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THE OPIOID CRISIS, HEALTH, HEALTHCARE, AND CRIME: A REVIEW OF QUASI-EXPERIMENTAL ECONOMIC STUDIES

Johanna Catherine Maclean
Justine Mallatt
Christopher J. Ruhm
Kosali I. Simon

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The Opioid Crisis, Health, Healthcare, and Crime: A Review Of Quasi-Experimental Economic Studies

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ABSTRACT

Opioid use is one of the most substantial and long-lasting public health crises faced by the United States. This crisis, which began by the mid-1990s and continues through the time of writing, causes 136 fatal opioid overdoses each day and costs the U.S. at least $596 billion each year. These numbers, while incredibly large, likely do not capture the full toll of the crisis on American society. In this study, we review quasi-experimental studies that examine the relationship between opioids and health and healthcare, and crime outcomes in the U.S. We focus on the U.S., a country particularly hard hit by the crisis which has adopted a broad array of policies aimed at curbing it.

Our findings align with the general perception that the opioid crisis has negatively impacted a range of health outcomes and increased healthcare costs, with limited evidence that opioids (which are designed to reduce chronic pain) have enhanced work capacity or other metrics that might capture intended benefits from appropriate use of these medications. While opioids have worsened many health outcomes, the healthcare system played a role in the emergence of the epidemic and its continuation. Further, studies suggest that opioids increase crime, although the link is not as strong as has been observed in previous drug epidemics; this finding is consistent with the pharmacological difference between opioids and stimulant substances (e.g., cocaine) that dominated earlier drug epidemic periods characterized by higher levels of crime. Through the provision of treatment to address underlying addiction and the development of strategies to effectively curtail access to opioids, the healthcare system potentially has an important role in attempts to end the crisis.

Johanna Catherine Maclean
Department of Economics
Temple University
Ritter Annex 869 Philadelphia,
PA 19122
and NBER
catherine.maclean@temple.edu

Justine Mallatt
Bureau of Economic Analysis
U.S. Department of Commerce
Justine.Mallatt@bea.gov

Christopher J. Ruhm
Frank Batten School of
Leadership and Public Policy
University of Virginia
235 McCormick Rd.
P.O. Box 400893
Charlottesville, VA 22904-4893
and NBER
ruhm@virginia.edu

Kosali I. Simon
O'Neill School of Public and
Environmental Affairs
Indiana University
1315 East Tenth Street
Bloomington, IN 47405-1701
and NBER
simonkos@indiana.edu

1. Introduction

Each day, there are 136 fatal overdoses in the United States recorded as involving opioids, leading to over 49,000 deaths per year (CDC, 2021c). Between 1999 and 2019, the opioid crisis has claimed over 500,000 American lives (CDC, 2021c). (These are actually under-counts since opioid involvement is not completely reported on death certificates, as discussed below.) The scale of this crisis is immense and it is challenging to meaningfully quantify its impact on American society. For comparison 58,220 Americans died in the Vietnam war (National Archives, 2018) and in 2019 there were 37,595 motor vehicle fatalities (CDC, 2021a). The opioid crisis, beginning in the mid-1990s, has entered its third decade and shows no sign of abating. Figure 1, which reports fatal opioid overdoses from 1999 through 2020, demonstrates that death rates have increased in virtually every year. The economic costs of the crisis are large: the Council of Economic Advisers estimates that the crisis costs the U.S. $596 billion dollars each year (White House Council of Economic Advisers, 2017) and some calculations indicate that the costs are considerably higher (Florence et al., 2016).[1]

We view the opioid crisis from an economic perspective and contend that it results from an interaction between supply-side and demand-side factors, and feedback between the two. In particular, supply-side factors created a setting ripe for the over-use of this extremely addictive medication. In the 1980s and 1990s prescribing regulations were limited in the U.S. pharmaceutical suppliers (both manufacturers and distributors) responded to this permissive regulatory environment by engaging in an extraordinarily well-financed, aggressive, and sophisticated marketing strategy aimed at changing social norms around opioids and targeting states with relatively lax prescribing laws. These forces interacted with demand-side factors that determined which groups would be most susceptible to the crisis in its initial stages: fundamental changes in the U.S. labor market (e.g., foreign competition, automation of routine tasks, declining strength of labor unions) weakened economic prospects for specific groups of Americans, in particular White men with lower levels of education, and these individuals were disproportionately and negatively impacted during the initial stages of the crisis (please see Monnat (2022), in this volume, for a discussion of disparities). Over time, interactions between supply- and demand-side factors, public policies designed to curb opioid use, and changes in the types of opioids available in drug markets allowed the crisis to continue, expand in scope, and impact a larger, and more diverse, share of the U.S. population.

In this paper, we use our previously developed conceptual model (Maclean et al., 2020)

[1]This number is inflated from the original estimate ($504 billion) to 2021 terms by the authors using the Consumer Price Index.

and review relationships between opioids, health outcomes, healthcare, and crime.[2] Our review focuses on U.S. economic studies using quasi-experimental methods (e.g., difference-in-differences models) designed to elicit causal inference from observational data using policy-induced variation in relevant variables. We located studies by searching online sources[3] and through conversations with economists and researchers conducting research using quasi-experimental methods to estimate the effect of public policies on opioid outcomes. We focus on the U.S. as this country has arguably been hardest hit, to date, by the opioid crisis which is generally viewed as originating in this country. Further, the U.S. has adopted a wide range of policies − targeting both supply- and demand-side factors − at the local, state, and federal levels designed to curtail the crisis. Collectively, these features suggest that the U.S. is an interesting and important 'laboratory' to understand the global opioid crisis.[4] Our focus on quasi-experimental methods leveraging variation from policy changes is motivated by an interest in understanding the role of public policies in curbing the crisis. We consider both health and medical care, as well as crime, as crime outcomes are directly determined by demand for opioids, which are a type of healthcare and are driven by addiction.

While our study is, by design, narrow, this does not imply that carefully examining other facets of the opioid crisis is less crucial. We refer interested readers to excellent reviews of the literature outside economics (Barry and Frank, 2019; Mauri et al., 2020), state actions to curtail opioid use (Pacula and Stein, 2020), and factors that lead to the emergence and decline of illicit drug epidemics more broadly defined (Moore and Pacula, 2020).

Five principle findings emerge from our review. First, researchers have allocated substantial efforts to studying relationships between opioids, health, medical care, and crime. Second, greater use of opioids has negatively impacted both health and healthcare outcomes in the U.S., worsening a range of health metrics and increasing the use of medical services. Moreover, there is at best only limited evidence that opioids improve quality of life or work capacity by allowing for better management of chronic pain (i.e., the indicated use of these medications). The opioid crisis is an unusual example of additional healthcare leading to worsening of health outcomes, which poses an unconventional challenge to economic measurement. Third, the healthcare sector in the U.S. has played an important role in the emergence and propagation of the opioid crisis. Fourth, opioids are related to crime, although the linkages are not strong as those identified in previous illicit drug epidemics, consistent with the pharmacological

[2]We also discuss measures of labor supply as a proxy for work capacity and given the tight link between health and labor supply Currie and Madrian (1999).

[3]In particular, we draw studies from our earlier paper and we searched through Google Scholar in October 2021. We describe more details on our search in that study.

[4]While we focus on the U.S., we encourage future studies that examine the crisis in other counties.

properties of opioids compared with the substances dominating earlier drug epidemics in the U.S. (e.g., cocaine). Fifth, while the federal government and states have adopted a range of policies, both those targeting the supply of opioids and demand for these medications, research shows that policies have not been unilaterally successful. Furthermore, in some cases (e.g., policies emphasizing curtailing the supply of prescription opioids as well as the reformulation of OxyContin) the literature finds that policies may have had unintended consequences in the course of the crisis' evolution from prescription to illicit opioids. The literature on policy impacts emphasizes the need for comprehensive interventions that pair reduced access to opioids with increased support for treatment. There is stigma and an incomplete understanding regarding addiction science among many Americans, leading to a common perception emphasizing the role of personal choices and moral failings as sources of addiction, rather than treating addiction as a chronic medical condition.

