment (Lagisetty et al., 2019, 2021), which again leads to illicit drug use for certain patients (Ti et al., 2015). Overly restrictive applications of CDC's prescription guidelines have been reported (Dowell et al., 2019), leading to opioid dose tapering and sudden discontinuation even for patients with pain associated with cancer, surgical procedures, or acute sickle cell crises (Kroenke et al., 2019) and severe withdrawal symptoms, uncontrolled pain, psychological distress, and suicide (Food et al., 2019).

3 Data

3.1 Homicide Rates

I use the publicly available version of the National Vital Statistics System's (NVSS) Multiple Cause of Death data from CDC WONDER to construct state-level homicide rates from 2000 to 2017. Operated by the National Center for Health Statistics (NCHS), this is the census of certificate-based deaths in the United States. I define homicide victims as those whose cause of death was due to

assault or sequelae of assault. This definition is consistent with CDC's Web-Based Injury Statistics Query and Reporting System (WISQARS) Fatal Injury Report's characterization of homicide and suicide in terms of ICD-10 codes[11]. Table 5 in the appendix displays the ICD-10 coding schemes for homicide.

For constructing state-level homicide rates, I choose NVSS Multiple Cause of Death data over police report-based sources, such as the FBI's Uniform Crime Report (UCR) or National Incidence-Based Reporting System (NIBRS), because it is more representative of the United States residents population. Police report-based data are known to systematically underreport yearly homicide counts due to non-participating police agencies and homicide cases not reported to the police. Moreover, some participating agencies only report part of the year's data (Kaplan, 2019). On the other hand, the limitation of the public version of this data is missing data due to privacy restriction[12]. I impute those missing values with murder counts obtained from the UCR Offenses Known and Clearances by Arrest data.

3.2 OxyContin and Pain Relievers Misuse

I follow Alpert et al. (2018) and use the National Survey of Drug Use and Health (NSDUH) for the 2004-2009 average of state-level nonmedical use rates of OxyContin as well as other pain relievers. Conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA) annually, NSDUH is a nationally representative, household-level survey collecting self-reported substance use and mental health information on individuals aged 12 or above. In particular, the survey asks about its takers' history of nonmedical use of pain relievers, including OxyContin, since 2004. These measures are publicly available from NSDUH's Restricted-Use Data Analysis System (RADS)[13] in aggregated two-year, four-year, or eight-year waves. The 2004-2009 state-level measures are obtained by averaging the 2004-2005, 2006-2007, and 2008-2009 corresponding values to mitigate the concern for measurement errors (Powell and Pacula, 2021).

Although NSDUH has its limitation[14] The main advantage of NSDUH is that the survey questions are substance-specific. Moreover, they specify non-medical use of these substances[15]. This

[11]Excluding deaths due to terrorism. The underlying data for the WISQARS Fatal Injury Report is also NVSS's Multiple Cause of Death. In this sense, the two data sources are equivalent. Another data source of violent death is WISQARS's National Violent Deaths Reporting System (NVDRS); however, only a handful of states participated in this program in the early 2000s.

[12]CDC WONDER has the following restriction regarding output on its data portal: if the requested number of deaths is smaller than 10, the number will be suppressed and labeled as such. If the number of deaths is lower than 20, this number will be reserved. However, the crude and age-adjusted rates will be labeled "Unreliable."

[13]https://datatools.samhsa.gov/. Note that the variable of interest, OXYCONTIN, with the label "EVER USED OxyContin NONMEDICALLY," is not directly available from RADS at the state level. When requested, the system will suppress the results on the grounds of confidentiality. However, the website allows its users to recode the requested variables. After grouping the original codes into either 0 or 1, state-level OxyContin can be accessed.

[14]Underreporting is common in such survey questions. Harrell(1997) documents that for questions in NSDUH asking about the use of illicit drugs, the accuracy rates range from 68 to 96 percent. Another limitation of NSDUH is that it only surveys individuals with valid addresses (i.e., it leaves out the homeless population).

[15]NSDUH does not have information on legitimate use of OxyContin and other pain relievers; such information would have to come from data sources such as DEA's Automation of Reports and Consolidated Orders System (ARCOS).

makes NSDUH ideal for information measuring OxyContin and other pain reliever misuse rates for the years before the reformulation of OxyContin.

3.3 Summary Statistics

I present the averages of state-level intentional death rates, substance misuse rates, socio-economic characteristics, and demographics between year 2000 and year 2009 (inclusive) in Table 1. Consistent with prior literature, I group these statistics into three groups. The "All" column corresponds to statistics of all 50 states plus the District of Columbia. I then characterize states either as "high" or "low," depending on whether their 2004-2009 OxyContin misuse rates are above or below the median.

A few patterns can be observed in this table. Regarding demographics, The "high" states are typically smaller in population sizes, whiter, and older. They also exhibit higher misuse rates of pain relievers other than OxyContin, suggesting a positive correlation between nonmedical use and related substances. Lastly, the "high" states, on average, saw lower homicide rates in the ten years before OxyContin reformulation. These findings suggest the possible omitted variable bias in the baseline specification. I will investigate this possibility in the main results and the robustness checks sections.

3.4 Descriptive Statistics on Homicide Rates

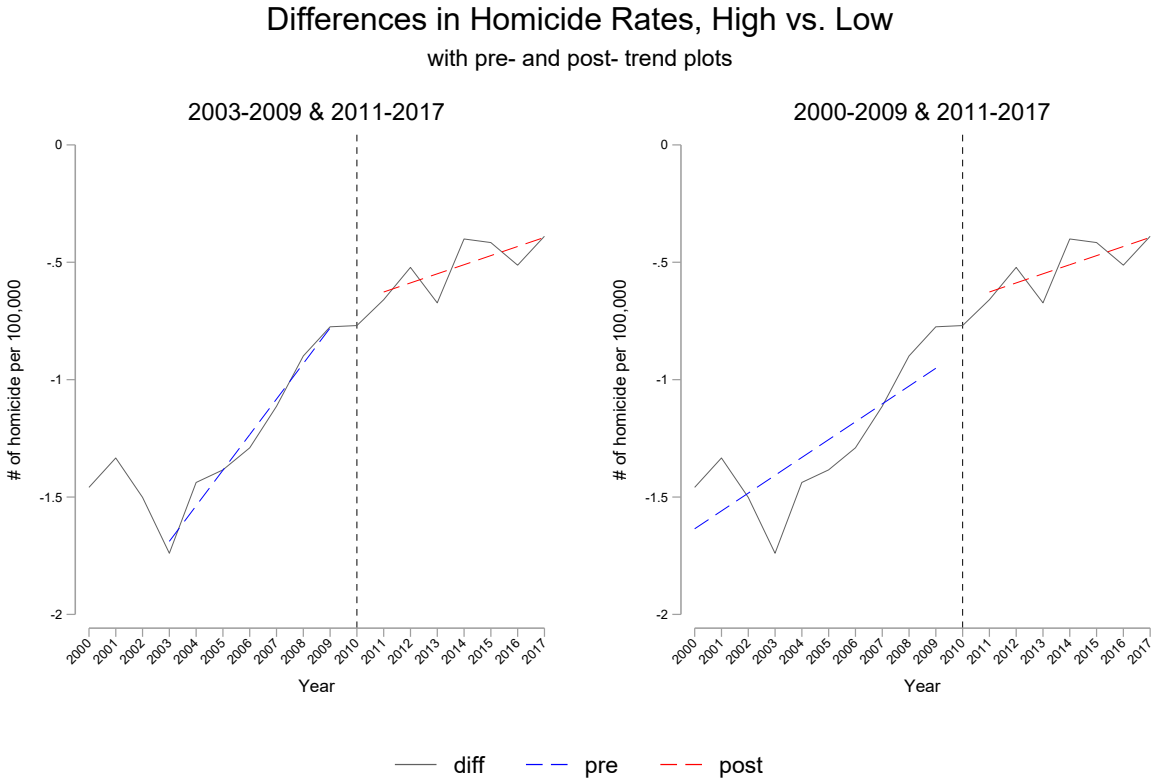
This paper begins the investigation of the effects of OxyContin Reformulation on homicide rates by describing how these rates evolved differently by pre-reformulation OxyContin misuse rates, categorizing states into "high" OxyContin nonmedical exposure states (greater-than-median 2004–2009 misuse rates) and "low" exposure states. This paper presents the the differences between the "high" OxyContin nonmedical exposure and "low" OxyContin nonmedical exposure state homicide rates in Figure 2. Figure 2 presents these differences, with Panel (a) showing matched lines for "symmetric" study periods (excluding 2010) and Panel (b) covering the entire study period. A clear "trend break" is observable in Panel (a) suggesting that OxyContin reformulation is graphically associated with differential impacts on homicide rates depending on pre-reformulation misuse levels. However, this pattern is not presented in Panel (b). Whether this association is causal will be explored in subsequent sections.

Table 1: Summary Statistics, 2000 - 2009

	All	High	Low
Outcomes (per 100,000)			
Homicide Rate	5.71	4.35	7.12
Heroin Overdose Rates	0.38	0.42	0.34
Misuse Prior to Reformulation (%)			
2004-2009 OxyContin Misuse Rate	0.67	0.86	0.48
2004-2009 Other pain relievers Misuse Rate	6.48	7.13	5.79
Unemployment Rate (%)	5.24	5.11	5.37
College Degrees (%)	18.17	17.51	18.85
Gender (%)			
male	49.23	49.41	49.04
Race/Ethnicity (%)			
Hispanic	9.12	8.21	10.06
White	81.97	88.15	75.55
Black	11.72	6.67	16.98
Age (%)			
0-19	27.66	27.53	27.80
20-39	28.72	28.54	28.91
40-59	20.87	21.30	20.42
60+	9.07	9.19	8.95
Population	5770436.27	3431583.07	8202843.60
# of States	51	26	25

Notes: This table presents the unweighted average of state-level homicide death rates, heroin overdose death rates, substance misuse rates, socio-economic characteristics, and demographics between the years 2000 and year 2009 (inclusive). I report these statistics over three groupings for states: all 50 states in the US plus the District of Columbia, states with pre-reformulation OxyContin misuse rates above the median (the "high" states), and states with pre-reformulation OxyContin misuse rates below the median (the "low" states). The homicide and heroin overdose rates are calculated by dividing the year-state counts of deaths obtained from the National Vital Statistics System's (NVSS) Multiple Cause of Death data by corresponding state population estimates. Misuse rates are obtained using data from the National Survey of Drug Use and Health (NSDUH) and averaging over the 2004-2005, 2006-2007, and 2008-2009 waves. Unemployment rates are from Federal Research Economic Data (FRED). The population's percentage of people with at least a college degree is calculated using American Community Service (ACS) data. Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

Figure 2: Differences in Homicide Rates Between States with Different Levels of Pre-Reformulation OxyContin Misuse, 2000 - 2017



Notes: This figure presents the differences in average state-level homicide rates between the "high" and "low" states from the year 2000 and year 2017. The averages are weighted by state-year population estimates from the SEER program. The "high" states are those states with 2004-2009 OxyContin misuse rates above the median, and the "low" states are the rest. The data source for OxyContin misuse rates is the National Survey of Drug Use and Health (NSDUH).

4 Empirical Strategy

4.1 Effects of OxyContin Reformulation on Homicide Rates

To explore how Oxycontin reformulation affected homicide rates, this paper uses an event study specification and a fully parameterized specification. Both specifications use the same data and leverage the cross-state variation of nonmedical use of Oxycontin before the reformulation.

The event study specification is given by

$$y_{st} = \alpha_s + \beta_t + \delta_t * oc_s + \gamma_t * op_s + \sum_{i=m,f} \sigma_i * [tl_{2000} \times loc_i] + \epsilon_{st}$$

The independent variable of interest *oc* is 2004-2009 state-level OxyContin misuse rates, averaged using 2004-2005, 2006-2007, and 2008-2009 waves of NSDUH data to reduce measurement errors from the individual waves. It measures the scale of nonmedical users who would turn to

illicit alternatives after the reformulation of OxyContin, modeling its impact on the homicide rate. The estimates of interest for the event study specifications is the vector of δ_t. These estimated coefficients capture the would-have-been differences in each year's homicide victims per 100,000 individuals that would result from increasing pre-reformulation rates from their lowest to highest levels, conditional on the set of restrictions included. This paper further assumes states have "strong" parallel trends in the sense of Callaway et al. (2024) in homicide rates as the identifying assumption[16]. Although this assumption could not be tested directly in this context, visually inspecting the pattern of pre-reformulation estimated coefficients would provide suggestive evidence of its validity (Miller, 2023). Caetano and Callaway (2024) suggests including additional control variables would mitigate concerns over non-parallel pre-trends at the cost of more restrictive interpretations for the treatment effect coefficients. In addition, including "bad controls" could unintentionally undermine the causal interpretation when using two-way fixed effects (TWFE) linear regression estimators.

For this reason, the baseline event study specification includes a minimum set of control variables that help mitigate concerns over non-parallel pre-trend. How demographic and socio-economic variables influence the estimated results will be tested in Section 6.2. For a convenient comparison between pre- and post- reformulation estimates, the interaction term of the pre-reformulation OxyContin nonmedical exposure and the dummy variable for 2009 is excluded, and its coefficient is normalized to zero. This paper reports the point estimates of δ_t graphically, along with their upper and lower bands of 95% confidence intervals.

The fully parameterized specification is given by

$$y_{st} = \alpha_s + \beta_t + \sum_{i=m,f} \sigma_i * [tl_{2000} \times loc_i] + \eta_1 * [tl_{2000} \times oc_s] + \theta_1 * [tl_{2000} \times op_s]$$
$$+ \eta_2 * [tl_{2010} \times oc_s \times post_t] + \theta_2 * [tl_{2010} \times op_s \times post_t] + \eta_3 * [oc_s \times post_t] + \theta_3 * [op_s \times post_t] + \epsilon_{st}$$

The key estimates in the fully parameterized specifications are η_2 and η_3. η_2 represents the conditional post-reformulation counterfactual difference in homicide victims per 100,000 individuals, reflecting the impact of increasing pre-reformulation rates from their lowest to highest levels. η_3 captures the additional post-reformulation counterfactual difference in homicide rates not explained by η_2, assuming a constant rate of change over time for this residual difference. Together, η_2 and η_3 represent the static and time-varying components of the treatment effect, referred to in this paper as the "shift" and "posttrend" parameters. The identifying assumption aligns with that used for the event study specifications. In the main results section, this paper presents both the estimated values of η_2 and η_3 and the joint test results for $\eta_3 + t\eta_2$ (for $t = 0, 1, \ldots, 7$), a series of "X-year effects" that facilitate consistency comparisons with the event study specification results.

[16] This is an alternative definition to the standard parallel trend assumption. Suppose two states, A and B, have pre-reformulation OxyContin misuse rates r_A and r_B. The standard parallel trend assumption requires that the homicide rates in these two states would continue if the OxyContin Reformulation had not happened. The strong parallel trend assumption, however, requires that if r_B was assigned to state A, the evolution path of homicide would be the same as if state B had received its treatment. In other words, the global counterfactual should equal local counterparts.

The baseline fully parameterized specification includes linear time trends of pre-reformulation nonmedical OxyContin use rates. The corresponding coefficient is η_1, referred to as the "pretrend" parameter in this paper. The purpose is to control for spillover effects linked to pre-reformulation nonmedical OxyContin use that may have contributed to post-reformulation homicide rates, independent of the reformulation itself. As discussed in Section 2.2, nonmedical OxyContin users began switching to heroin well before the reformulation, driven by the cost difference between diverted OxyContin and heroin, which likely increased local heroin demand and, consequently, homicide rates. Without accounting for these dynamics, it would be difficult to distinguish whether the observed post-reformulation increase in homicide rates is due to pre-existing heroin market violence or new demand created by the reformulation.

post is a dummy variable indicating the passage of OxyContin Reformulation, which equals one if current year is greater than or equal to 2010. Motivated by the positive heroin price hikes observed in Figure 1, this paper defines year 2010 as the first year of receiving complete treatment even though it is partially treated[17]. Panel (b) of Figure 1 shows rapid decline of post-reformulation heroin street prices, though Panel (a) finds persistence in heroin prices among Midwestern states. These finding suggests that the US heroin market around 2010 was able to swiftly absorb the demand shock caused by OxyContin Reformulation. Therefore, changing the first treatment period from 2010 to 2011 would likely bias the estimated coefficient of interest toward zero. This possibility will be explored in Section 6.1.

In both baseline estimation models, subscripts s and t represent state and year, respectively. y is the outcome of interest, a vector of state-level homicide rates by year. The estimation includes all 50 states plus the District of Columbia. The study period spans from 2000 to 2017. The error terms, ϵ, are assumed to be normally distributed, and standard errors are clustered at the state level. All specifications are weighted by state population estimates sourced from the SEER program. *tl* calculates the difference between current year and the year indicated in the subscript. Lastly, α_s represents state fixed effects, capturing time-invariant differences across states, and β_t to control for national-level shocks, such as federal drug regulations or economic recessions, that vary over time.

op is a vector of 2004-2009 state-level misuse rates of other commonly used painkillers, controlling for possible substitution between OxyContin and legal alternatives (e.g., prescription opioids whose active substance is hydrocodone). Another reason for controlling nonmedical use rates of other painkillers is to mitigate concerns of omitted variable bias. States with high nonmedical OxyContin misuse in the late 2000s likely experienced factors such as overprescription and increased prescription drug diversion, which may have influenced homicide rates long before the OxyContin reformulation. However, measures for these factors are not present in the current data. Since prescribing patterns for OxyContin are likely correlated with those for similar painkillers, including exposure to close substitutes in the analysis helps address this issue. Alternatively, this paper also tests the baseline specification where the independent variable of interests is replaced by ratios

[17]Previous literature uses 2011 as the first year of receiving full treatment (e.g., Alpert et al. (2018))

of OxyContin misuse rates and other pain relievers misuse rates as in (Alpert et al., 2018) as a robustness check.

$loc_i, i = m, f$ is a set of two linear pre-reformulation time trends, where m denotes states bordering Mexico[18] and f denotes Florida. The majority of illicit substances consumed within the United States are trafficked illegally into the country internationally, with heroin mainly originating from Central American and South American countries. While Florida was traditionally the primary first stop of South American heroin distribution, from 2000 onward, states bordering Mexico have gradually become hubs for initial trafficking and distribution of heroin within the United States. The relatively high level of drug trafficking and distribution activities in these areas had existed long before the reformulation of OxyContin, possibly driving up post-reformulation homicide rates in those states through mechanisms unrelated to the substitution toward heroin. Another reason to include these trends, especially for the states bordering Mexico, is to mitigate the concern for competing substitutes of heroin. It is well documented that the counterfeit drug markets in Mexico allow US medical tourists to obtain fake prescription drugs without a prescription (Mackey and Liang, 2011; Dégardin et al., 2014; Friedman et al., 2023). Suppose a fake original formulated Oxycontin could be obtained just by crossing the border post-reformulation. In that case, some nonmedial users of OxyContin might opt for the counterfeit version of the original OxyContin instead of heroin, thereby reducing the validity of the treatment in these states. Although the sign of the net effect of omitting these trends is ambiguous, not including them will likely bias the estimated effects of the reformulation of OxyContin on post-reformulation homicide rates. To mitigate the concern that impact of the chosen geography time trends on homicide is spurious and/or incidental, this paper extends the baseline event study specification to with additional set of trends, including states bordering Canada, Hawaii and Alaska (the "offshore" states), and states reported by the police to have frequent, significant heroin seizures before the reformulation of OxyContin[19].

4.2 Specification for Studying the Heterogeneous Effects on Age Groups

This section investigates the heterogeneous effects of OxyContin reformulation on homicide rates by age group. It is well documented that homicide occurrences are distributed unequally across the age spectrum (Almgren et al., 1998; Gartner, 1990; Pampel and Williamson, 2001; Cook, 1981). Typically, the victimization rate quickly climbs during the adolescent years, peaks around 20, and gradually declines afterward (Perkins, 1997). Whether OxyContin reformulation causally shifts this distribution remains to be tested.

This section augments the baseline difference-in-differences specification by interacting with age group indicators to achieve this goal. Specifically, It test the following triple-difference specification

[18] CA, AZ, NM, TX.

[19] AZ, CO, FL, IL, NY, WA. Source: Metropolitan Areas Most Often Identified as Origination and Destination Points for Seized Drug Shipments, by Drug, 2008-2009 (National Drug Threat Assessment, 2010)

with the same notations as in Section 4.1

$$
\begin{aligned}
y_{ast} = \alpha_s + \beta_t + \gamma_a + \eta_1 * [tl_{2000} \times oc_s] + \eta_2 * [tl_{2010} \times oc_s \times post_t] + \eta_3 * [oc_s \times post_t] \\
+ \eta_4 * [tl_{2000} \times age_a] + \eta_5 * [tl_{2010} \times age_a \times post_t] + \eta_6 * [age_a \times post_t] \\
+ \eta_7 * [tl_{2000} \times oc_s \times age_a] + \eta_8 * [tl_{2010} \times oc_s \times age_a \times post_t] + \eta_9 * [oc_s \times age_a \times post_t] + \epsilon_{ast}
\end{aligned}
$$

In this specification, y_{ast} is homicide per 100,000 individuals at age group a, year t, and state s. This paper consider seven age groups: 5-14, 15-24, 25-34, 35-44, 45-54, 55-64, and the reference group of victims below five or above 65. The age-specific homicide victim counts are similarly obtained from the National Vital Statistics System (NVSS) and complemented by Supplemental Homicide Reports (SHR)[20]. It estimates age-state homicide rates by dividing these counts by population estimates in their corresponding cells, calculated from the SEER program. The standard errors are clustered at the state and age group levels.

All regressions include a set of state, year, and age group dummies in this specification. In particular, it includes age group dummies instead of age group-by-state dummies. This is based on the following two observations. First, institutions and the culture in the United States display differential attitudes towards their subjects based on age. However, such differences are not likely to differ massively across states. Second, and more closely related to the current discussion, homicide-generating activities are associated with participants' age, and such associations are not likely to differ across states. For example, New York and Montana have different rates of homicide related to drug trafficking. This is most likely due to varying levels of organized crimes operated by similarly aged individuals in these two states. Still, it is unlikely (hypothetically) that in Montana, most of the drug trafficking activities are conducted by senior citizens.

age_a is an indicator of a specific age group a, equals one if an observation is of that age group and zero otherwise. The specification allows pre-reformulation OxyContin misuse rates and the chosen age group to have a linear time trend effect on homicide rates, captured by η_1 and η_4. It also allows these variables to have separate post-reformulation average treatment effects, captured by η_3 and η_6, respectively. Furthermore, these two effects can have their post-reformulation time trends on homicide rates, measured by η_2 and η_5. However, the estimates of interests are η_7, η_8, and η_9 as they capture the various OxyContin misuse-induced effects between the chosen age group and the rest. Precisely, η_7 measures possible differential time trend of pre-reformulation OxyContin misuse rates on homicide rates between the chosen age group and all others. η_9 measures the age group-specific average treatment effect of reformulating the selected age group over the other age groups. η_8 captures this effect's possible lieanr post-reformulation time trend.

[20] Due to missing data.

Table 2: Main Regression Results

Panel A: Estimated Coefficients								
Outcome	Homicide Victims per 100,000							
Parameters	OxyContin Misuse			Other Pain Relievers Misuse			Trends	
	pretrend	posttrend	shift	pretrend	posttrend	shift	South Boarder	Florida
Estimates	-0.0309	-0.0768	0.945***	0.0190	0.0184	-0.153	-0.103***	0.0194
	(0.093)	(0.212)	(0.328)	(0.016)	(0.038)	(0.115)	(0.036)	(0.017)
Panel B: Predicted Treatment Effects								
Outcome	shift + (year - 2010) × posttrend for OxyContin Misue							
Year	2010	2011	2012	2013	2014	2015	2016	2017
Estimates	0.945***	0.868**	0.791	0.715	0.638	0.561	0.484	0.407
	(0.328)	(0.410)	(0.565)	(0.749)	(0.945)	(1.147)	(1.352)	(1.559)

Notes: * p < 0.1, ** p < 0.05, *** p < 0.01. This table presents results of the baseline regression specification, where Panel A presents the estimated coefficients and Panel B presents the joint test results for the linear predicted treatment effects over time. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The regression includes a full set of state and year dummies and time trends for Florida and the states bordering Mexico. The regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

5 Main Results

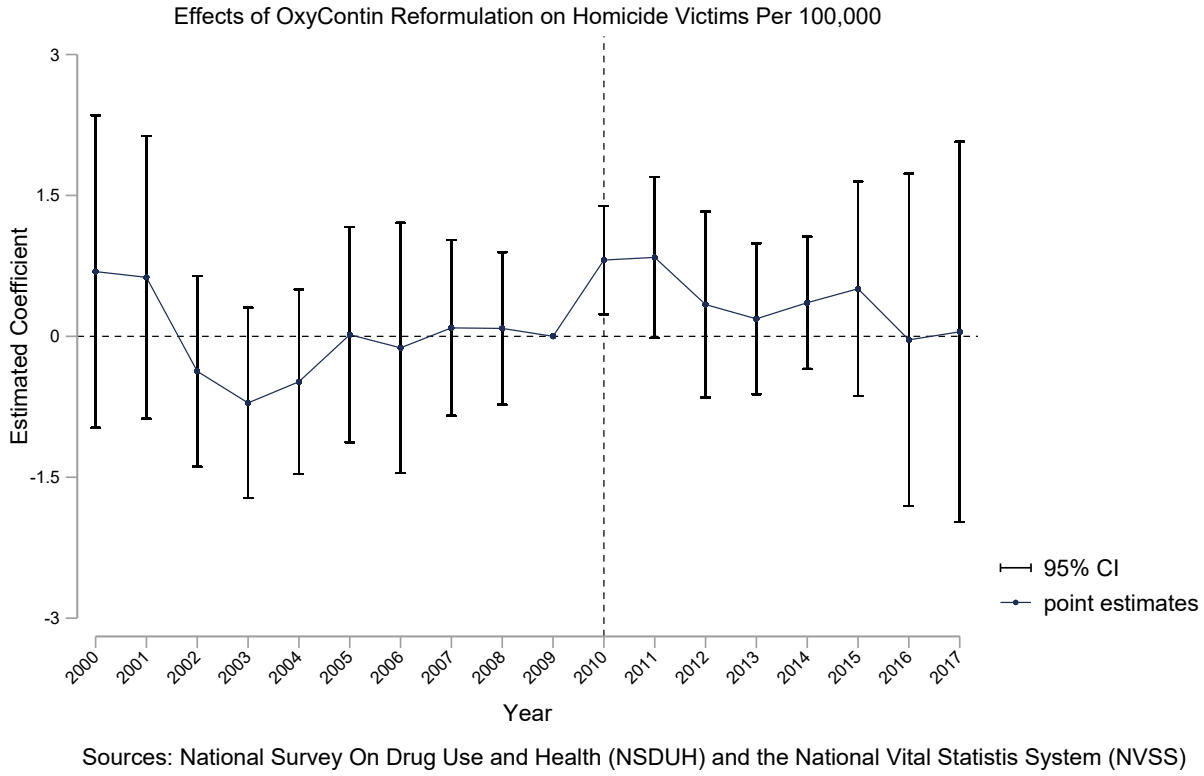
5.1 Fully Parametrized Specification

Panel A of Table 2 presents the estimated coefficients for the baseline specification. The point estimate of the "shift" parameter is 0.945, approximately 16% of the pre-reformulation mean homicide rate, and is statistically significant at the 99% confidence level. In contrast, the "posttrend" parameter is estimated at -0.0768 and there is little evidence to suggest that it is distinguishable from zero. This finding indicates intuitively that the increase in post-reformulation homicide rates due to differences in pre-reformulation Oxycontin nonmedical use exposure is unlikely to persist in the long run. However, the findings in Panel B is inconsistent with this intuition. Even though the estimated yearly aggregate effects became insignificant beyond the year 2011, its magnitude is measured at 0.407. This is inconsistency will be discussed in full details in Section 5.3.

5.2 Event Study Specification

Figure 3 graphically presents OxyContin reformulation's estimated effects on homicide rates from the baseline event study specification. The estimated coefficients in the pre-reformulation period, $\delta_t, t = 2000, 2001, ..., 2008$, exhibit a declining trend in the early 2000s, which reverses quickly, stabilizing around zero. Notably, all of them are statistically indistinguishable from zero at the 95% confidence level, supporting the assumption of parallel trends prior to the reformulation. In contrast, δ_{2010} is positive and is statistically significant at the 95% confidence level. with δ_{2011} showing a similar magnitude, though significant at only the 90% confidence level. Beyond 2011, the coefficients trend downward and remain statistically indistinguishable from zero.

Figure 3: Estimated Coefficients of State-Level Pre-Reformulation OxyContin Misuse Rates on Homicide Rates, 2000 - 2017



Notes: This figure presents the estimated coefficients of state-level pre-reformulation OxyContin misuse rates on homicide rates using the baseline event study specifications. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. For all regressions, standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. The regression includes a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

The findings in Figure 3 suggest that the reformulation of OxyContin led to a differential

increase in post-reformulation homicide rates, and this increase is larger in states with higher pre-reformulation OxyContin misuse rates. Notably, the pattern of post-2009 estimated coefficients show that this increase is transitory. This is in contrast to Park (2021), where the author found that the differential increase in post-reformulation homicide rates persisted or even amplified in the long run. As discussed in the empirical strategy section, this could be (at least) partly attributed to the pre-existing trends in homicide rates due to factors unlikely to be accounted for by the inclusion of demographic and economic variables, such as proximity to international sources of illicit drugs. The implication of this finding on the underlying victim-generating mechanisms will be discussed in detail in Section 6.1.