The paper proceeds as follows. Section 2 provides a brief review of the emergence and growth of the opioid crisis as described in our earlier work (Maclean et al., 2020). Section 3 discusses the prevalence of opioid use disorder and mortality rates as well as the costs to the healthcare system, and outlines an economic model of the demand for health and healthcare. The section situates opioids in this model, and reviews the economic literature on opioids, health, and medical care. Section 4 provides a theoretical basis for a relationship between substance use and crime, and reviews the literature on opioids and crime. Both Sections 3 and 4 highlight key opioid-related policies adopted by state and federal governments in the U.S. in attempts to curb the crisis, and discuss the effectiveness of the policies and unintended consequences. Section 5 offers a discussion and lays out potential avenues for future research.

2. Emergence of the opioid crisis

This section outlines how we view the opioid crisis as emerging over time, divided in three waves. Understanding the evolutionary path is necessary to appreciate the tight link between the crisis and the healthcare system.

Figure 1 plots fatal overdoses in the U.S. in each year between 1999 and 2020 related to: (i) any opioid, (ii) prescription opioids ('natural and semi-synthetics'), (iii) heroin, (iv) synthetic opioids such as fentanyl and tramadol, and (v) methadone (which can be used to treat chronic pain and is used in the treatment of opioid use disorder). Data in this figure have been corrected for incomplete reporting of opioid involvement on death certificate records. See Ruhm (2018) for a discussion of this issue and our empirical approach to correct for mis-reporting.

2.1 Wave I: Mid-1990s through 2010

Prior to the current crisis, there was relatively limited use of opioids in the treatment of chronic pain within the U.S. In particular, some scholars characterize the U.S. healthcare system pre-crisis as having 'opia-phobia,' in part because misuse of opioids extends back as far as the Civil War (Macy, 2018). Healthcare professionals were therefore hesitant to prescribe opioids for chronic pain even in settings where such medications could be expected to have large benefits to patients – such as treatment for cancer-related pain and among terminally ill patients (Quinones, 2016; Hill Jr, 1993; Paice et al., 1998; Weissman, 1993). Somewhat ironically, given the massive toll the opioid crisis has taken on the U.S., for much of the 20th century, opioids were arguably under-used in this country.

The 1996 approval and release of OxyContin by Purdue Pharma is often seen as the trigger event for the current opioid crisis. A key feature of OxyContin (vs. other prescription pain relievers) is that the medication does not have added acetaminophen or other NSAID (which can cause harmful side effects if taken in toxic doses). While Purdue Pharma played a prominent role in the emergence of the epidemic, other opioid companies also contributed heavily to the crisis in terms of marketing and distributing opioids to patients without adequate oversight (Haffajee and Mello, 2017). One consequence was that, in 2021, three of the largest prescription drug distributors (McKesson, Cardinal Health, and Amerisource Bergen) and Johnson & Johnson (a large U.S. company that develops medical devices and pharmaceuticals) reached a $26 billion settlement with U.S. state and local governments for their role in propagating the opioid epidemic.[5] We emphasize Purdue Pharma in our discussion due to the popularity of OxyContin, but other producers and distributors of opioid companies also facilitated the distribution and sale of this medication and other opioids.

Purdue Pharma's marketing and promotion of OxyContin was unprecedented (United States General Accounting Office, 2003; Van Zee, 2009). The marketing budget allocated to the OxyContin launch was orders of magnitude larger than any other medication produced by Purdue Pharma or its competitors. In 2001, the company spent $200 million ($314 million in 2021 dollars) on the marketing and promotion of OxyContin alone (United States Senate, 2002). Interestingly, clinical trials at the time did not show that OxyContin was more efficacious than similar prescription pain medications available (Heiskanen and Kalso, 1997; Kaplan et al., 1998; Mucci-LoRusso et al., 1998; Hale et al., 1999; Stambaugh et al., 2001). Further, an earlier Purdue Pharma extended release pain reliever product (MS Contin) was heavily, although not to the level of OxyContin, misused in the 1980s and early 1990s in

[5]Please see https://www.nytimes.com/2021/07/21/health/opioids-distributors-settlement.html (last accessed December 17, 2021)

the U.S. (Crews and Denson, 1990; Van Zee, 2009). Moreover, Purdue Pharma focused its marketing and promotional efforts for OxyContin on areas of the country that had the weakest prescribing regulations as these areas were deemed most profitable (Van Zee, 2009; Alpert et al., 2019). The advertising campaign emphasized normalizing the use of opioids within the general population (e.g., comparing OxyContin to over-the-counter pain medications), a departure from previous norms emphasizing the use of pain medications for, predominately, cancer and terminally ill patients, and it downplayed the potential for addiction (e.g., stating that the risk of addiction was less than one percent) (Meier, 2003; Van Zee, 2009).

In addition to these efforts at promoting OxyContin, Purdue Pharma and other opioid companies funded the American Pain Society, which lobbied the Joint Commission (a well-regarded non-profit hospital accreditation organization in the U.S.) to emphasize the treatment of pain through the use of medications by healthcare professionals (McGreal, 2018). The actions of the Joint Commission lead to changes in treatment protocols and resulted in much wider use of medications to treat pain. The results were observable in the number of prescriptions filled for opioid pain relievers. For example, in 2012, there were 259 million opioid prescriptions dispensed and one in four Americans was prescribed an opioid medication each year (Kilby, 2016; Mallatt, 2019). Although the Joint Commission revised standards in 2001, the inertia in prescribing was hard to break. Notably, the Affordable Care Act (ACA) uses patient experience with pain management as a component of satisfaction surveys completed by patients. Scores on this survey impact future hospital reimbursements. Policymakers may wish to closely evaluate the incentives (i.e, to emphasize pain management through medications) created by this reimbursement structure.

Figure 2 plots the rate of opioid prescriptions filled at retail pharmacies in morphine milligram equivalents (MME)[6] per capita in the U.S. from 1992 to 2020 using data from the IQVIA Institute (2020).[7] In 1992 (the first year these data are available) the rate was 106 MME per capita and by 2011 (the height of opioid prescribing) the rate was 790 MME per capita. By 2020, the rate had declined to a low of 334 MME per capita, a 58 percent decline from 2011. Prescription opioids were misused by patients themselves[8] and diverted to non-patients through the illicit market.

[6]MME are values that represent the potency of an opioid dose relative to morphine and are a standardization common in the opioid literature.

[7]These data are based on IQVIA all-payer claims data. IQVIA collates data from various sources and covers approximately 90 percent of prescriptions filled at retail pharmacies.

[8]The Centers for Disease Control and Prevention defines drug (including opioid) misuse as follows: 'The use of illegal drugs and/or the use of prescription drugs in a manner other than as directed by a doctor, such as use in greater amounts, more often, or longer than told to take a drug or using someone else's prescription' (CDC, 2021b)

2.2 Wave II: 2010-2013

Beginning in 2010, there was a dramatic acceleration in deaths involving heroin (Figure 1). In 1999, there were 2,434 fatal heroin overdoses. By 2010 this number had increased to 3,880 deaths and by 2013 it has risen to 10,280. The growth starting in 2010 is generally believed to be, at least partially, an unintended consequence of state and federal policies aimed at reducing access to prescription opioids but failing to take into account economic substitution between different types of opioids. Economists refer to two goods (here prescription opioids and heroin) as substitutes when consumers view them as sharing similar features and are willing to use either. In practical terms, if two goods are economic substitutes, then raising the full price (including access, which was curtailed for prescription opioids by the above-noted state and federal policies) of one tends to lead people to increase use of the other. Further, this potential substitution of heroin for prescription opioids was probably aggravated by severe constraints on the availability of effective treatment for opioid use disorder.