5.3 Long-Run Impact of OxyContin Reformulation on Homicide

The findings in Section 5.2 suggest that the differential increase in post-reformulation homicide is transitory, approaching zero in the long run. However, the linear predicted treatment effect shown in Panel B, Table 2, is estimated at 0.407 at the end of the study period, albeit statistically indistinguishable from zero. To mitigate the concern for this inconsistency, this paper propose including 2005 - 2009 age-adjusted cancer mortality rates in the baseline specifications. Cancer mortality rates may serve as a proxy for legitimate demand for prescription opioids attributed to the need for pain management in cases of cancer pain and palliative care. These patients typically depend on powerful medications such as OxyContin for pain relief and are less likely to use these drugs nonmedically. Nevertheless, if they face barriers to obtaining appropriate prescription medications, they might resort to illicit drug markets to meet their pain management needs.

This section begins by examining the extent to which 2005 - 2009 state-level total cancer mortality rates serve as a proxy for pre-reformulation OxyContin misuse. Panel A of Table 3 shows that the predictive power is weak. In addition, this relationship is not severely confounded by the inclusion of nonmedical use rates for other commonly abused painkillers. Building on this evidence, Panel (a) of Figure 4 shows the results of including interactions of cancer mortality rates and year in the baseline event study specification. This adjustment strengthens the pattern observed in Figure 3. Notably, the estimated coefficients plateau from 2012 to 2015 before rapidly declining to sub-zero levels. By contrast, Panel (b) displays results where cancer mortality rates are treated as the independent variable of interest. The estimated coefficients beyond 2014 show an upward trend. Notably, Figure 7 in the appendix shows that this pattern persists even when the cancer mortality rates from 1999 - 2003 are used. These findings align with the results presented in Panel B of Table 2, which reports estimates from the fully parameterized specification incorporating pre-trend, posttrend, and shift parameters for 2005–2009 total cancer mortality rates. Estimates of this augmented specification show that the coefficient associated with the level (or linear time trend) component linked to the pre-reformulation OxyCOntin nonmedical exposure is measured at 1.121 (-0.222) homicide victims per 100,000 individuals and is statistically significant (insignificant) at the 99% (90%) confidence level. By contrast, the linear time trend component linked to cancer mortality is measured at 0.00773 homicide victims per 100,000 individuals and is statistically sig-

nificant at the 99% confidence level. As shown in Panel C, the linear predicted treatment effects approach zero by 2015.

If cancer mortality has weak correlation with misuse and the shift parameter associated with it is negative and insignificant, then the effect captured by the posttrend parameter can be largely attributed to later events such as the influx of illicit fentanyl from foreign sources(Ciccarone, 2019; Powell and Pacula, 2021), nationwide opioid tapering (Busse et al., 2016; Dowell et al., 2016; Guy Jr et al., 2017), and protests against police militarization (Premkumar, 2019). Figure 8 provide further supporting evidence by showing the timing of association between cancer mortality and opioid overdose excluding heroin as the underlying cause of death coincides with the pattern in Panel (b) of Figure 4. Taken together, these findings suggest that while the OxyContin reformulation initially contributed to a rise in homicide rates, its effect unlikely persisted beyond 2014.

5.4 Heterogeneous Effects On Age Groups

I conducted six tests, each regarding one designated age group excluding the reference group. I test six specifications for each age group-specific test with different combinations of year-state-age group level demographics, including log population, percentage male, percentage white, and percentage of Hispanic origin. I only report $\hat{\eta_9}$ for each specification. I organize test results into panels A through F in Table 4. Within each panel, I present the point estimate and standard error (in parenthesis) of η_9 in columns (1) through (6) for each specification.

In column (1) of Table 4, I find that the estimated age group-specific differential average treatment effect for victims aged 15-24 is positive at 8.152, the largest among all age groups. I cannot reject the null that it is statistically significant at the 95% confidence level. It is about 2.7 times the size of that for victims aged 25-34, measured at 3.062 and statistically significant at the 95% confidence level. In contrast, this effect is negative for all other victim age groups. This pattern largely persists through the rest of the specifications. In particular, the estimated impact for victims aged 15-24 is not sensitive to inclusions of demographic covariates. The significance level stays constant across these specifications, and the point estimate increases by about four percentage points when estimated with a full set of controls. These findings suggest that OxyContin reformulation induces a differential rise in young homicide victims aged 15-34 compared to other age groups. Moreover, this differential effect concentrates on homicide victims aged 15-24.

This research suggests that the observed increase in homicides is not primarily driven by psychopharmacological violence, i.e., violence under the influence of drugs. This conclusion is drawn from the difference-in-difference estimator, which compares the impact in states with high and low levels of OxyContin misuse. The data does not support the hypothesis that heroin, a common substitute for Oxycodone, has a distinctly different effect on users' propensity for violence.

Similarly, the rise in homicides does not appear to be motivated by the need for financial resources to sustain drug habits. If this were the case, it would imply higher prices for OxyContin substitutes like heroin and hydrocodone, but the opposite is true. Heroin, notably cheaper than OxyContin by 2009, had already seen a switch by users before OxyContin's reformulation due to

Table 3: Main Regression Results: The Long Run Impact of OxyContin Reformulation on Homicide

Panel A: Association Among Pre-Reformulation Nonemdical Use Rates of OxyContin (OC), Other Commonly Used Pain Relievers (OP), 1999 - 2003 Total Cancer Mortality Rates (CM), and 2006 - 2009 OxyCodne Supply Per Capita (OS)

Outcome	OC			OP	OS			
Regressor	CM	CM + OP		CM	CM	CM + OC		OC
Estimates	0.00400	0.00371	0.0911***	0.00315	0.000169	-0.00151	0.461***	0.219***
	(0.0314)	(0.00317)	(0.0212)	(0.082)	(0.00102)	(0.00173)	(0.117)	(0.0518)

Panel B: Estimated Coefficients Associated with Pre-Reformulaton OxyContin Misuse Rates (OC) and 2005 - 2009 Total Cancer Mortality Rates (CM)

Outcome	Homicide Victims per 100,000							
Parameters	CM			OC			Trends	
	pretrend	posttrend	shift	pretrend	posttrend	shift	South Border	Florida
Estimates	-0.000112	0.00773***	-0.00913	0.0318	-0.222	1.121***	-0.0546	0.049**
	(0.00117)	(0.00229)	(0.00589)	(0.0805)	(0.179)	(0.416)	(0.0366)	(0.0192)

Panel C: Predicted Treatment Effects Associated with Pre-reformulation OxyContin Misuse Rates , Controlling for 2005 - 2009 Cancer Mortality Rates

Outcome	shift + (year - 2010) × posttrend for OxyContin Misue							
Year	2010	2011	2012	2013	2014	2015	2016	2017
Estimates	1.121***	0.899**	0.677	0.455	0.235	0.0117	-0.210	-0.432
	(0.416)	(0.441)	(0.529)	(0.655)	(0.801)	(0.958)	(1.122)	(1.290)

Notes: * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Panel A presents the associations among state-level Pre-Reformulation nonemdical use rates of OxyContin (OC), other commonly used pain relievers (OP), 1999 - 2003 total cancer mortality rates (CM), and 2006 - 2009 OxyCodne supply per capita (OS), estimated using linear regression. The rest of this table presents results of the baseline fully-parametrized specification controlling for the pre-reformulation time trend, post-reformulation time trend, and post-reformulation shift of 2005-2009 cancer mortality rates, where Panel A presents the estimated coefficients and Panel B presents the joint test results for the linear predicted treatment effects over time.

Regressions in Panel A are run at the state level with robust standard errors, weighted by 2000 - 2009 average state populations. Data are for all 50 US states plus the District of Columbia.

For the regression in Panel B and Panel C, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The regression includes a full set of state and year dummies and time trends for Florida and the states bordering Mexico, weighted by state-year population estimates from the SEER program.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). 2005 - 2009 state-level total cancer mortality rates are obtained from the American Cancer Society. Lastly, the source for 2006 - 2009 oxycodone prescriptions is Automation of Reports and Consolidated Orders System (ARCOS).

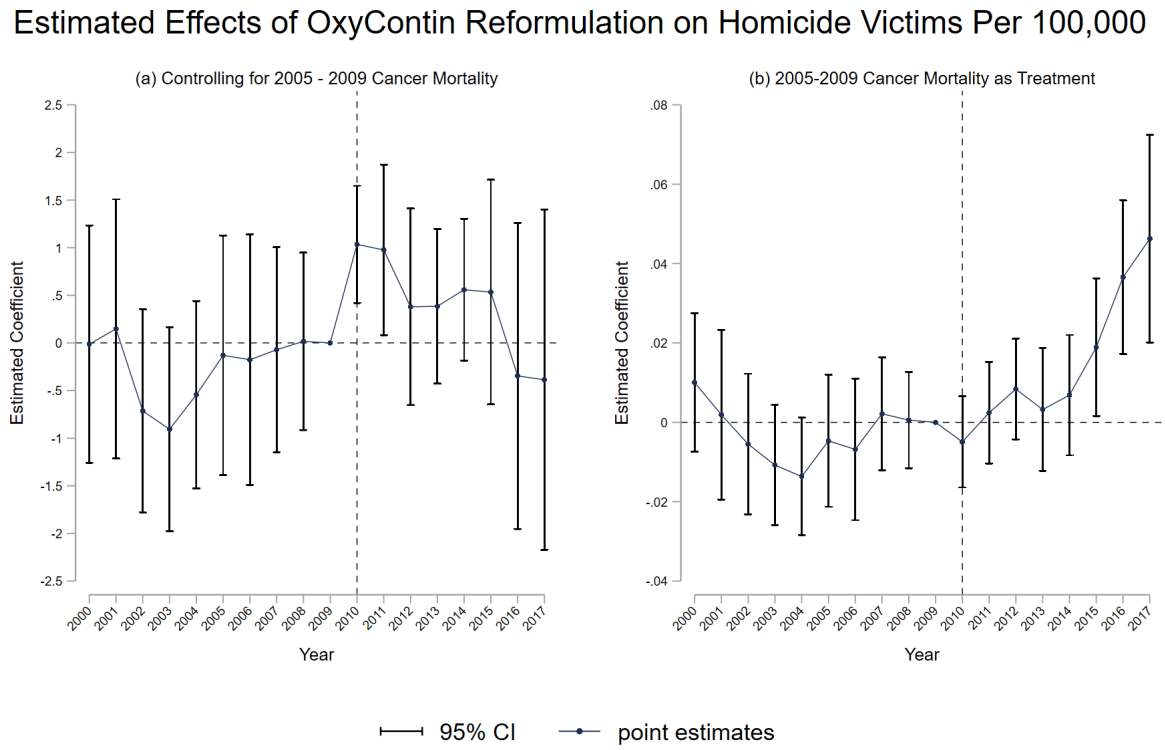
Table 4: Heterogeneous Effects of OxyContin Reformulation on Homicide Across Age Groups

	Dependent Var.: Homicide per 100,000					
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A: 5-14						
$oxy \times \mathbf{1}\{5 \leq age \leq 14\} \times \mathbf{1}\{year \geq 2010\}$	-3.081**	-2.969**	-3.155**	-3.309**	-3.043**	-3.265**
	(1.270)	(1.302)	(1.255)	(1.357)	(1.286)	(1.351)
Panel B: 15-24						
$oxy \times \mathbf{1}\{15 \leq age \leq 24\} \times \mathbf{1}\{year \geq 2010\}$	8.152**	8.202**	8.441**	8.179**	8.495**	8.526**
	(3.329)	(3.362)	(3.375)	(3.309)	(3.409)	(3.381)
Panel C: 25-34						
$oxy \times \mathbf{1}\{25 \leq age \leq 34\} \times \mathbf{1}\{year \geq 2010\}$	3.062**	3.290**	3.059**	2.963*	3.288**	3.212**
	(1.501)	(1.554)	(1.512)	(1.568)	(1.567)	(1.628)
Panel D: 35-44						
$oxy \times \mathbf{1}\{35 \leq age \leq 44\} \times \mathbf{1}\{year \geq 2010\}$	-1.401	-1.408	-1.360	-1.406	-1.365	-1.341
	(1.380)	(1.351)	(1.397)	(1.353)	(1.370)	(1.344)
Panel E: 45-54						
$oxy \times \mathbf{1}\{45 \leq age \leq 54\} \times \mathbf{1}\{year \geq 2010\}$	-2.131*	-2.285*	-2.188*	-2.053*	-2.342**	-2.230**
	(1.206)	(1.174)	(1.195)	(1.163)	(1.162)	(1.121)
Panel F: 55-64						
$oxy \times \mathbf{1}\{55 \leq age \leq 64\} \times \mathbf{1}\{year \geq 2010\}$	-1.724	-2.164**	-1.878*	-1.592	-2.308**	-2.161**
	(1.144)	(1.099)	(1.127)	(1.115)	(1.076)	(1.079)
log population	No	Yes	No	No	Yes	Yes
gender	No	No	Yes	No	Yes	Yes
race/ethnicity	No	No	No	Yes	No	Yes
age FE	Yes	Yes	Yes	Yes	Yes	Yes
state FE	Yes	Yes	Yes	Yes	Yes	Yes
time FE	Yes	Yes	Yes	Yes	Yes	Yes

Notes: * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. This table presents evidence that the effect of OxyContin reformulation on homicide differs between a chosen victim age group and all the other victim age groups. Six victim age groups are considered: 5-14, 15-24, 25-34, 35-44, 45-54, 55-64. Within each panel, columns (1) through (6) correspond to the estimation results with various combinations of demographic variables at the state, year, and age group level, including (1) log state populations, (2) male percentage, percentage white, percentage black, percentage Hispanic, and (3) share of the population aged between 20 and 40. For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered by state and victim age group. All regressions include state, year, and victim age group dummies and are weighted by state-year population estimates from the SEER program.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

Figure 4: Comparison of Treatment: Pre-Reformulation OxyContin Misuse Rates and Cancer Death Rates



Notes: Panel (a) presents the estimated coefficients of state-level pre-reformulation OxyContin misuse rates on homicide rates using the baseline event study specification, controlling for 2005 - 2009 age-adjusted cancer death rates. Panel (b) presents the baseline event study specification results, replacing mesures of OxyContin misuse with cancer mortality. In both regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. The regression includes a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

its lower cost. Cicero et al. (2013) also found that cost was not a primary factor in the choice of OxyContin over hydrocodone. Furthermore, police reports indicate that while robberies and assaults are common among drug users seeking money, homicides are rare in these circumstances.