Alpert et al. (2018) and Evans et al. (2018) highlight the importance of a reformulation of OxyContin in 2010. OxyContin had emerged as a popular prescription opioid in the 1990s and 2000s. The original formulation, which paradoxically was designed to prevent misuse, extended the release of the active ingredients. However, consumers quickly learned that they could circumvent the extended release mechanism and access the full dose through crushing and then swallowing, snorting, or injecting the drug (Van Zee, 2009). In particular, to circumvent the time release, users crushed the OxyContin pill. The time release feature of the pill was part of its physical (not chemical) structure. In August 2010, Pharma Purdue responded rapidly switched to a re-formulated version of OxyContin. The decision to reformulate the drug reflected a combination of pressure to do so by the Food and Drug Administration (FDA), the agency with the authority to regulate drugs at the federal level, as well as financial incentives whereby Purdue Pharma received additional patent protection (Keefe, 2021). The reformulated product was crush-resistant and therefore harder to swallow, snort, or inject, decreasing the value of OxyContin to consumers using the drug for non-medical purposes. Fatal heroin overdoses tripled between 2010 and 2013, whereas prescription opioid overdoses plateaued or subsided slightly. This pattern suggests that some consumers switched to heroin rather than other prescription opioids such as codeine, hydrocodone, or morphine. While the OxyContin reformulation was one important change, various state-level policies targeting access to prescription opioids generally (not exclusively OxyContin) also contributed to rising heroin use over this time period (Mallatt, 2020b) which may explain why all consumers did not simply transition to other prescription opioids. That said, some consumers (particularly older individuals) did switch to other prescription opioids in response to OxyContin reformulation

and the other policy changes. Mallatt (2021) uses Medicare (a public insurance program that predominantly covers older adults) claims data to show that consumers substituted to off-brand slow-release (non-reformulated) oxycodone and regular oxycodone.

2.3 Wave III: 2013 and onward

The opioid crisis entered its third wave in 2013, characterized by the adulteration of heroin, and other drugs such as cocaine, with fully synthetic opioids including fentanyl and its analogs (e.g, acetylfentanyl, furanylfentanyl, and carfentanil). Scholars have not yet fully determined why this relatively sudden emergence of fentanyl occurred, but negative shocks to the heroin supply, attractive properties of synthetics for suppliers vs. heroin and prescription opioids (e.g., synthetics can be entirely created in labs and are relatively cheap to produce, and easier to transport and smuggle since smaller quantities are required to achieve the same potency), and the increasing sophistication of e-commerce (which is a common platform for synthetic opioid sales) have been suggested as possible factors (Pardo et al., 2019). Whatever the reasons for the switch, drug combinations that involve fentanyl will increase the risk of death for given levels of opioid use disorder or related drug problems.

Synthetic opioids are considerably more potent than the prescription opiods or heroin that were more prevalent in Waves I and II of the crisis with the result that overdose fatalities have increased substantially in the third wave (see Figure 1). For example, two milligrams of fentanyl can be be fatal and carfentanil is 10,000 times more potent than morphine. The potency of these drugs is so substantial that law enforcement officers responding to a related crime are at risk of exposure from touching the drugs and/or breathing contaminated air at the crime scene. Many consumers are not aware that the drugs they have purchased contain fentanyl or its analogs as dealers often mix synthetics in with other opioids. This lack of information combined with the substantial differences across opioids in terms of potency led to a surge in fatal overdoses in the third wave. In particular, synthetic opioids were involved in 4,090 fatal overdoses in 2013, but this number increased to 11,612 and 59,726 in 2015 and 2020 respectively. Fentanyl is increasingly identified in other drugs such as cocaine, methamphetamine, and methylenedioxy-methamphetamine (MDMA) as an inexpensive means to increase supply (NIDA, 2021). Further, counterfeit prescription opioid pills that contain fentanyl have become more common. These consequences have raised alarm among policymakers, with the Drug Enforcement Agency (DEA) − the federal law enforcement agency within the U.S. tasked with combating domestic drug trafficking and distribution − releasing a Public Safety Alert (the first such release in six years) on this issue

in the second half of 2021 (Drug Enforcement Agency, 2021). The human costs imposed on American society are expected to continue to rise as synthetic opioids permeate a larger swath of U.S. illicit drug markets.

3. The opioid crisis, health, and healthcare outcomes

This section first discusses the prevalence and costs associated with the opioid crisis. Next, quasi-experimental studies of the relationships between opioid use, health outcomes, and medical care are reviewed. This relationship is bi-directional: opioids can impact health and medical care, but as outlined in Section 2, the healthcare system played, and continues to play, and important role in the spread of the opioid crisis. We then discuss a basic economic model of the demand for health and medical care, and highlight that, *ex ante*, greater access to prescription opioids have ambiguous impacts on health outcomes. We also discuss the role of the healthcare system in treating opioid use disorder, which is important in efforts to mitigate the opioid crisis. Fourth, we review studies that identify the healthcare system as an important driver of the opioid crisis, in particular during the first wave that was largely characterized by misuse of prescription opioids. Finally, research documenting the impact of opioid use on health and medical care is summarized, and we emphasize state and federal policies used to combat the opioid crisis; many studies in this literature leverage such policies as sources of quasi-experimental variation and provide insight on the effectiveness of public policies designed to end, or at least mitigate, the crisis.

3.1 Prevalence and costs of the opioid crisis

Official government data (National Survey of Drug Use and Health [NSDUH]) show that in 2019, 2.4 million Americans 12 years and older had an opioid use disorder (Substance Abuse and Mental Health Services Administration, 2020). NSDUH is a survey of civilian non-institutionalized individuals and excludes some groups that are at elevated risk for opioid use disorder or 'OUD' (e.g., those experiencing homelessness); therefore prevalence rates based on these data likely underestimate the true rate. Further, due to stigma, many respondents do not respond truthfully to questions designed to identify OUD. Data on mortality, while reflecting a blunt measure of opioid misuse, suggest that between 1999 and 2019 over 500,000 Americans died from an opioid overdose (CDC, 2021c).

The costs to the healthcare system extend well beyond mortality. Opioid misuse increases emergency department visits, costs of pharmaceuticals, addiction treatment, overall healthcare

costs, and costs associated with neonatal abstinence syndrome (NAS). Economic studies have attempted to construct estimates of the total costs of the opioid crisis to the U.S. across these outcomes. Estimates vary, but all suggest that the costs are high. For example, the Council of Economic Advisers estimated that the opioid crisis cost the U.S. $504 billion in 2015 alone (White House Council of Economic Advisers, 2017). Other recent estimates of the cost of the opioid epidemic range from $179 billion in 2018 (Davenport et al., 2019) and over $1 trillion in 2017 (Florence et al., 2020).

Some health scholars attribute the opioid crisis to a prolonged period of reduced economic prosperity for specific groups within the U.S. This argument is eloquently described by the 'deaths of despair' hypothesis documented in Case and Deaton (2015). The authors note that due to a range of domestic and global economic changes (e.g., automation, import competition, increased market concentration, outsourcing, productivity clusters in abstract tasks, weakening unions), less educated White workers lost economic ground and social capital compared to other demographic groups over the past several decades. As a result of their worsening economic options, these individuals consume substances (including opioids) to self-medicate the imposed mental strain (Deaton, 2020). Using this argument, the opioid crisis might be viewed as an outcome of sustained changes in the American economy rather than an manifestation of changes in the healthcare system combined with weak regulations surrounding prescribing of controlled substances.

However, there are important reasons to question the deaths of despair hypothesis, as just described. Among these are the relatively favorable experiences of Blacks and Hispanics, relative to Whites in terms of overdose mortality, during the first decade of the 21st century and the timing of mortality trends, where the causal factors described by Case and Deaton occurred several decades prior to the rapid increases in drug, suicide, and chronic liver disease mortality that they emphasize. See Ruhm (2021b) for a more comprehensive discussion.

We view the deaths of despair hypothesis as useful in determining which groups were most vulnerable to the crisis rather than as a key driver of the epidemic itself. As outlined in our earlier work, the timing of supply-side changes, such as Purdue Pharma's introduction and promotion of OxyContin in the mid-1990s, and related actions of other opioid manufacturers and distributors in subsequent years (Haffajee and Mello, 2017), better fit the timing of the crisis than the deaths of despair hypothesis, since large-scale declines in economic propriety for lower wage workers commenced much earlier in the 20th century. Further, Ruhm (2019) shows that county-level changes in economic conditions from 1999 to 2015 were essentially unrelated to changes in opioid mortality rates over the same period and Currie et al. (2018) demonstrate little relationship between the employment-to-population ratio and opioid prescriptions across

U.S. counties. Similarly, Currie and Schwandt (2020) indicate that declining labor market opportunities during the second and third decades of the 21st century cannot explain a substantial portion of the trends in opioid-related outcomes.

3.2 An economic model of the demand for health and healthcare

In a canonical economic model, consumer demand for medical care is derived from the demand for good health (Grossman, 1972). Consumers combine healthcare and non-medical inputs (e.g., food, illicit substances, sleep) to produce health in what is refereed to by economists as a 'household production function.' We can use this model to understand how opioids may have dual impacts on health and healthcare outcomes.

Somewhat ironically, given the current scope of the crisis, the goal of prescribed opioids is to improve health. That is, these medications, when used correctly under the guidance of a well-meaning, accurately informed, and careful healthcare professional, have potential health benefits. For example, their use may reduce pain for patients with end-stage cancer or, for short periods of time, after certain surgical interventions.[9] When used in this manner, we might hope that opioids *improve* health status, or at least reduce patient's disutility from poor health (i.e., as a result of less chronic pain).

Indeed, previous research suggests that access to effective non-opioid pain management treatments can sometimes improve work capacity (a proxy for health status). For instance, studies examining the removal of Vioxx – a Cox-2 inhibitor used to treat chronic pain – from the U.S. healthcare market indicate that effective pain management has substantial benefits for various work capacity metrics (Garthwaite, 2012; Bütikofer and Skira, 2018).[10]

However, opioids, even when used as intended under the supervision of a healthcare professional, have side effects. In particular, patients report sedation, dizziness, nausea, vomiting, constipation, respiratory depression, hyperalgesia, immunologic and hormonal dysfunction, muscle rigidity, and myoclonus. These side effects, even for legitimate users, can offset the pain reduction benefits of opioids. Non-medical use of opioids has few, if any, health benefits. For example, when misused, opioids (still viewed as a market good but more similar to substances such as cocaine or other illicit drugs) can harm health through addiction, intoxication, and in extreme cases reduced respiration can lead to death.

Taken together, while theoretically the impact of opiods on health is mixed, most evidence

[9] However, as noted in Section 2, opioids are generally not more effective at treating chronic pain than alternative interventions.

[10] Vioxx, approved by the FDA in 1999, was voluntarily removed by the manufacturer (Merck & Co) in 2004 due to increased risk of heart attack and stroke associated with long-term, high-dosage use of the medication.

suggests that the harms imposed by opioids outweigh the benefits. The literature provides little evidence that prescription opioids improve health (Harris et al., 2019; Beheshti, 2019b).

3.3 The role of the healthcare system

As described in Section 2, an aggressive, sophisticated, and well-financed marketing campaign of highly addictive medications created an environment ripe for over-use of prescription opioids, and initial policy responses, largely focusing on the healthcare sector, targeted fairly blunt reductions of opioid use without sufficient consideration of substitution possibilities. This suggests that consideration of the healthcare sector and its changing role over time is critical to understand the epidemic and to develop effective strategies to bring it to an end. In this section, we discuss studies that document, to vary degrees and along different margins the role the healthcare sector broadly defined played, and continues to play in shaping the opioid crisis. We conclude this section with a broad summary of possible policy responses that leverage the healthcare sector in fighting the opioid crisis.

3.3.1 Emergence and continuation of the opioid crisis

Given the nature of the opioid crisis that emerged through the use of opioids prescribed by healthcare professionals, the healthcare system is closely related to both the initiation and continuation of the crisis. We next review a series of studies that examining these issues.

Alpert et al. (2019), using recently unsealed court documents, show that Pharma Purdue specifically targeted OxyContin marketing in states with limited prescribing regulations. In particular Pharma Purdue allocated fewer marketing dollars to 'triplicate states,' that is states that required healthcare professionals to create three copies of any opioid prescriptions. These state regulations imposed additional hassle to healthcare professionals which deterred prescribing of OxyContin. The authors further document that triplicate states were less adversely impacted by the opioid crisis, likely due to the lowered prescribing of opiods attributable to protection afforded to them by state regulations on prescribing in the 1990s. Arteaga Cabrales and Barone (2021), using the above-noted unsealed court documents, also show that marketing of Purdue Pharma led to worse opioid-related outcomes over time. Collectively, these studies empirically document the role of the pharmaceutical industry in igniting the epidemic in the 1990s through marketing efforts.

Healthcare professionals conceptually continue to play an important roll in dispensing prescription opioids through the time of writing. Such professionals provide access to these medications for appropriate uses, but the prescriptions are also potentially misused by

some patients and/or diverted to illicit drug markets. Empirical research establishes this importance. For example, differences across physicians in their prescribing practices can explain a substantial amount of cross-section variation in opioid misuse. Finkelstein et al. (2019) examine changes in opioid misuse among individuals who migrate across counties in the U.S. to understand the importance of the local prescribing environment. They establish that the local environment plays an important role in cross-sectional variation in opioid misuse: 30 percent of the variation in opioid deaths across U.S. counties is explained by place-specific effects which include physician prescribing behavior. Schnell and Currie (2018) empirically explore how differences across physicians in prescribing behavior are affected by the quality of physician medical training (proxied by medical school rank) and find that physicians with degrees from lower-ranked medical schools prescribe opioids at higher rates than observably similar physicians with degrees from higher-ranked schools. While not speaking to specific mechanisms that drive differences in prescribing patterns across physicians, Barnett et al. (2017) exploit plausibly exogenous physician assignment in emergency departments to understand how cross-physician differences in the propensity to prescribe opioids impact downstream misuse of these medications. One can view assignment of patients to emergency department physicians as essentially as good as random as there is arguably little scope for patients in this setting to select physicians (and vice-versa). Using this source of variation among Medicare beneficiaries with no opioid prescriptions in the six months prior to the episode, being assigned to a physician with a higher (vs. lower) pattern of opioid prescribing leads to an increase in the probability that the beneficiary receives a along-term opioid prescription. Schnell (2018) shows that there are important differences across physicians in their response to changes in the supply of prescription opioids. Finally, Lin et al. (2020) show that counties providing more intensive medical care (of all types) have higher rates of opioid mortality than those offering less intensive care.

How best to address differences across providers in their propensity to prescribe opioids is not immediately clear. Improving the quality of medical training, highlighted as empirically important by Schnell and Currie (2018), is likely challenging given the decentralized nature of medical schools and such a policy approach would impact, at most, future cohorts of physicians, leaving prescribing patterns among incumbent physicians unchanged. 'Lighter touch' interventions to date have not offered substantial promise to adjust prescribing patterns. For example, Sacarny et al. (2016) show that sending information to physicians with elevated prescribing patterns in the form of letters does not appear to change behaviors. However, more extensive continuing education efforts could plausibly have a more positive effect.

3.3.2 Treatment of opioid use disorder

Many factors can increase an individual's risk for developing OUD, ranging across individuals and including: experiencing trauma, environment, genetics (e.g., some individual's brain chemistry may lead to greater 'reward' in terms of euphoria from substance use), and opportunity. However, effective treatment options are available. We focus on OUD treatment here but refer readers to Maclean et al. (2020) for a more detailed discussion.

The gold standard of treatment incorporates the use of medications. The effectiveness of buprenorphine, methadone, and naltrexone has been established (Murphy and Polsky, 2016; Onuoha et al., 2021). Buprenorphine is a partial opioid agonist and methadone is a full opioid agonist. These medications act on the same opioid receptors in the brain as prescription opioids, heroin, and fentanyl and its analogs, but produce a less intense sense of euphoria, and reduce withdrawal symptoms and cravings. Naltrexone is an opioid antagonist and blocks activation of opioid receptors. Instead of controlling withdrawal symptoms and craving like (partial or full) opioid agonists, naltrexone prevents any opioid from producing feelings of euphoria, highs, or other rewarding effects for the user. Buprenorphine and naltrexone are frequently prescribed by healthcare professionals in outpatient settings whereas methadone is generally dispensed in standalone specialized facilities. Healthcare professionals must receive a 'waiver' from the DEA to dispense buprenorphine. Waivers, which are awarded by the DEA following the 2000 Drug Addiction Treatment Act, initially allowed only physicians to dispense buprenorphine and to no more than 30 patients. The DEA gradually granted waivers to a wider set of healthcare professionals (e.g, nurse practioners) and set higher patient limits (the current limit is 100 and healthcare professionals can apply for an increase to 275 patients after one year). Patient response to these medications varies, as they work in heterogeneous ways, suggesting that there is no 'one-size-fits-all' treatment protocol. Instead, patient characteristics, history, and circumstances should be considered when selecting treatment.