Therefore, the increase in homicides likely stems from illegal market-generated violence. Three lines of evidence support this hypothesis. First, prior literature in criminology, sociology, and economics links gang activities to homicide, emphasizing violence in illicit markets due to the absence of formal contracting. Second, research shows that gang violence is often related to protecting territory, with younger, low-level gang members most involved in these conflicts and facing higher mortality rates. Third, Owen (2014) points out that homicide victims in market-based crimes

tend to be younger, a pattern I have replicated in my research (Figure 11), further supporting the market-generated homicide hypothesis.

6 Additional Results

6.1 Robustness Tests

To mitigate the concerns that the differential increase in post-reformulation homicide rates is spurious, this paper implements a series of additional checks to challenge the assumptions of the identification strategy. Figure 11 and 12 present evidence that the dynamic pattern of the estimated coefficients is robust to the inclusion of additional geographical time trends, alternative estimator and measures of interest, shortening of the study period, and random, marginal changes to study sample. Findings in Table 6 further show that the fully parametrized specification is robust to alternative geographical time trends, unweighted estimation, and the relaxation of the assumption that within-state error terms are correlated across years.

Notably, findings in 13 indicate that the pattern observed in Figure 3 is driven mainly by states in the highest and lowest quintiles of pre-reformulation nonmedical OxyContin use, which is consistent with findings in Table 7. Another finding is, suggested by column (4) of Table 6, that the fully parametrized specification is not robust to the length of study periods prior to the reformulation of OxyContin. Changing the first treatment period from 2010 to 2011 biases the "shift" parameter toward zero, as expected.

6.2 Sensitivity Tests

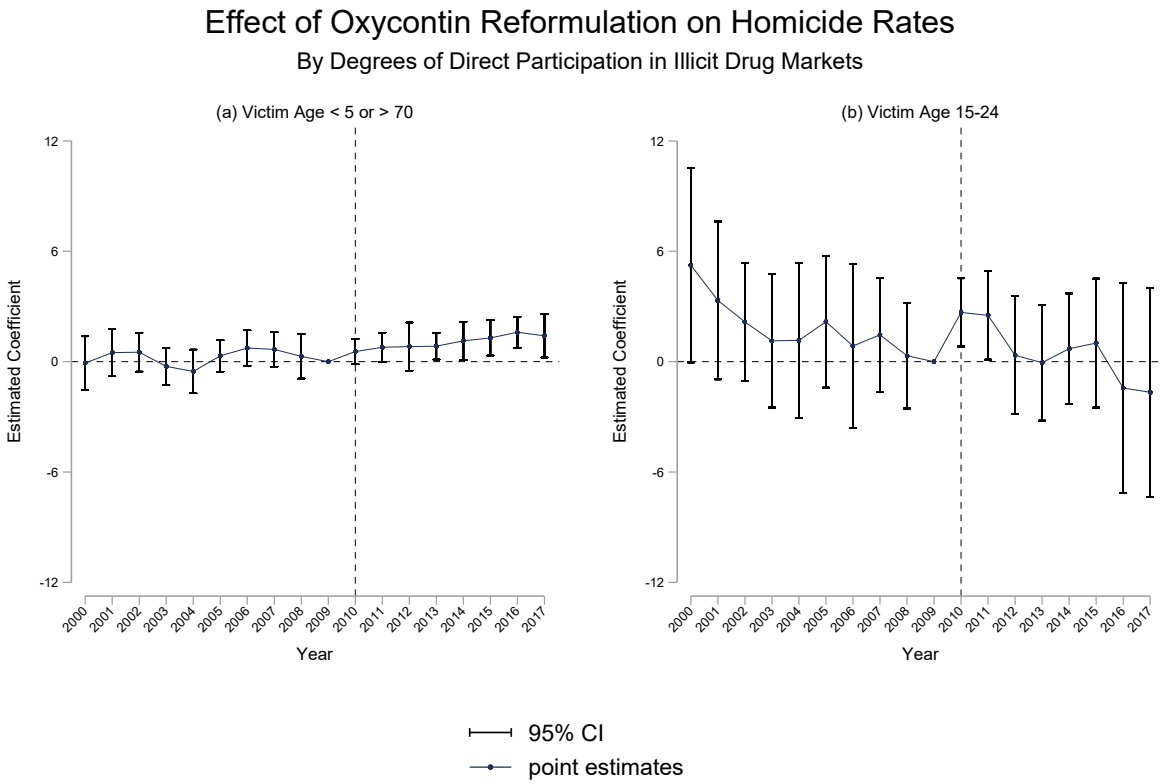
To mitigate the concerns that the results in Section 5.1 and 5.2 are driven by factors not included in the baseline specifications, this paper administers tests with different sets of demographic and socio-economic variables to investigate whether the results presented in Figure 3 and Table 2 hold across specifications with combinations of log population, common drug control policy dummies, unemployment rate, percentage of people with college degrees or above, dummies for gender, race/ethnicity, and share of population aged between 20 and 40. Figure 14, 15 show that the pattern of estimated coefficients in general aligns well with that of the baseline event study specification. Table 8 and 9 demonstrate that the estimates of causal parameters "shift" and "posttrend" are largely insensitive to the inclusion of demographic and socio-economic controls. It is worth noting that the variation of the estimated "shift" parameter across specifications in Table 9 is greater than that when only demographic variables are included, suggesting these socio-economic control variables could be affected by pre-reformulation nonmedical use of OxyContin.

6.3 Falsification Test

This section investigates whether the reformulation of OxyContin influenced outcomes that are not directly associated with illicit drug market activities. Specifically, it examines the homicide

rates of victims under five years old or over 70 years old. The underlying hypothesis is that post-reformulation increases in homicide are primarily driven by escalated illicit drug market activities, which typically involve the active participation of victims. However, indirect mechanisms, such as child maltreatment (Evans et al., 2022) and violence targeting non-participants due to intoxication, could also result in homicide. Since individuals younger than five or older than 70 are generally not active in the illicit drug market, concerns would be raised if the reformulation of OxyContin is found to have a similar impact on this population.

Figure 5: Falsification Test for the Baseline Event Study Specification



Notes: This figure presents the estimation results from estimating OxyContin reformulation's effect on the homicide rates of victims under five years old or over 70 years old (panel (a)) and victims between 15 and 24 (panel (b)) using the event study specification. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. Both regressions include a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH).

This section also explores the effect of the reformulation of OxyContin on victims between 15 and 24. Unlike the under-five or over-70 age groups, those between 15 and 24 are much more likely to be involved in illicit drug markets directly. According to the 2021 National Survey on Drug Use and Health (NSDUH), individuals between 18 and 25 have the highest rate of illicit drug use and

dependency. Street gangs also consist of members primarily from this age range, with the younger ones being most vulnerable in conflicts between gangs. If the estimated coefficient patterns for this group mirror those in Figure 3, it would further mitigate concerns about the effect being primarily driven by indirect mechanisms.

Panel (a) in Figure 5 presents the estimated effects of the reformulation of OxyContin on the homicide rates of victims under five years old or over 70 years old. The estimated coefficients show an upward trend post-reformulation, with δ_{2010} statistically indistinguishable from zero at the 95% confidence level. Significant effects are consistently observed only after 2012, diverging from the pattern in Figure 3. Moreover, this pattern resembles previous findings on the impact of the reformulation on heroin overdose deaths (Powell and Pacula, 2021), suggesting the increase in homicides in this age group is indirectly linked to long-term opioid use.

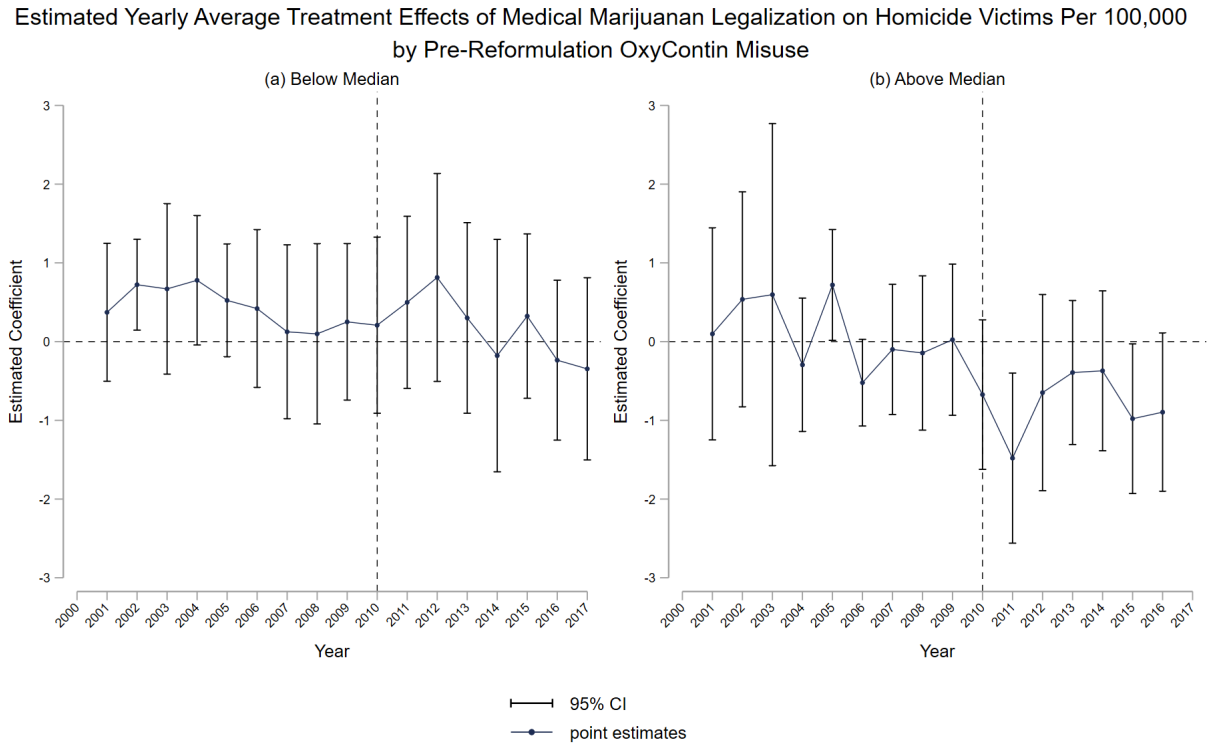
Panel (b) in Figure 5 presents the estimated effects of the reformulation of OxyContin on the homicide rates of victims between 15 and 24. The pre-reformulation estimated coefficients show a consistent downward trend till 2010, where a significant, positive effect is observed. This increase is transitory, as the post-2011 coefficients resume the pre-reformulation downward trend. This pattern contrasts with the one observed in panel (a) but aligns more with Figure 3. This comparison indicates that indirect mechanisms do not dominate the effect of the reformulation of OxyContin on homicide rates, suggesting that the impact of the reformulation on homicide rates is less likely to be spurious.

6.4 Moderation Effect MML on Post-Reformulation Homicide Rate

Existing literature suggests that cannabis could effectively replace prescription opioids for pain management in specific conditions due to its analgesic properties (Reiman et al., 2017; Caldera, 2020; Carlini, 2018; Bicket et al., 2023). Theoretically, this substitution could lower post-reformulation demand for illicit opioids like heroin, thereby reducing violence associated with the illegal drug market. In reality, there are several reasons why an individual would opt for cannabis over or with prescription opioids (Wiese and Wilson-Poe, 2018; Nielsen et al., 2017; Rogers et al., 2019; McCabe et al., 2012). Moreover, both existing medical (Nguyen et al., 2024; McGinty et al., 2023; Shover et al., 2019; Bachhuber et al., 2014; Chihuri and Li, 2019) and economics (Mathur and Ruhm, 2023; Powell et al., 2018; Chan et al., 2020) literature lack consensus regarding the impact of medical marijuana laws on opioid prescription and opioid overdose deaths. As summarized in Mathur and Ruhm (2023), this effect is sensitive to the choice of studying periods: extending study periods tends to show zero or positive, estimated effects of these laws on opioid overdose death, which raises questions about the argument that these laws reduce post-reformulation homicides.

The paper attributes this inconsistency to changing prescription opioid policy stringency over time, reducing the population affected by medical marijuana access. Since cannabis cannot replace prescription opioids for all conditions, especially for severe, cancer-related pain, when the prescribing culture is liberal, there are likely a relatively more significant number of patients whose underlying health conditions are manageable by medical marijuana but use prescription opioid for

Figure 6: Effects of Medical Marijuana Laws on Homicide



Notes: This figure presents the yearly average treatment effect of medical marijuana laws (MML) on homicide by states' pre-reformulation OxyContin misuse rates. States that passed MML before 2001 and after 2009 are excluded[a]. For both estimations, standard errors are clustered at the state and age group level. The confidence interval for all estimated coefficients is set at 95% level. Both estimations use linear OLS estimator, with each regression weighted by state-year-age group population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

[a]States that passed MML before 2001 are considered "always treated units" and therefore not included in the estimation. States that passed MML after 2009 might leverage MML to curb the rising opioid overdose deaths. Such states are excluded to mitigate the policy endogeneity concern.

pain management purposes. However, as the overall prescription behavior became more restrictive, the relative proportion of this population will likely decrease. The estimated net effects might reflect the impact from other channels or possibly spurious correlation, thus becoming more positive. This is illustrated in Figure 20 in the appendix.

This discussion suggests that the effect of medical marijuana laws on homicide is moderated by the size of underlying population whose condition could be managed by cannabis but seeking prescription or illicit opioids instead. This paper posits that Pre-Reformulatioon OxyContin misuse rates is a reasonable proxy for such populations. Section 2.3 suggests that, since the cross-state variation in opioid prescription could not be explained by cross-state variations in underlying health conditions, it is likely contributed mainly by how physicians prescribe opioids as a solution to

various pain conditions. Furthermore, the main difference likely occurs among patients with non-cancer related pain or mild to moderate level pain. This paper provides three additional sets of evidence in support this assumption. First, Panel A of Table 3 shows that there is little correlation between cancer mortality and both legal opioid prescription and nonmedical use of prescription opioids. Second, Figure 18 uses publicly available National Health Interview Survey (NHIS) data shows there are positive pre-reformulation associations between health insurance coverage and cross-region OxyContin nonmedical use rates among individuals reporting any level of work-limiting pain, a pattern that disappears for those with severe pain. Third, Figure 19 uses Medical Expenditure Panel Survey (MEPS) data to show a positive correlation before 2010 between chronic low back pain and OxyContin misuse but not among individuals with cancer diagnoses. These findings, although not causal, suggest that misuse misuse was not primarily driven by cancer-related or severe pain management. Taken together, these findings support the prediction that the moderation effect of MML on homicide should be stronger among states with higher pre-reformulation OxyContin misuse rates.

To address variation in the timing of medical marijuana law passage, this paper uses a staggered difference-in-differences approach (Callaway and Sant'Anna, 2021) to estimate the effect of medical marijuana laws on homicide. To help mitigate the concern for policy endogeneity due to OxyContin Reformulation, states that passed medical marijuana laws after 2010 are excluded. However, this design cannot rule out policy endogeneity before 2010, such as using state MML implementation to counter high drug use and crime rates. By grouping states based on their pre-reformulation OxyContin nonmedical use rates and summarizing treatment effects by year, Figure 6 shows that treatment effects are negative in the years immediately following OxyContin reformulation, but only in states with above-median pre-reformulation misuse exposure.

The analysis of this section provides suggestive evidence that indirect intervention could be effective in reducing the unintended, adverse effects on crime outcomes due to the implementation of restrictive, supply-side drug policies. On the other hand, this analysis suggests that the effectiveness of medical marijuana legalization in moderating violent crime outcomes depends on the size of the underlying population whose opioid use are expected to be affected by legal access to marijuana. It is recommended that a critical evaluation of this population to be included in the process of legalizing medical marijuana.

7 Conclusion

This study examines the effect of one of the most significant supply-side drug control policies, the reformulation of OxyContin, on homicide, documenting the following results. First, difference-in-difference estimates show that this policy generates a positive gap in homicide rates between states with high pre-reformulation exposure to OxyContin and the rest, and this effect is likely transitory. Second, this effect is primarily concentrated among young homicide victims, especially for those between 15 and 24. This empirical evidence primarily reflects an increase in illicit drug market

activities due to greater demand for substitutes such as heroin. Furthermore, the analgesic potential of marijuana suggest that medical marijuana legalization could moderate this adverse effect. Using pre-reformulation OxyContin misuse rates as a proxy for this population and comparing states with similar exposure, difference-in-differences estimates show that medical marijuana legalization is associated with post-reformulation a decrease in homicide victims only for states with the high pre-reformulation OxyContin exposure.

These results provide suggestive evidence how medical marijuana legalization reduces the incentives to substitute illicit opioids, thereby indirectly mitigating the adverse effects on public health and crime outcomes post-reformulation. However, a critical evaluation of *who* will be affected is recommended to accompany considerations involving legalizing medical marijuana.

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APPENDIX

A Data

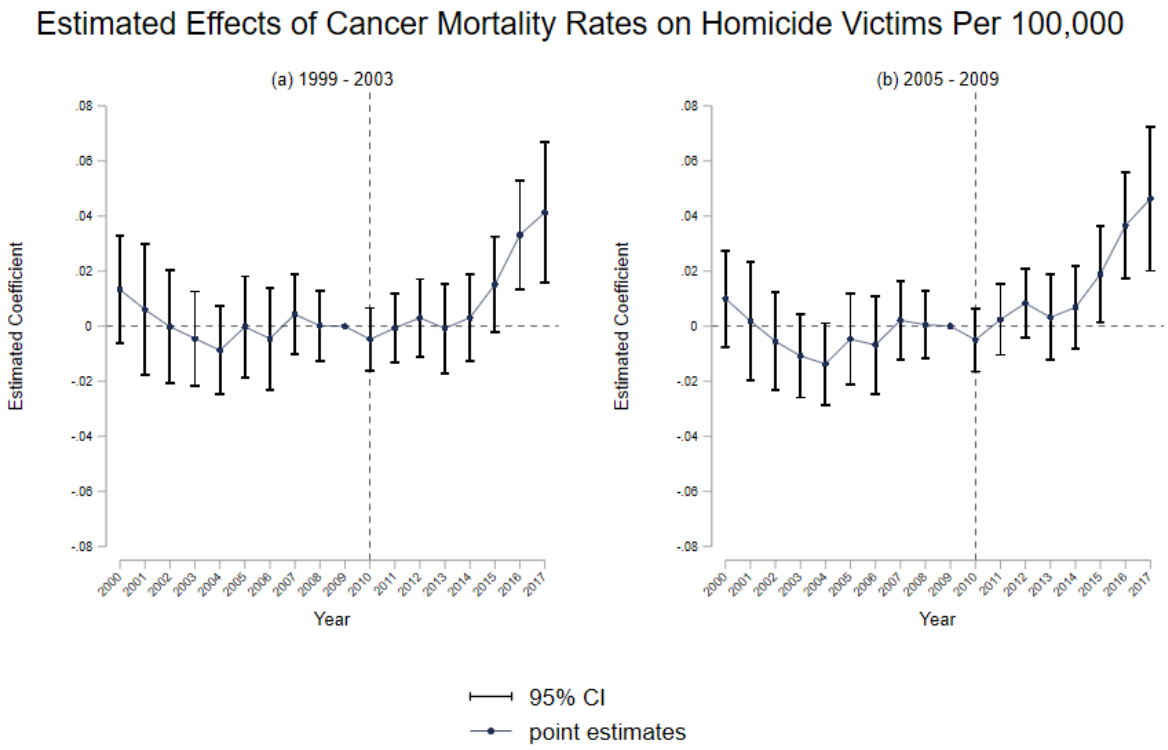
Table 5: ICD-10 Codes in the Assault Category (NVSS)

ICD-10 codes	description
X85	Assault by drugs, medicaments and biological substances
X86	Assault by corrosive substance
X87	Assault by pesticides
X88	Assault by gases and vapours
X89	Assault by other specified chemicals and noxious substances
X90	Assault by unspecified chemical or noxious substance
X91	Assault by hanging, strangulation and suffocation
X92	Assault by drowning and submersion
X93	Assault by handgun discharge
X94	Assault by rifle, shotgun and larger firearm discharge
X95	Assault by other and unspecified firearm discharge
X96	Assault by explosive material
X97	Assault by smoke, fire and flames
X98	Assault by steam, hot vapours and hot objects
X99	Assault by sharp object
Y00	Assault by blunt object
Y01	Assault by pushing from high place
Y02	Assault by pushing or placing victim before moving object
Y03	Assault by crashing of motor vehicle
Y04	Assault by bodily force
Y05	Sexual assault by bodily force
Y87.1	Sequelae of assault

Notes: ICD-10 coding for death certificates-based homicide rates. These codes only include categories specified as the underlying cause of death for the deceased from the National Vital Statistics System's (NVSS) Multiple Causes of Death data.

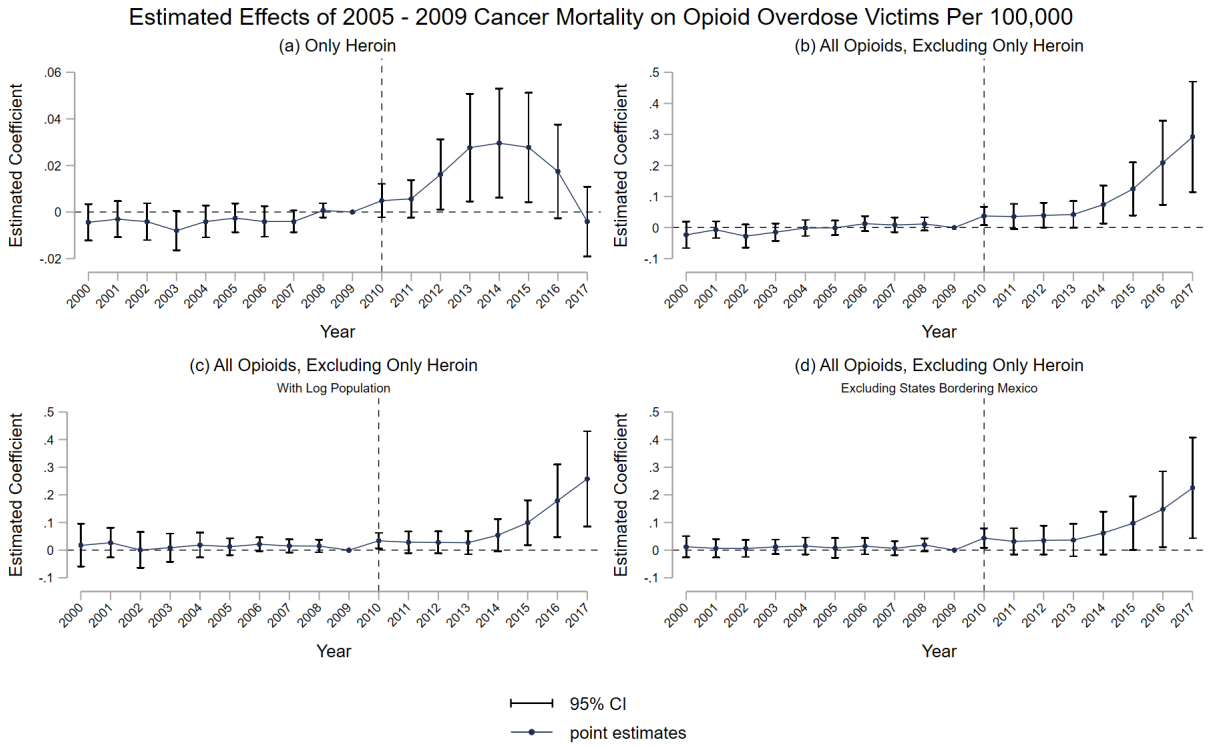
B Main Results

Figure 7: Diagnostic Test: Percentage Insured by Pain Level



Notes: This figure presents the estimated coefficients of state-level pre-reformulation OxyContin misuse rates on homicide rates using the baseline event study specifications. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. For all regressions, standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. The regression includes a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

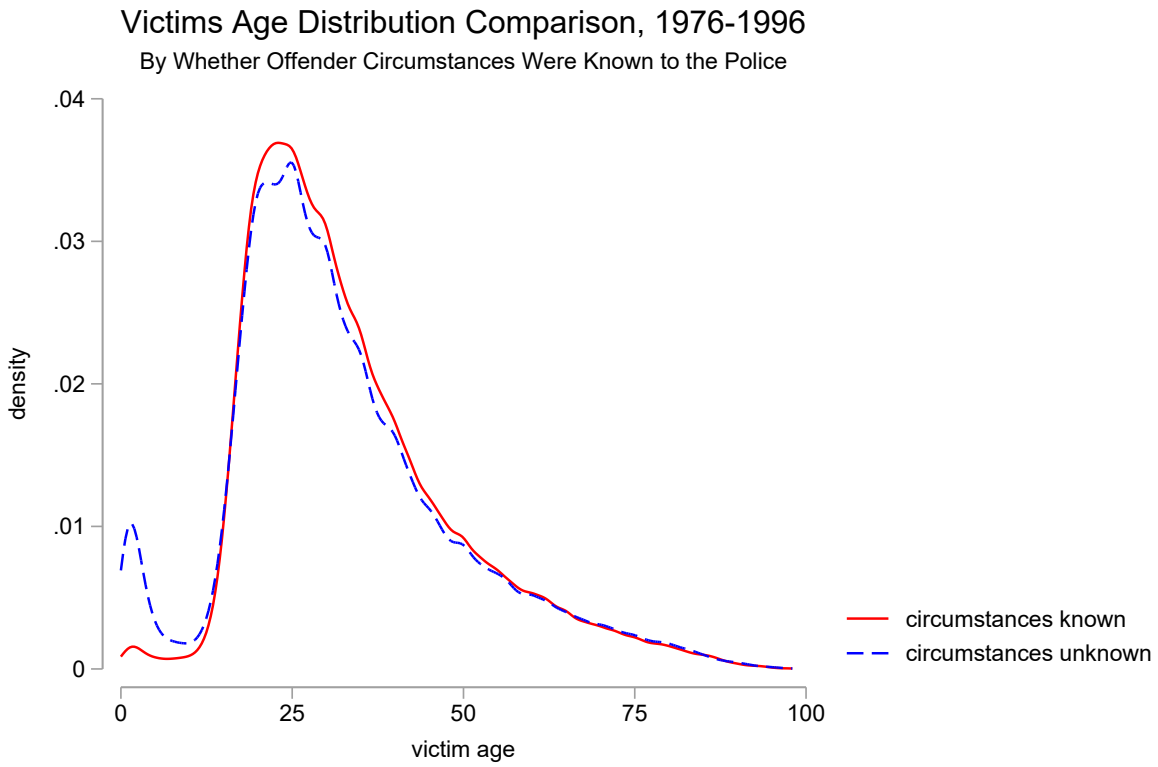
Figure 8: Estimated Coefficients of State-Level Pre-Reformulation OxyContin Misuse Rates on Homicide Rates, 2000 - 2017: Sources of Variation



Sources: National Vital Statistis System (NVSS) and American Cancer Society

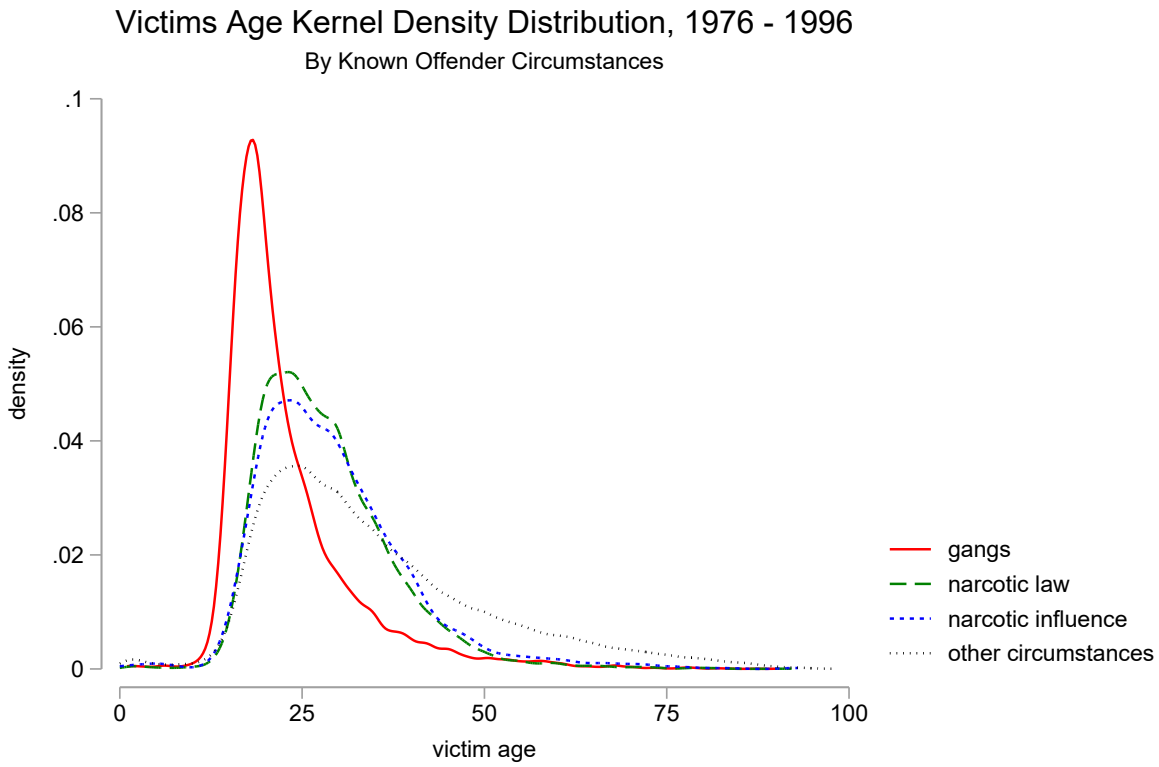
Notes: This figure presents the estimated coefficients of state-level pre-reformulation OxyContin misuse rates on homicide rates using the baseline event study specifications. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. For all regressions, standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. The regression includes a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

Figure 9: Victims Age Distribution: Known vs. Unknown Offender Circumstances



Notes: This figure presents the kernel density estimations of victim age distribution from the year 1976 to the year 2021 by whether the offender circumstances were known. The data source is the Supplemental Homicide Reports (SHR).