Time in treatment may allow those with OUD to re-establish normal brain function. The frontal lobe of the brain (responsible for higher level executive functions) shows reduced activity among those with OUD (and other SUDs). However, addiction science suggests that re-establishing normal activity of the brain typically requires 100 substance-free days and most treatment programs are of much shorter duration, which may pose challenges to patients' sobriety post-treatment.

While medications used to treat opioid use disorder are effective, they are under-used: studies suggest that less than 50 percent of privately funded substance use disorder (SUD) treatment facilities offer medications for opioid use disorder (MOUD) and roughly a third of OUD patients receiving care in such facilities receive medication as part of their treatment

(Knudsen et al., 2011). There are many reasons for under-use of MOUD, but stigma is identified as an important barrier by healthcare scholars (Stone et al., 2021). There is a view among a subset of healthcare professionals, and various segments of the general public, that using opioid agonists and opioid antagonists is 'replacing one addiction with another.' This view, while considered incorrect by leading health organizations, such as the World Health Organization which lists medications used to treat opioid use disorder as 'essential medicines' (World Health Organization, 2005), leads to under-use of effective treatment for OUD.

The isolation of the U.S. substance use disorder (including OUD) treatment delivery system from the broader healthcare system may pose barriers to treatment receipt. Reasons for the the segregation of SUD treatment include: stigma, limited understanding of addiction by healthcare professionals and the public generally, lack of training among healthcare providers, concerns among insurers and public payers that the demand for treatment is elastic and that covering such services in insurance contracts can lead to overuse and escalating healthcare costs, inadequate payments to providers (e.g., reimbursement rates for wrap around services are often limited and salaries for behavioral healthcare providers are often low, leading to workforce shortages), and informal treatment options that are designed to operate outside a structured healthcare system (e.g., Narcotics Anonymous). There are likely feedback loops across these different factors, but collectively they have created an isolated system.

In addition to clinical research, economic studies using quasi-experimental designs to estimate causal effects show that (i) expanding access to SUD treatment generally (including OUD, although most studies to date have not exclusively examined this modality) as measured by the number of providers in a healthcare market, and (ii) expansions of insurance coverage that includes such treatment induces individuals to take up treatment and reduces measures of SUD (including OUD). For example, Wen et al. (2017), Swensen (2015), and Bondurant et al. (2018) find that increases in the number of SUD treatment facilities lower SUD-related mortality. Studies that exploit variation in state (public and private) insurance policies that increase coverage for SUD treatment demonstrate that treatment utilization increases (Maclean and Saloner, 2018; Maclean et al., 2018; Meinhofer and Witman, 2018; Cher et al., 2019; Grooms and Ortega, 2019; Saloner and Maclean, 2020). As a specific example, Meinhofer and Witman (2018) find that a major expansion of Medicaid (the primary insurer of low-income people in the U.S.) that occurred with the Affordable Care Act (a major policy implemented in 2010 that fundamentally transformed many aspects of the U.S. healthcare system) doubled prescriptions for medications used to treat OUD, increased admissions to drug treatment centers, and raised the probability that OUD treatment providers accepted

Medicaid as a form of payment.[11]

The literature is not fully consistent, with some studies showing limited evidence that treatment use increases post-insurance expansion. For example, in 2010, young adults became eligible to be covered by their family's insurance plans until age 26 under the Affordable Care Act. Saloner and Lê Cook (2014) find no evidence this ACA dependent coverage mandate changed rates of reported SUD treatment among young adults in the NSDUH.[12] Interestingly, exploiting variation from the same policy, Saloner et al. (2018) document that post-expansion, admissions to publicly-funded standalone SUD treatment facilities decline among younger adults. The structure of payments to providers can also have implications for service use. Donohue et al. (2018) show that a global payment and accountable care initiative implemented in 2009 by Blue Cross Blue Shield of Massachusetts − designed to integrate care and improve outcomes − had no measurable impact on utilization of OUD treatment. Thus, insurance policies, both aggregate (e.g., state or federal level) and micro (e.g., specific insurers), must be carefully devised to ensure that the policies promote treatment possibilities.

The effect of insurance expansions on measures of opioid misuse is inconclusive to date.[13] The above-noted ACA Medicaid expansion does not appear to have impacted opioid-related mortality (Averett et al., 2019; Abouk et al., 2019) while the dependent coverage mandate appears to have reduced such fatalities among young adults impacted by the policy (Wettstein, 2019). Economic theory suggests that insurance coverage can lead to moral hazard, a term economists use to describe changes in people's behavior when they do not face the full cost of their actions; insurance reduces the cost of medical care faced by consumers and therefore can affect behaviors. In this context, moral hazard could induce *over-use* of prescription opioids. The findings from Medicaid expansion and the dependent coverage provision do not reveal evidence of such moral hazard. However, Powell et al. (2020) study how the introduction of Medicare prescription drug coverage ('Part D') in 2006 impacted opioid misuse. The authors use this insurance expansion (which covers prescription opioids) to show that a ten percent increase in the supply of (legitimate) opioids leads to a seven percent rise in opioid fatalities among individuals who are not likely eligible for Medicare (e.g., non-elderly persons). The authors interpret their findings to suggest that Medicare Part D expanded access to

[11]Within the U.S., many providers do not accept Medicaid. Many potential reasons have been raised by healthcare scholars including low reimbursement rate, slow payments, complex patients, and administrative burden. See Rosenbaum (2014) for a thoughtful discussion of these issues.

[12]Young adults may be reluctant to seek care following this policy as their parents may now know about the associated care (as the service will be recorded as a covered service) and therefore substance use. This 'reporting' feature may explain the somewhat unexpected findings.

[13]We note that recent work suggests that estimation of mortality effects from federal- and state-level policies may face issues related to statistical power (Black et al., 2019).

prescription opioids, which led to increased diversion of prescriptions into the illicit market.

3.4 The impact of the opioid crisis on health: Quasi-experimental evidence from policy responses

A large literature examines the impact of the opioid crisis on health outcomes, often using quasi-experimental methods that leverage variation offered by policy responses. Here, we integrate these findings with a discussion of relevant state and federal policies. Policies can usefully be defined as supply-side, those that attempt to curb access to prescription opioids, and demand-side, those that aim to reduce demand for opioids generally through provision of treatment and/or harm reduction strategies. As already discussed, an important challenge facing supply-side policies is economic substitution, that is when the full 'price' of prescription opioids rises, consumers can use an alternative substance, which may be more harmful, rather than simply abstaining from opioid use altogether as is the object of such policies.

3.4.1 Evidence from supply-side policies

One of the earliest and most comprehensively studied policies implemented to address the opioid crisis are prescription drug monitoring programs ('PDMP'), which share some features of the original 'triplicate' policies previously discussed. The first PDMP was adopted in 1939 in California. This PDMP, and other early programs, were designed to curb prescription medication misuse generally and were not specific to prescription opioids (Holmgren et al., 2020). By 2017, all states had some type of PDMP (Holmgren et al., 2020), although in Missouri (the last state to formerly adopt a PDMP in 2017) the program has been contested since it became effective and many healthcare scholars do consider it not to be an operational.

While each state PDMP is different, these programs share a broadly similar structure. A PDMP is a centralized database that includes patients' histories of prescriptions for scheduled medications. The DEA assigns substances a 'schedule' of I through V. Scheduling is determined by considering both the medical benefits of a drug and potential for misuse or addiction. Schedule I drugs are prohibited and are deemed by the DEA to have no medical benefits and a high potential for misuse and addiction. There are fewer restrictions on access to drugs in lower schedules (II to V), as these drugs are determined to have increasingly medical benefits or lower risk for addiction and misuse. Heroin is a schedule I drug while prescription opioids such as oxycodone, fentanyl, and hydrocodone are schedule II pharmaceuticals. The objective of a PDMP is to increase patient information available to healthcare professionals when a prescription is filled. Operationally, pharmacists are mandated to enter a patient's filled

prescriptions for scheduled drugs (including opioids) into the PDMP and, when prescriptions are being written, healthcare professionals can check the database to determine if the patient has a prescription history that suggests misuse or diversion. Policymakers hope that the PDMP will prevent misuse of opioids without limiting access to legitimate patients.

The extent to which PDMPs can meaningfully reduce opioid misuse is tightly linked to design features that encourage (or discourage) use by healthcare professionals at the time of prescribing. A feature that has received substantial research attention within the literature is whether healthcare professionals mandated to check the PDMP around the period of prescribing. These are sometimes referred to as mandatory or 'must access' (vs. voluntary) programs.[14] States began to adopt mandatory PDMPs in approximately 2007.

The literature is mixed on the impact of overall PDMPs on prescription opioid misuse. These studies frequently do not differentiate between voluntary and mandatory PDMPs, and instead treat both types of programs homogeneously; therefore the estimated effects likely reflect a weighted average of voluntary and mandatory PDMPs. Several studies suggest that voluntary PDMPs do not have a measurable impact on opioid misuse (Meara et al., 2016; Buchmueller and Carey, 2018). On the other hand, other studies offer more conclusive evidence that voluntary programs do so. Kilby (2016) documents a 12 percent reduction in opioid-related mortality post-voluntary PDMP, and a ten percent decline in prescribing among patients with employer-sponsored insurance. Voluntary PDMPs may have larger effects on the Medicaid population (Bao et al., 2016) and on patients with previous patterns of behavior indicative of opioid misuse (Mallatt, 2019). Finally, Popovici et al. (2018) show that a PDMP reduces prescription opioid-related admissions to standalone SUD treatment.

Conceptually, mandatory PDMPs may have more impact than voluntary systems and empirical evidence confirms this expectation. Using data from the state of Kentucky, which transitioned from a voluntary to mandatory PDMP, Carey et al. (2021) show that prior to the mandate 12 percent of prescribers checked the PDMP but this share increased to 56 percent after the PDMP became mandatory. This study, while descriptive, suggests two important facts: (i) mandatory PDMPs appear to induce perscribers to check the database and (ii) compliance with a mandatory PDMP may be lower than desired by policymakers.

Studies that distinguish mandatory PDMPs from voluntary programs offer more conclusive evidence that these programs reduce opioid prescribing, prescription opioid misuse and mortality, and medical care utilization (e.g., emergency department episodes) related to the

[14]In all PDMPs to date, pharmacists are mandated to enter information, thus this additional 'mandatory' feature pertains to prescribers. There is a distinction between mandatory and 'must access.' Some mandatory PDMPs allow healthcare professionals the opportunity to consult the database within seven days of prescribing, whereas must-access requires providers to consult the patient's history in order to prescribe.

misuse of these drugs (Dowell et al., 2016; Ali et al., 2017; Buchmueller and Carey, 2018; Deiana and Giua, 2018a; Bao et al., 2018; Grecu et al., 2019; Mallatt, 2019, 2020b; Kaestner and Ziedan, 2019; Sacks et al., 2019a; Wen et al., 2019; Alpert et al., 2020; Buchmueller et al., 2020; Ziedan and Kaestner, 2020; Ellyson et al., 2021; Neumark and Savych, 2021). Grecu et al. (2019) demonstrate that mandatory PDMPs reduce opioid-related admissions to standalone[15] SUD treatment facilities. The declines attributable to the mandatory PDMP are substantial (20 to 25 percent), emerge two-years post-policy, and are concentrated among younger adults (18 to 24 years of age). Further suggesting that PDMPs can have heterogeneous effects across individuals, Gupta et al. (2021) examine changes in opioid prescribing and mortality in Kentucky post-PDMP (this state is viewed as having a particularly well-designed PDMP) relative to Indiana over the period 2012 to 2013. The authors show that prescribing and mortality declined most substantially among 15 to 34 year olds, the sub-population with the greatest incidence of opioid-related mortality. Ellyson et al. (2021) document that physicians in different specialities respond heterogeneously to the adoption of a mandatory PDMP, with declines in opioid prescribing concentrated among primary care and internal medicine providers and, specifically, physicians in the lower tail of the opioid prescribing distribution. However, a recent study shows that mandatory PDMPs lead to an increase in fatal heroin overdoses, suggesting that consumers substitute to the more dangerous opioid when prescription opioid access declines (Kim, 2021).

Reductions in opioid misuse attributable to mandatory PDMPs have positive spillovers to health and well-being metrics among children. For example, children's birth outcomes improve, and rates of neonatal abstinence syndrome, foster care admissions, and child abuse and neglect decline follwing adoption of such a policy (Gihleb et al., 2019; Evans et al., 2020; Gihleb et al., 2020; Ziedan and Kaestner, 2020).

While the key channel through which PDMPs are expected to curb prescription opioid misuse is through more appropriate prescribing patterns by healthcare professionals, several studies suggest that there may be additional mechanisms. Nguyen et al. (2019) document a potential feedback loop: post-mandatory PDMP pharmaceutical companies reduce prescription opioid promotions to physicians which can plausibly reduce demand by patients for these medications. Sacks et al. (2019b) find that PDMP laws reduce opioid use among opioid-naive populations, and Alpert et al. (2020) use detailed data from Kentucky to note that rather than conveying information to healthcare professionals, PDMPs may reduce opioid prescribing by increasing the hassle costs associated with checking the database.

A recent study argues that the salient feature of a PDMP is not whether or not they are

[15]That is treatment received in outpatient, residential, and hospital settings.

must access but rather if the database is electronic. Kaestner and Ziedan (2019) document that the coefficient estimate on a mandatory PDMP variable loses statistical significance, after adding controls for whether the PDMP is electronic, in a regression of prescription opioid shipments on various opioid-related policies, while the electronic PDMP program indicator is associated with statistically significant reductions of shipments.[16] Wang (2020) documents decreased opioid misuse when PDMPs are connected with state-wide health integration technology that facilitates the sharing of electronic health records within the healthcare system.

A concern with PDMPs is that they will reduce access to patients who could benefit from pain medications, such as those with chronic conditions leading to significant pain that impedes daily activity. Ozturk et al. (2021) analyze detailed health and healthcare information available in the Medical Expenditure Panel Survey and find that individuals with long-standing disabilities are not adversely affected by a PDMP adoption in terms of their ability to be prescribed opioids. This study suggests that PDMPs do not have negative spillovers to legitimate patients.

The 2010 reformulation of OxyContin has received considerable attention. As described in Section 2, the original formulation of OxyContin was designed for extended release, with the hope that this formulation would mitigate the potential for abuse. However, users quickly learned that the extended release formulation could be broken, allowing the user to swallow, snort, or inject the drug and immediately access the full potency and resulting euphoria. In August 2010 Purdue Pharma abuptly and (by all accounts) unexpectedly reformulated OxyContin so as to be much harder to misuse. Upon breaking the extended release pill, the drug deteriorated into a slimy substance that is difficult to swallow, snort, or inject. Several studies show that prescription opioid misuse declined rapidly after the reformulation (Alpert et al., 2018; Evans et al., 2018; Wolff et al., 2020; Powell and Pacula, 2021). However, the policy, while well-meaning, did not consider the possibility that consumers, when faced with a shock to the supply of OxyContin, could substitute to other substances that offered similar euphoric effects. Further, while all opioids have the potential for misuse, these substances exist along a risk continuum, with OxyContin arguably being of somewhat lower risk than heroin or synthetic opioids. Interestingly, and unfortunately from a public health perspective, following the reformulation of OxyContin many consumers substituted to heroin rather than fully abstaining from opioids or substituting to alternative prescription opioids such as hydrocodone (Alpert et al., 2018; Evans et al., 2018).[17] Heroin is likely to be more dangerous to consumers

[16] An electronic PDMP is defined by Kaestner and Ziedan (2019) as: 'Systems that are not paper-based and allow the prescriber to transmit the prescription information electronically to the state authority.'

[17] Wolff et al. (2020) find less evidence of substitution, but they focus on a sample that reported using

since it is often injected with needles shared among different consumers and because purity of the drug (which is procured from illicit sources) is uncertain. Indeed, several studies show that, due to the nature in which heroin is consumed, blood-borne diseases increased following the reformulation (Beheshti, 2019a; Powell et al., 2019) and the costs of this reformulation appear to have spread to other health outcomes. Park and Powell (2021) show that following the reformulation there was an increase in disability claiming and reduction in labor supply (a proxy for health status). Further, the transition to heroin was a positive boost to the black market and lead to an expansion in the scope and sophistication of U.S. drug markets that would not have occurred without the reformulation of OxyContin (Powell and Pacula, 2021).