Figure 10: Victims Age Distribution: Offender Circumstances Known

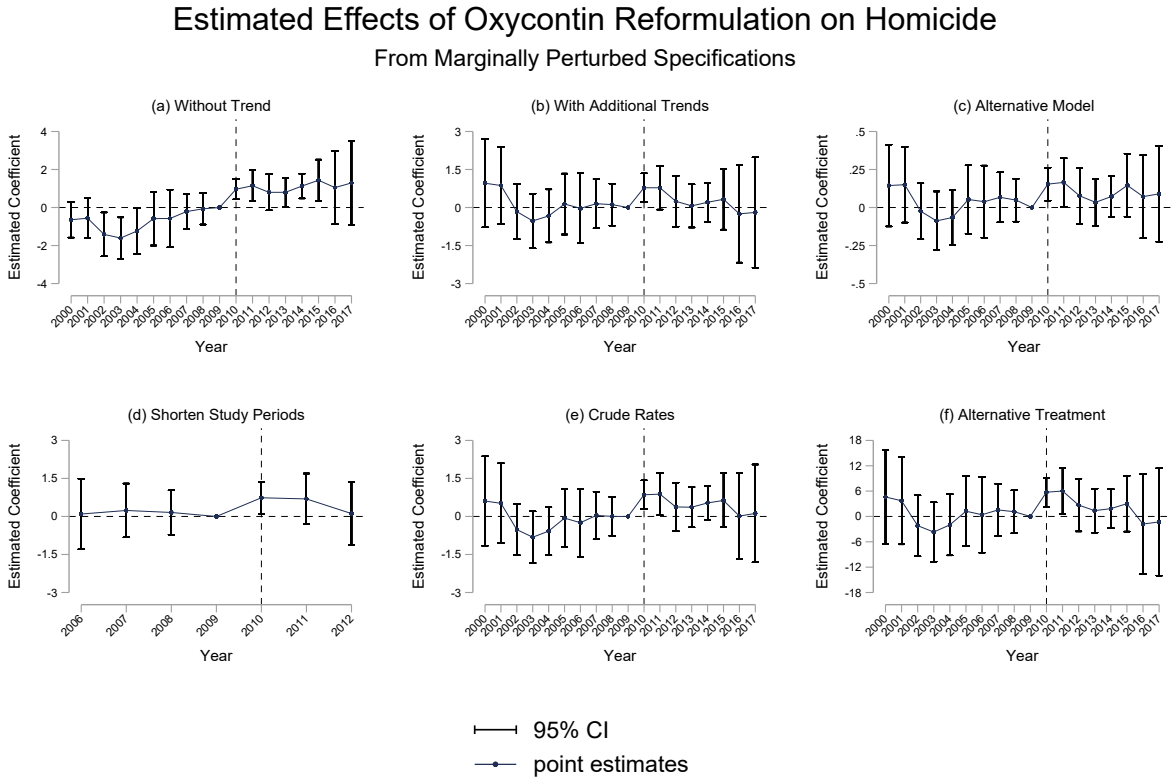


Notes: This figure presents the kernel density estimations of victim age distribution due to gang activities, violation of narcotic laws, influence of illicit drugs, and all other circumstances. The study period is from 1976 to 2021. The data source is the Supplemental Homicide Reports (SHR).

C Additional Results

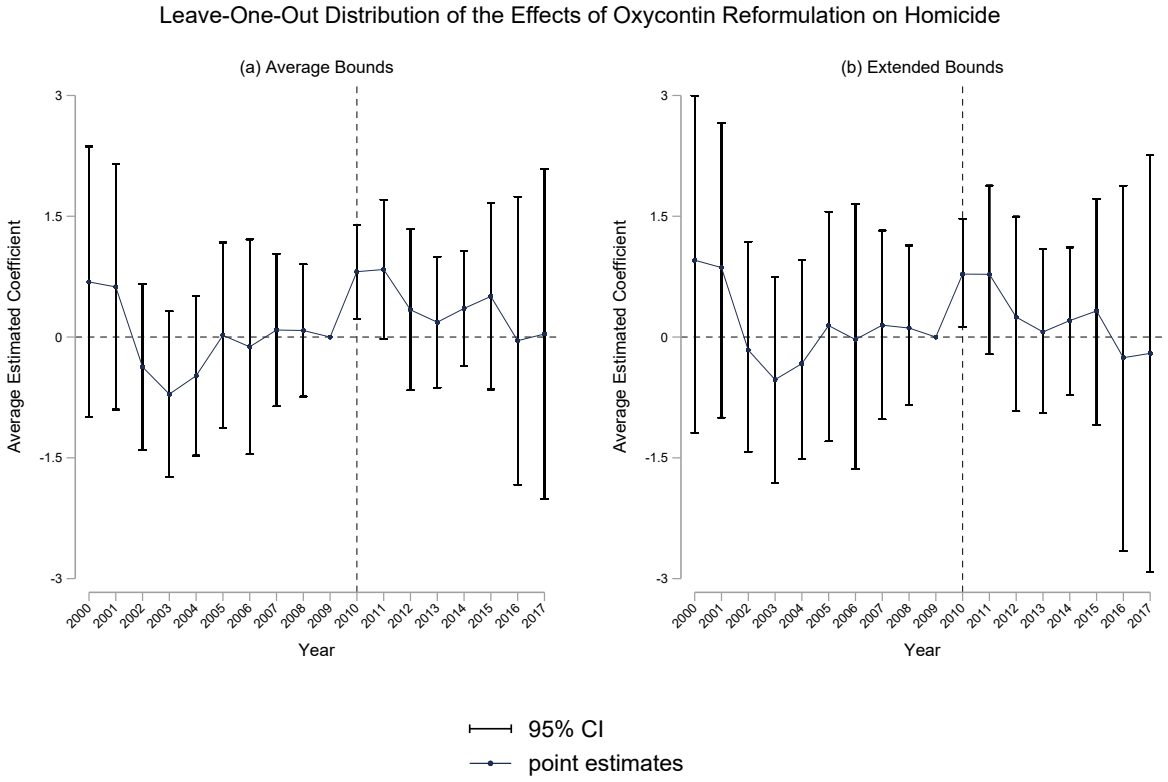
C.1 Robustness Tests

Figure 11: Robustness Checks for the Baseline Event Study Specification: Alternative Measures and Estimation Parameters



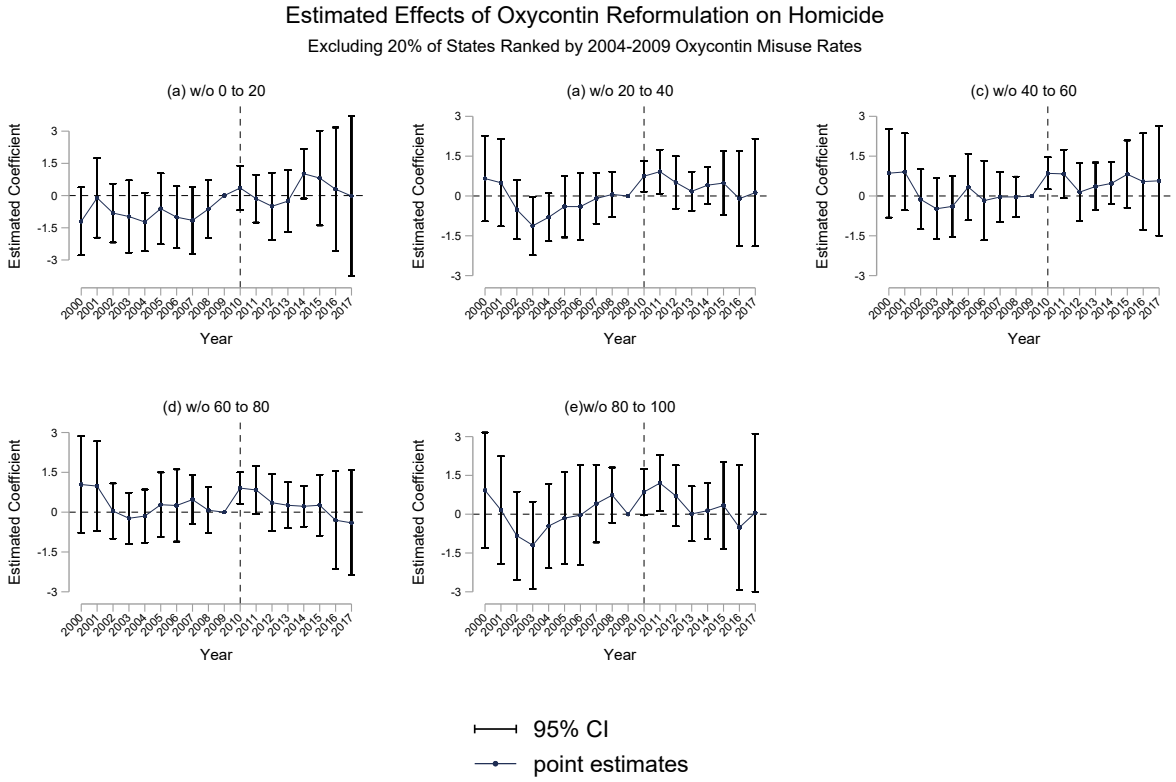
Notes: This figure presents the estimation results from six perturbations applied to the baseline event study specification, which are (a) estimating without time trends for Florida and states bordering Mexico, (b) estimating with additional time trends for states considered sources and distribution hubs of heroin, (c) using Poisson estimator instead of OLS, (d) shortening study periods, (e) using crude rates instead of age-adjusted rates, and (f) using ratios of pre-reformulation OxyContin and other pain relievers misuse rates as treatment intensity. For all regressions, the study period is from the year 2000 to the year 2017, and standard errors are clustered at the state level. Data are for all 50 US states plus the District of Columbia. The confidence intervals for all estimated coefficients are set at 95% level. Unless otherwise noted, all regressions include a full set of state and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH).

Figure 12: Robustness Checks for the Baseline Event Study Specification: Random Deletion of Observations From One State



Notes: This figure presents the estimation results of the baseline event study specification from randomly deleting one state. Panel (a) presents the mean point estimates of the regression coefficients and the mean values of the confidence interval limits. Panel (b) presents that the upper (lower) limit of a calculated coefficient corresponds to the upper (lower) limit of the 95% confidence interval within the distribution of the upper bounds. For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia, minus one state randomly. Standard errors are clustered at the state level. Both regressions include a full set of state and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH).

Figure 13: Robustness Checks for the Baseline Event Study Specification: Deletion of 20% of States Ranked by Pre-reformulation OxyContin Misuse Rates



Notes: This figure presents the estimation results of the baseline event study specification from removing states from one of the five quantiles in the distribution of pre-reformulation OxyContin misuse rates. Unless otherwise noticed, for all regressions, the study period is from the year 2000 to the year 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH). All regressions include a full set of state (only for states with the designated range of pre-reformulation OxyContin misuse rates) and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.

Table 6: Robustness Checks for the Fully Parameterized Specification: Perturbing Specification Setup and Excluding Selected States

	Dependent Var.: Homicide per 100,000							
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
2004-2009 OxyContin Misuse Rates								
pretrend	-0.0847	-0.255***	-0.144	-0.0591	-0.138**	-0.0228	-0.0805	-0.0850
	(0.127)	(0.093)	(0.287)	(0.101)	(0.063)	(0.112)	(0.131)	(0.111)
posttrend	0.00975	-0.00779	-0.320	-0.204	0.0468	-0.227	0.0227	0.0107
	(0.258)	(0.209)	(0.392)	(0.158)	(0.132)	(0.282)	(0.270)	(0.292)
shift	0.950***	1.222***	0.874*	0.509	0.987**	0.694*	0.855**	0.540
	(0.331)	(0.445)	(0.484)	(0.335)	(0.406)	(0.404)	(0.376)	(0.339)
2004-2009 Other Pain relievers Misuse Rates								
pretrend	0.0321	0.0496***	0.0523	0.0253	0.0315***	0.0157	0.0325	0.0216
	(0.023)	(0.016)	(0.058)	(0.019)	(0.012)	(0.015)	(0.020)	(0.018)
posttrend	0.0123	0.0101	0.134*	0.0471	0.0101	0.0507	-0.00916	-0.0124
	(0.047)	(0.040)	(0.079)	(0.032)	(0.025)	(0.049)	(0.043)	(0.0568)
shift	-0.162	-0.0743	-0.192*	-0.0954	-0.152*	-0.112	-0.116	-0.0306
	(0.118)	(0.168)	(0.110)	(0.086)	(0.085)	(0.118)	(0.116)	(0.10015)
pop.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
gender/race/ethnicity	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
age	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
state FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: * p < 0.1, ** p < 0.05, *** p < 0.01. This table presents a broader set of estimation results from the robustness checks of the fully parameterized specification. In column (1), the model is estimated with additional state by region time trends. In column (2), no weighting population is used. In column (3), study period is changed to from 2007 to 2012. In column (4), study period is changed to from 2003 to 2014. In column (5), robust standard errors is used. In column (6), California is excluded. In column (7), New York and Texas are excluded. In column 8, the first treatment period is set at 2011 instead of 2010. For all regressions, unless otherwise noted, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. Unless otherwise specified, all regressions include a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program. Lastly, all specifications are estimated with a full set of demographic controls, including (1) log state population, (2) male percentage, percentage white, percentage black, percentage Hispanic, and (3) share of the population aged between 20 and 40.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

Table 7: Robustness Checks for the Fully Parameterized Specification: Deletion of States Ranked by Pre-reformulation OxyContin Misuse Rates