States have adopted other policies in attempts to curb the supply of prescription opioids. We focus our attention here on two: pain clinic management laws (PCMLs) and healthcare professional prescribing limits.

PCMLs are designed to give states authority to prevent the opening or continued operations of 'pill mills,' that is medical clinics that knowingly prescribe prescription opioids to illegitimate patients (those who seek prescription opioids to misuse themselves or to divert to the illicit market). Pill mills, particularly in the first wave of the crisis, were central to the supply of prescription opioids and PCMLs offered states the ability to reduce this supply. Operationally, PCMLs set minimum standards (e.g., education requirements for employed healthcare professionals) that clinics must meet in order to prescribe prescription drugs, including opioids. The available evidence suggests that PCMLs reduce the number of pill mills in operation, prescription opioid use, and associated harms such as opioid-related overdoses (Rutkow et al., 2015; Chang et al., 2016; Dowell et al., 2016; Lyapustina et al., 2016; Meinhofer, 2016; Mallatt, 2020b; Ziedan and Kaestner, 2020). For example, using national data on establishment counts, Mallatt (2020a) shows that PMCL adoption is associated with a ten to 15 percent reduction in the number of pain clinics. In a related study, Ziedan and Kaestner (2020) estimate a 15 to 50 percent decline in prescription opioid sales after implementation of a PMCL. Dowell et al. (2016) find that PCMLs reduce opioid prescribing and overdoses, with no change in heroin overdoses, when adopted in combination with a mandatory PDMP.

Prescribing limits restrict the length of initial prescriptions for opioids, typically to seven days. While this policy appears reasonable in terms of reducing supply, it does not consider compensatory behavior on the part of healthcare professionals. That is, these laws regulate a sub-set of all possible margins along which healthcare professionals have discretion in terms of writing prescriptions for patients. In particular, using detailed health insurance claims data, Sacks et al. (2019a) indicate that these laws actually *raise* the overall amount of opioids

opioids prior to the reformulation and may not capture individuals who initiated post-reformulation.

prescribed to new users. Healthcare professionals reduce the length of prescriptions but also increase the frequency of short prescriptions, and the latter effect dominates suggesting that, contrary to its objective, the policy increased the overall supply of prescription opioids. Using Workers Compensation claims data, Neumark and Savych (2021) find little evidence that prescribing limits have any effects on the extensive margin of prescribing (any prescription), but lead to reductions on the intensive margin (use among those with a prescription).

The federal government has leveraged the Controlled Substance Act (CSA) to help address the opioid crisis in a variety of ways. For instance, the scheduling of two specific prescription opioids was adjusted in 2014: (i) tramadol (a hydrocodone product) was added to the CSA (i.e., the drug became a scheduled or controlled substance for the first time) and (ii) hydrocodone combination drugs were rescheduled from Schedule III to the more restricted Schedule II (where no refills are allowed). Prior to the federal action, 12 states had adopted similar policies for tramadol but not for hydrocodone combination drugs.

While not examining a direct health outcome, Beheshti (2019b) shows that the re-scheduling of hydrocodone combination drugs increased labor supply (a proxy for health status). In particular a ten percent decrease in overall hydrocodone prescriptions was linked to a 0.7 percent increase labor force participation. Collectively, the CSA-related policy changes altered the relative 'full' price of two specific prescription opioids, but left this full price unchanged for other opioids which are potentially substitutes from the perspective of consumers. Gupta et al. (2020) examine the net effect of these policy changes. The authors show that increased restrictions on access to these two drugs reduced their use, but increased prescriptions for substitutes, with the overall supply of prescription opioids being unaltered.

3.4.2 Evidence from demand-side policies

There has been decidedly less empirical work on demand-side policies (relative to supply-side policies) within the U.S. We review a handful of evaluated policies here.

Doctor shopping laws (DSLs) prevent patients from receiving prescriptions from multiple healthcare professionals, with the goal of reducing the supply of opioids likely to be diverted to illicit markets or misused by patients themselves. While these policies could be viewed as supply-side interventions, we classify them here as demand-side since the patient (not the healthcare professional) is targeted by the law and and faces legal penalties associated with the prohibited behavior. While all states and DC have general laws that criminalize fraud (which theoretically covers doctor shopping),[18] 20 states have adopted standalone

[18]These laws directly use language from the Narcotic Drugs Import and Export Act of 1922 or the Uniform Controlled Substances Act of 1970.

laws that specifically address doctor shopping (Centers for Disease Control and Prevention, ND). Broadly, DSLs 'prohibit a patient from knowingly withholding information from the practioner about controlled substances or prescription they have received from other healthcare practitioners' (Centers for Disease Control and Prevention, ND). One study examines the impact of DSLs on prescription opioid and heroin deaths and admissions to treatment (Popovici et al., 2018); it finds only modest evidence that DSLs impact prescription opioid related outcomes and no observable changes in heroin-related outcomes .

Demand-side policies adopted in the second and third waves of the crisis address harm reduction much more so than policies common in the first wave. These do not (at least directly) attempt to reduce supply of or demand for opioids; instead they promote the safer consumption of them. This approach recognizes that substance use disorders may cause individuals to have impaired judgement and thus not be able to adequately weigh costs and benefits as intended in more ppunitive approaches to policies. Three common harm reduction policies are: naloxone access laws (NALs) which offer immunity to healthcare professionals who prescribe or administer naloxone − a medication used to reverse opioid overdoses; Good Samaritan Laws (GSL) which offer immunity or reduced sentencing to individuals who call 911 following an overdose; and syringe exchange programs (SEP) which allow injection drug users to return used and obtain unused syringes, thereby reducing the probability that 'dirty' syringes will be shared among users and spread blood-borne diseases.

Studies examining NALs and GSLs obtain inconclusive findings. Doleac and Mukherjee (2018) show that online searches for naloxone increase while searches for opioids decrease post-NAL, and opioid-related possession arrests, sales, and emergency department visits increase, with no observable change in opioid-related mortality. Conversely, Rees et al. (2019) find that NAL adoption reduces opioid-related mortality, although GSLs do not appear to lead to changes in these deaths. McClellan et al. (2018) also find that NAL adoption leads to a 14 percent reduction in opioid overdose deaths. However, their results suggest that that GSLs have a similarly sized impact, reducing opioid overdose deaths by 15 percent. Abouk et al. (2019) identify specific NAL features as important for reducing overdoses: laws that grant naloxone distribution authority to pharmacists reduce fatal opioid overdoses, but NALs without this feature do not.

Packham (2019) examines the impact of SEPs − exploiting county-level SEP openings for variation − on opioid-related outcomes and HIV diagnoses. The opening of an SEP within a county leads to increases in opioid-related emergency department episodes and mortality, but a reduction in HIV rates (HIV is a blood-borne disease that is transmitted through the sharing of contaminated needles between individuals who inject drugs).

While not specifically an opioid policy, several studies show that legalization of marijuana for medical or recreational purposes may have positive spillovers to opioid use. The rationale or the potential link between marijuana legalization and opioids is that these medications are both used by consumers to treat chronic pain, that is marijuana and opioids are what economists call 'therapeutic substitutes.' Several studies, across various populations, use insurance claims data to show that following marijuana legalization, prescriptions for opioids decline (which is what is expected if two medications are therapeutic substitutes) and proxies for chronic pain improve (Bradford and Bradford, 2017; Bradford et al., 2018; Wen and Hockenberry, 2018; Nicholas and Maclean, 2019; Ghimire and Maclean, 2020; Wen et al., 2021; Drake et al., 2021), suggesting that marijuana allows for better symptom management of chronic pain than opioids. Not all studies suggest that legalization leads to reduced reliance on opioids for pain relief (Maclean et al., 2020; Jayawardhana and Fernandez, 2021) and one study (Mathur and Ruhm, 2022) links retail marijuana sales to higher opioid death rates.

Finally, some demand-side policies have adopted a particularly punitive approach. For example, the state of Tennessee criminalized substance use among pregnant women. See Durrance et al (2022), in this issue, for a more complete discussion of such policies.