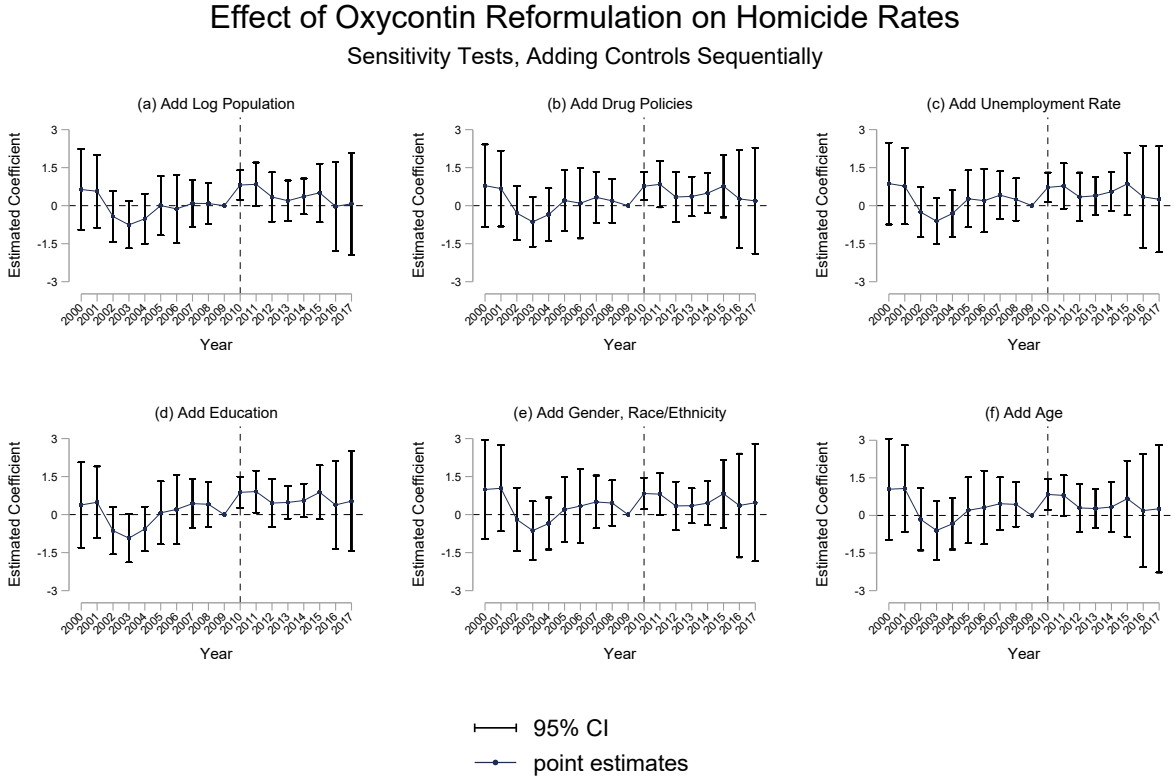
	Dependent Var.: Homicide per 100,000						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
2004-2009 OxyContin Misuse Rates							
pretrend	0.0435	-0.157	-0.200	-0.204	-0.0739	0.474**	-0.456***
	(0.110)	(0.132)	(0.128)	(0.137)	(0.170)	(0.209)	(0.150)
posttrend	0.0403	0.0257	0.242	-0.0293	-0.101	-0.227	0.290
	(0.304)	(0.280)	(0.300)	(0.280)	(0.388)	(0.580)	(0.315)
shift	0.562	1.183***	0.992**	1.047***	0.824*	-0.516	1.455***
	(0.811)	(0.229)	(0.411)	(0.332)	(0.473)	(1.512)	(0.234)
2004-2009 Other Pain relievers Misuse Rates							
pretrend	0.00444	0.0316	0.0434*	0.0432*	0.0339	0.000941	0.0940***
	(0.014)	(0.024)	(0.022)	(0.021)	(0.023)	(0.015)	(0.027)
posttrend	0.0475	0.00558	-0.0220	0.0230	-0.00709	0.0305	-0.0473
	(0.048)	(0.048)	(0.059)	(0.053)	(0.057)	(0.058)	(0.067)
shift	-0.0960	-0.219**	-0.123	-0.160	-0.153	-0.0843	-0.256**
pop.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
gender/race/ethnicity	Yes	Yes	Yes	Yes	Yes	Yes	Yes
age	Yes	Yes	Yes	Yes	Yes	Yes	Yes
state FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes
time FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Notes: * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. This table presents the estimation results from removing certain quantiles (out of five) of states in the pre-reformulation OxyContin misuse rates distribution. Columns (1) through (5) correspond to the estimation results from removing the states that fall into the bottom fifth, 20th-40th percentiles, 40th-60th percentiles, 60th-80th percentiles, and the top fifth of the pre-reformulation OxyContin misuse rates distribution, respectively. In column (6), the estimation removes the top and bottom fifth of states. In column (7), the estimation removes all but the top and bottom fifth of states. For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. All regressions include a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program. Lastly, all specifications are estimated with a full set of demographic controls, including (1) log state populations, (2) male percentage, percentage white, percentage black, percentage Hispanic, and (3) share of the population aged between 20 and 40.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

C.2 Sensitivity Tests

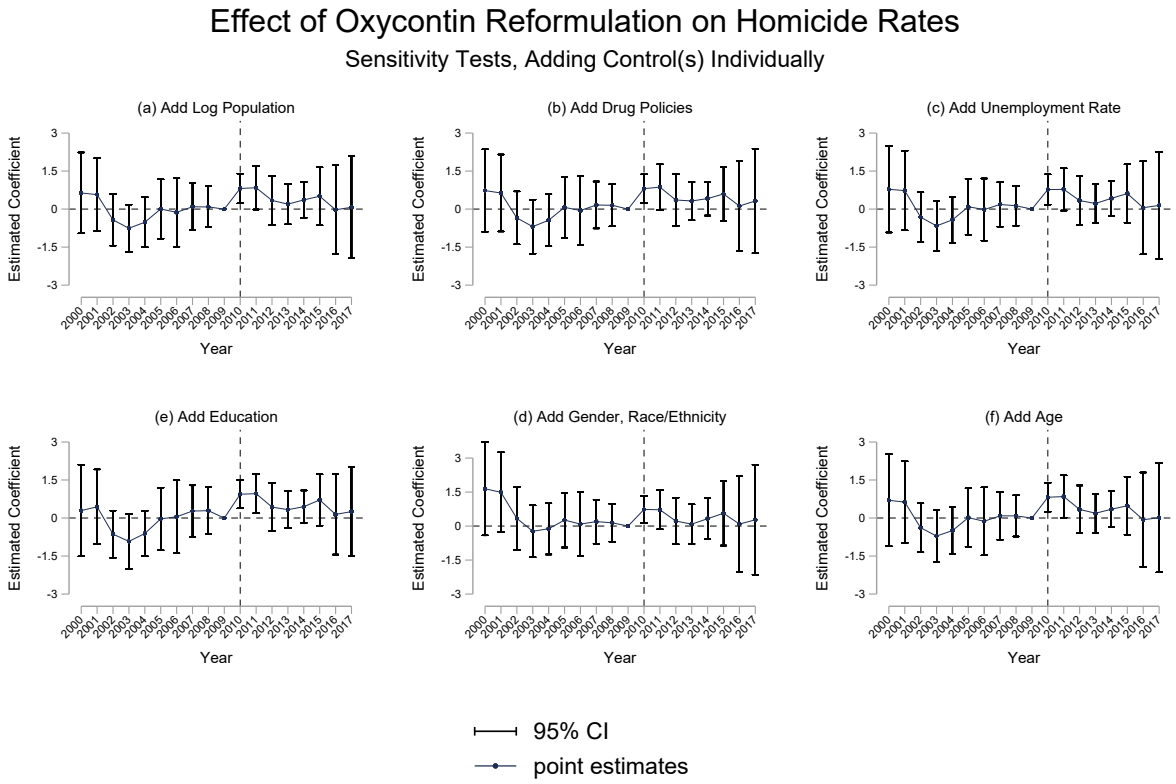
Figure 14: Sensitivity Test for the Baseline Event Study Specification: Adding Controls Sequentially



Notes: This figure presents the estimation results from adding state-level control variables to the baseline event study specification, which are (a) log state populations, (b) drug control policies, including naloxone laws, prescription drug monitoring programs (PDMP), medical marijuana laws, and recreational marijuana laws, (c) unemployment rate, (d) the percentage of state population with college degrees (e) male percentage, percentage white, percentage black, percentage Hispanic, and (f) share of population aged between 20 and 40. The addition of these variables is accumulative. For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. All regressions include a full set of state and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program. Unemployment rates are from Federal Research Economic Data (FRED). The population's percentage of people with at least a college degree is calculated using American Community Service (ACS) data. Drug policy data are from Rand's OPTIC-Vetted Policy Data Sets.

Figure 15: Sensitivity Test for the Baseline Event Study Specification: Adding Controls Individually



Notes: This figure presents the estimation results from adding state-level control variables to the baseline event study specification, which are (a) log state populations, (b) drug control policies, including naloxone laws, prescription drug monitoring programs (PDMP), medical marijuana laws, and recreational marijuana laws, (c) unemployment rate, (d) the percentage of state population with college degrees (e) male percentage, percentage white, percentage black, percentage Hispanic, and (f) share of population aged between 20 and 40. Control variables or sets of control variables are added individually. For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. All regressions include a full set of state and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program. Unemployment rates are from Federal Research Economic Data (FRED). The population's percentage of people with at least a college degree is calculated using American Community Service (ACS) data. Drug policy data are from Rand's OPTIC-Vetted Policy Data Sets.

Table 8: Sensitivity Test for the Fully Parameterized Specification: Demographic Controls

	Dependent Var.: Homicide per 100,000					
	(1)	(2)	(3)	(4)	(5)	(6)
2004-2009 OxyContin Misuse Rates						
pretrend	-0.0309	-0.0229	-0.138	-0.0312	-0.132	-0.138
	(0.093)	(0.091)	(0.109)	(0.104)	(0.115)	(0.122)
posttrend	-0.0768	-0.0827	0.0759	-0.0830	0.0674	0.0468
	(0.212)	(0.209)	(0.248)	(0.233)	(0.260)	(0.272)
shift	0.945***	0.927***	0.978***	0.963***	0.973***	0.987***
	(0.328)	(0.341)	(0.318)	(0.349)	(0.324)	(0.335)
2004-2009 Other Pain relievers Misuse Rates						
pretrend	0.0190	0.0217	0.0347*	0.0142	0.0345*	0.0315*
	(0.016)	(0.016)	(0.020)	(0.017)	(0.020)	(0.019)
posttrend	0.0184	0.0184	-0.00158	0.0292	-0.000644	0.0101
	(0.038)	(0.038)	(0.043)	(0.044)	(0.043)	(0.048)
shift	-0.153	-0.158	-0.161	-0.146	-0.161	-0.152
	(0.115)	(0.115)	(0.114)	(0.118)	(0.114)	(0.114)
pop.	No	Yes	No	Yes	Yes	Yes
gender/race/ethnicity	No	No	Yes	No	Yes	Yes
age	No	No	No	No	No	Yes
state FE	Yes	Yes	Yes	Yes	Yes	Yes
time FE	Yes	Yes	Yes	Yes	Yes	Yes

Notes: * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Columns (1) through (6) of this table present the estimation results from the sensitivity tests of the baseline fully parameterized specification with state-level demographic controls, including (1) log state populations, (2) male percentage, percentage white, percentage black, percentage Hispanic, and (3) share of the population aged between 20 and 40. For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. Unless otherwise noted, all regressions include a full set of state and year dummies and time trends for Florida and the states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

Table 9: Sensitivity Test for the Fully Parameterized Specification: Drug Policy and Economic Variables

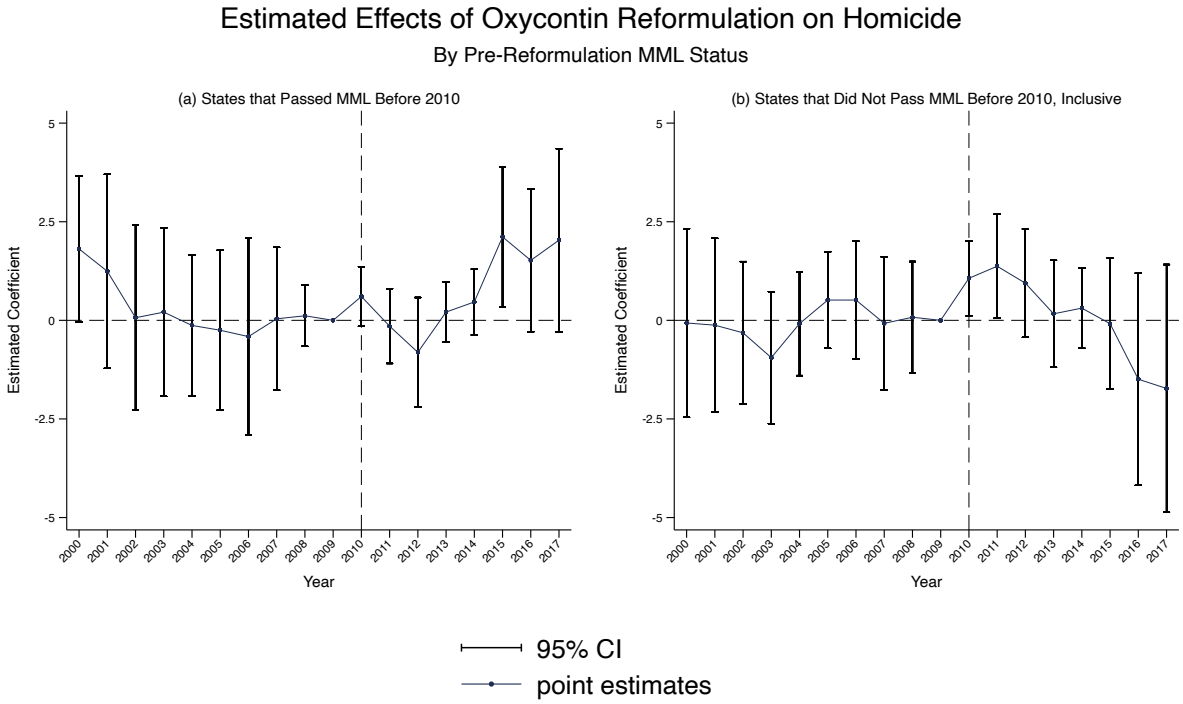
	Dependent Var.: Homicide per 100,000					
	(1)	(2)	(3)	(4)	(5)	(6)
2004-2009 OxyContin Misuse Rates						
pretrend	-0.138	-0.121	-0.153	-0.140	-0.134	-0.0536
	(0.122)	(0.121)	(0.122)	(0.122)	(0.118)	(0.105)
posttrend	0.0476	0.0421	0.00466	0.0565	0.0653	-0.0266
	(0.272)	(0.282)	(0.257)	(0.286)	(0.284)	(0.237)
shift	0.978***	0.890**	1.058***	0.961**	0.911***	0.811**
	(0.332)	(0.398)	(0.379)	(0.375)	(0.314)	(0.399)
2004-2009 Other Pain relievers Misuse Rates						
pretrend	0.0317*	0.0308*	0.0326*	0.0316*	0.0330*	0.0157
	(0.019)	(0.018)	(0.019)	(0.019)	(0.019)	(0.017)
posttrend	0.00973	-0.000321	0.0275	0.00939	0.00347	0.0191
	(0.048)	(0.046)	(0.049)	(0.050)	(0.052)	(0.043)
shift	-0.151	-0.123	-0.163	-0.149	-0.147	-0.168
	(0.113)	(0.133)	(0.117)	(0.117)	(0.113)	(0.119)
pop.	Yes	Yes	Yes	Yes	Yes	Yes
gender/race/ethnicity	Yes	Yes	Yes	Yes	Yes	Yes
age	Yes	Yes	Yes	Yes	Yes	Yes
state FE	Yes	Yes	Yes	Yes	Yes	Yes
time FE	Yes	Yes	Yes	Yes	Yes	Yes

Notes: * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. The table displays results from sensitivity analysis incorporating drug policy and economic factors. It examines the effects of Prescription Drug Monitoring Program (PDMP), Medical Marijuana Laws (MML), Recreational Marijuana Laws (RML), Naloxone Laws (NAL), state unemployment rates, and the proportion of the population with a college degree across columns (1) to (6). For all regressions, the study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. Standard errors are clustered at the state level. All regressions include a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program. Lastly, All specifications are estimated with a full set of demographic controls, including (1) log state populations, (2) male percentage, percentage white, percentage black, percentage Hispanic, and (3) share of the population aged between 20 and 40.

The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates and other pain reliever misuse rates are from the National Survey of Drug Use and Health (NSDUH). Demographic characteristics are calculated using the age-adjusted version of county-level population files from the SEER program.

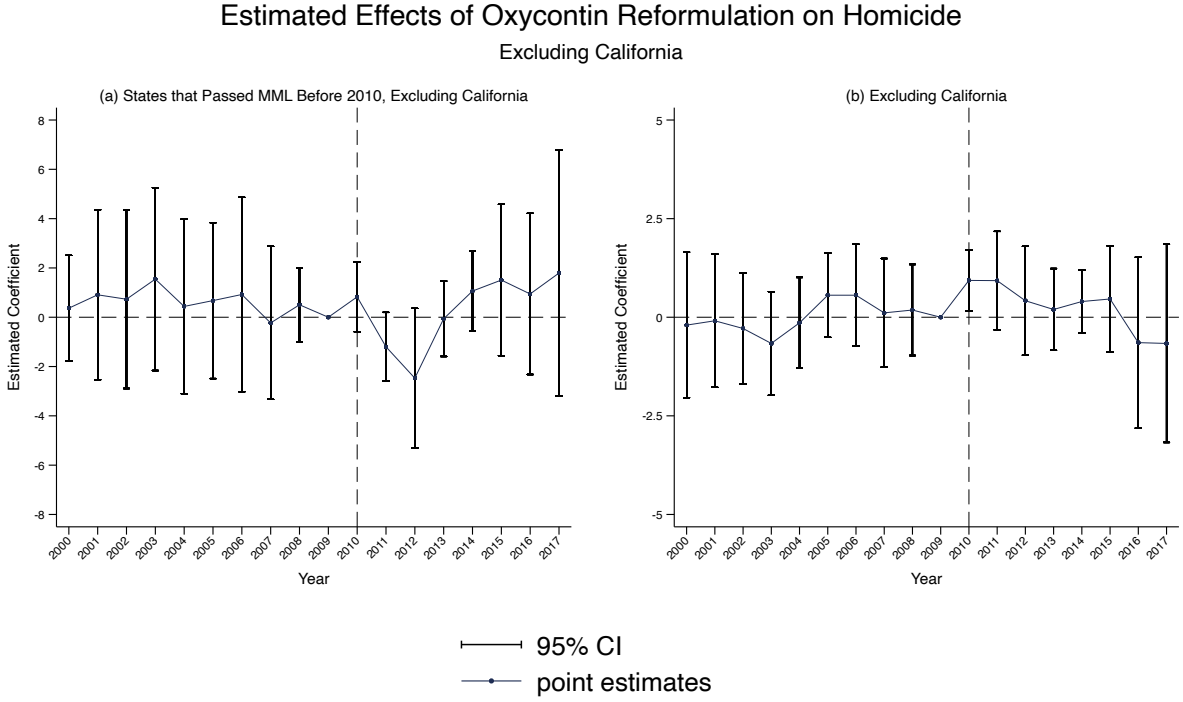
C.3 Homicide Reduction Hypothesis of MML

Figure 16: Effects of OxyContin Reformulation on Homicide: By Medical Marijuana Legalization Status



Notes: This figure presents the estimated effects of the OxyContin reformulation on homicide rates. Panel (a) shows results for states that enacted medical marijuana laws (MML) before 2010, while Panel (b) presents results for states that either passed MML after the reformulation or did not enact MML during the study period. For both specificatoins, the study period is from 2000 to 2017. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. All regressions include a full set of state and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH). Drug policy data are from Rand's OPTIC-Vetted Policy Data Sets.

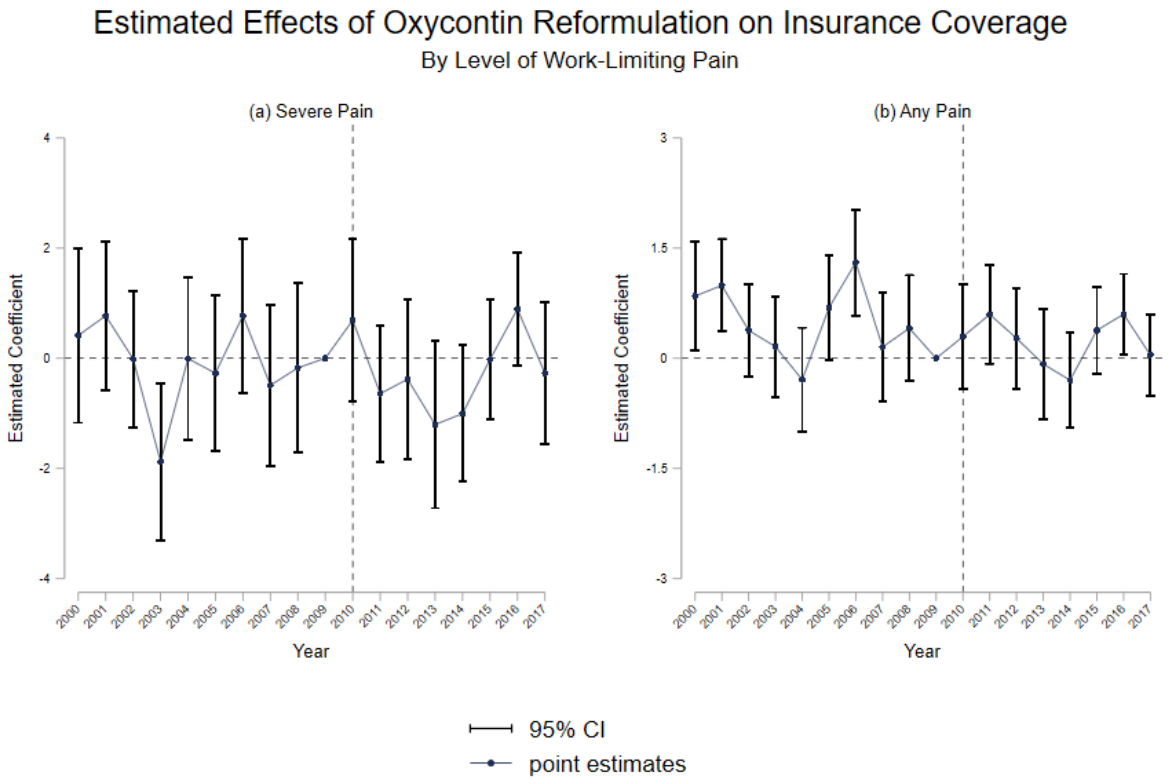
Figure 17: Effects of OxyContin Reformulation on Homicide: The Role of California



Notes: This figure presents the estimated effects of the OxyContin reformulation on homicide rates, with California excluded. Panel (a) shows results for states that enacted medical marijuana laws (MML) before 2010, excluding California, while Panel (b) displays results for the entire sample, also excluding California. For both specificatoins, the study period is from 2000 to 2017. Standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. All regressions include a full set of state and year dummies and a set of trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.

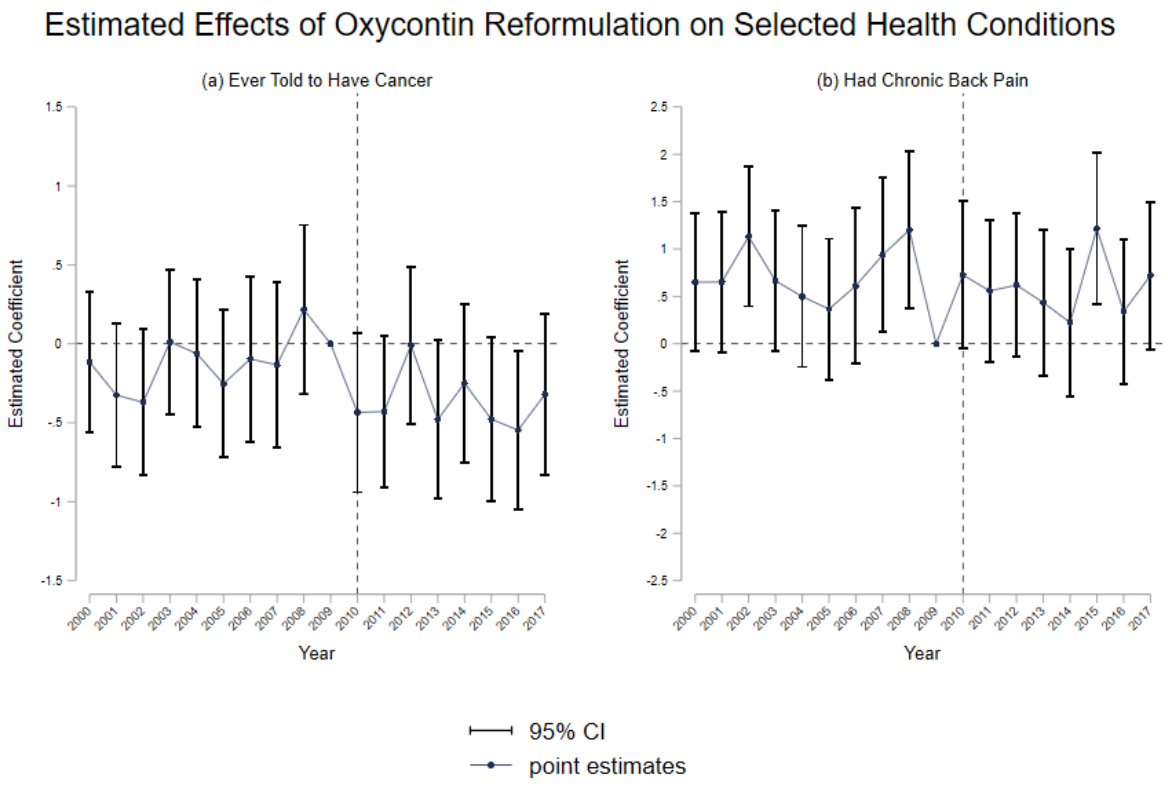
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates are from the National Survey of Drug Use and Health (NSDUH). Drug policy data are from Rand's OPTIC-Vetted Policy Data Sets.

Figure 18: Diagnostic Test: Percentage Insured by Pain Level



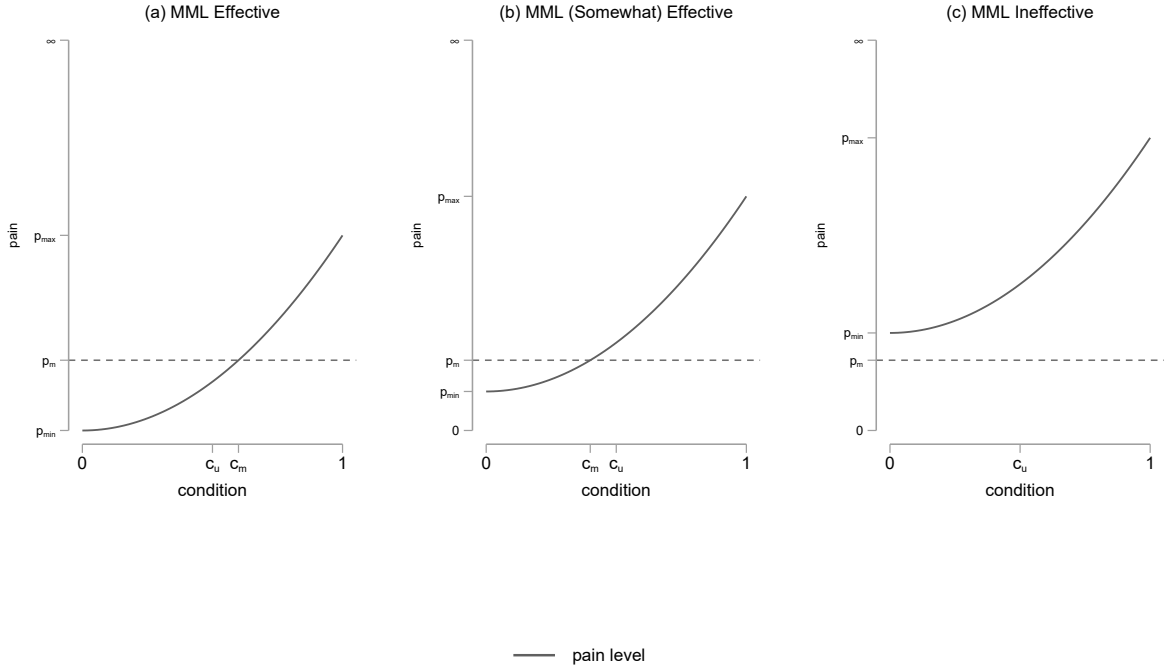
Notes: This figure presents the estimated coefficients of state-level pre-reformulation OxyContin misuse rates on homicide rates using the baseline event study specifications. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. For all regressions, standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. The regression includes a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

Figure 19: Diagnostic Test: Selected Health Outcomes



Notes: This figure presents the estimated coefficients of state-level pre-reformulation OxyContin misuse rates on homicide rates using the baseline event study specifications. The study period is from 2000 to 2017. Data are for all 50 US states plus the District of Columbia. For all regressions, standard errors are clustered at the state level. The confidence interval for all estimated coefficients is set at 95% level. The regression includes a full set of state and year dummies and time trends for Florida and states bordering Mexico. Additionally, each regression is weighted by state-year population estimates from the SEER program.
The data source for homicide rates is death certificate-based homicide data from the National Vital Statistics System (NVSS). 2004-2009 state-level OxyContin misuse rates obtained from the National Survey of Drug Use and Health (NSDUH).

Figure 20: Effectiveness of Medical Marijuana Laws in Substance Use Disorder Prevention: Position of the Max Level Manageable Pain



Notes: This figure illustrates how the position of the max level manageable pain by medical marijuana, p_m, relative to patient pain distribution, affects the size of possible switchers, c_m, from prescription opioids to medical marijuana if legal access to medical marijuana is provided. In all three panels of this figure, c_u is the fraction of untreated patients.