4. The opioid crisis and crime

4.1 An economic model of crime

Becker (1968) describes a model, in which a potential offender weighs the costs and benefits of committing criminal offenses, that can easily be adapted to consider opioid-related crime. The potential offender has differing benefits of committing drug-related crimes which range from financial incentives to euphoria from using drugs or the alleviation of withdrawal symptoms and cravings. However, the potential offender also faces the direct costs of purchasing opioids, and also (potential) expected costs of remaining dependent on opioids, and of being punished if these crimes are detected.

Thus, opioids may contribute to crime by (i) increasing the need to secure finances to procure substances, (ii) leading to intoxication which may impede accurate assessment of the expected costs and benefits of crime, (iii) illicit market activities (i.e., procuring opioids from drug dealers), and (iv) victimization, where opioid intoxication makes the individual an 'easy target' to potential offenders. Third factors may influence both crime and opioid use (e.g., socioeconomic background) without a causal connection.

Policymakers have various levers that can alter the costs and benefits of opioid-related

crime. To date, in the U.S., the primary focus has been on policies that adjust the costs of drug use, for example the supply- and demand-side factors discussed in Section 3. This contrasts with past drug crises − like the 1970s urban heroin crisis and crack-cocaine epidemic of the 1980s − where the risk of apprehension and punishments were increased substantially as part of the 'War on Drugs.'

4.2 Trends in crime over the opioid crisis

Unlike the heroin wave of the 1970s, the crack epidemic of the 1980s, or the 2000s methamphetamine crisis (Fryer et al., 2005; Dobkin and Nicosia, 2009; Plüddemann et al., 2010; Pollack and Reuter, 2014), there has not been an increase in gun or property crimes during opioid crisis. While it is initially surprising that the most widespread drug crisis in U.S. history has not been associated with any discernible increase in crime (Szalavitz and Rigg, 2017), this may have occurred because crime rates in the U.S. have been falling since the 1990s, and for reasons that are not fully understood (Levitt, 2004; Fryer et al., 2005).

A possible reason for the weaker relationship between opioids and crimes than in previous drug epidemics is the quite different response of the criminal justice system. There has been much a 'softer' approach to opioids, often focusing on treatment rather than incarceration.[19] More specifically, drug misuse during the opioid crisis has been treated more as a medical disease than previously. For example, numerous police departments across the U.S. have adopted diversion programs that attempt to offer treatment to those arrested for non-violent drug crimes (Collins et al., 2019; Ahmad, 2020). Further, some jurisdictions have developed specialized drug courts − there are over 3,500 drug courts in the U.S. (Office of Justice Programs, 2021) − that are separate from the broader criminal court system and emphasize addiction recovery through the provision of treatment rather than punitive measures or incarceration. Some states are prioritizing medication used to treat opioid use disorder during incarceration for opioid-addicted inmates (Arora and Bencsik, 2021) and jail-based methadone maintenance treatment programs have been shown to have the added benefit of reducing recidivism (Horn et al., 2020). Economic evaluations suggest that drug courts can be both effective and cost-effective (Logan et al., 2004). Several states have also downgraded most forms of drug possession to misdemeanors and have raised the amount of scheduled drugs an individual can possess before being charged with a felony. Finally, states have also passed GSLs (see Section 3.4.2), which grant legal immunity to bystanders who call in overdoses.

Not all judicial system changes brought on in response to the opioid crisis have relaxed

[19]For example, please see https://www.app.com/in-depth/news/local/public-safety/2019/12/02/crack-heroin-race-arrests-blacks-whites/2524961002/ (website last accessed December 17, 2021).

the enforcement of drug crime, however. For example, a few states have criminalized prenatal substance use, even though these laws have been shown to reduce reunification rates between infants in foster care and their biological mothers (Sanmartin et al., 2020), increase reports of child neglect to child protective agencies (Maclean et al., 2021), and increase rates of neonatal withdrawal symptoms (Meinhofer et al., 2021).

Finally, lower rates of crime during Wave I of the opioid crisis may be attributable to the fact that these substances originated from legal sources and were, in many cases, subsidized for low costs to consumers through their health insurance. However, diversion was common with more than half of mis-using individuals reporting that they did not obtain prescription opioids through legal channels, as demonstrated in Figure 3. In Waves II and III, opioids were increasingly sourced entirely from the black market, which eliminated the role of insurance and necessitated interaction with illicit markets.

4.3 Evidence on the opioid-crime link from policy changes

While examination of trends in crime and the opioid crisis do not reveal that the opioid crisis has led to an overall increase in crime rates, such analyses are challenging to interpret causally. For example, Figure 3 shows that a substantial fraction of individuals who use opioids report (i) diverting prescription opioids to illicit uses and (ii) using heroin (which is procured in illicit markets).

Studies that employing quasi-experimental or experimental methods suggest that opioid misuse is related to crime outcomes. Bondurant et al. (2018), Wen et al. (2017), and Vogler (2020) find that expanding access to SUD treatment (measured by the number of providers in a local healthcare market or through expansions of insurance coverage that includes SUD services) decreases both violent and financially-motivated crimes.[20] Similarly, Swensen (2015) shows that fatal drug overdoses decrease as treatment access increases. More generally, Dave et al. (2018) document − using variation offered by state adoption of PDMPs − that reducing the supply of prescription opioids decreases violent crime. Several other recent studies leveraging variation from policy changes or randomized control trials document broadly similar patterns of declines in crime as access to opioids falls (Meinhofer, 2016; Deiana and Giua, 2018b; Smart and Reuter, 2021).

Now that the crisis has evolved into one mainly involving illicit opioids, there are new studies looking into the effect of criminal justice crackdowns on illicit opioid access and crime. From Australia's heroin crisis, Moore and Schnepel (2021) find that a series of operations

[20]Since SUD treatment in the U.S. is heavily financed by public payers it can appropriately be viewed as a 'policy' (Substance Abuse and Mental Health Services Administration, 2019).

targeting the heroin supply caused long term reductions in property and violent crime in the Sydney area. However, attempts to limit the supply of chemical precursors to the production of fentanyl has not had a meaningful effect on access to fentanyl thus far (Miller, 2020). Due to the difficulty of controlling the supply of fentanyl, states have shifted to harm reduction approaches, as discussed in a previous section.

5. Discussion

The opioid crisis is one of the most substantial public health emergencies the United States has faced. Particularly in the third Wave, the opioid epidemic has evolved to polysubstance use, that is consumers use opioids (prescription, heroin, fentanyl, etc.) with other substances (e.g., stimulants). The annual economic cost of the crisis is at least $596 billion dollars (White House Council of Economic Advisers, 2017)[21] and between 1999 and 2019 over 500,000 Americans died from a fatal opioid overdose (CDC, 2021c). This paper reviews relationships between the opioid crisis, health and medical care outcomes, and crime.

The literature reveals a bi-directional relationship between the opioid crisis and the health-care system: prescription opioids in combination with aggressive pharmaceutical company efforts to increase use, limited regulation of prescriptions, and healthcare professionals prescribing of opioids combined to create the crisis. In turn, the crisis led to addiction, mortality, and healthcare utilization. On the other hand, the healthcare system − through providing addiction treatment, limiting the supply of opioids, and offering alternative approaches to treating chronic pain − has a role to play in abating the crisis.

While the relationship is perhaps not as strong as observed during previous drug epidemics, the opioid crisis is linked increased crime, both violent and non-violent crimes. However, and perhaps in a more conclusive way than for health or medical care, policies reducing access to prescription opioid appear to decrease crime. Further, increasing the availability of treatment − either through direct openings of treatment centers or provision of insurance coverage that includes MOUD − can reduce crime rates.

While state and federal governments have adopted multiple policies designed to curb the misuse of opioids, the crisis of overdoses and addiction persists. Numerous studies have examined the effects of key policy levers utilized by government, but there are many questions remaining. For example, demand-side policies have been less studied than supply-side policies, leaving opportunities to better understand how policy can be harnessed to fight the crisis. A

[21]This number is inflated by the authors from the original estimate ($504 billion in 2015) to 2021 terms using the Consumer Price Index.

theme that emerges from a review of the available evidence is that have been shown to be more effective in addressing adverse health outcomes include both levers that reduce access to opioids, recognizing that consumers (and suppliers) are nimble and can substitute across substances when policy changes the relative attractiveness of opioids, and ensure that people can access treatment to address underlying addiction to opioids.

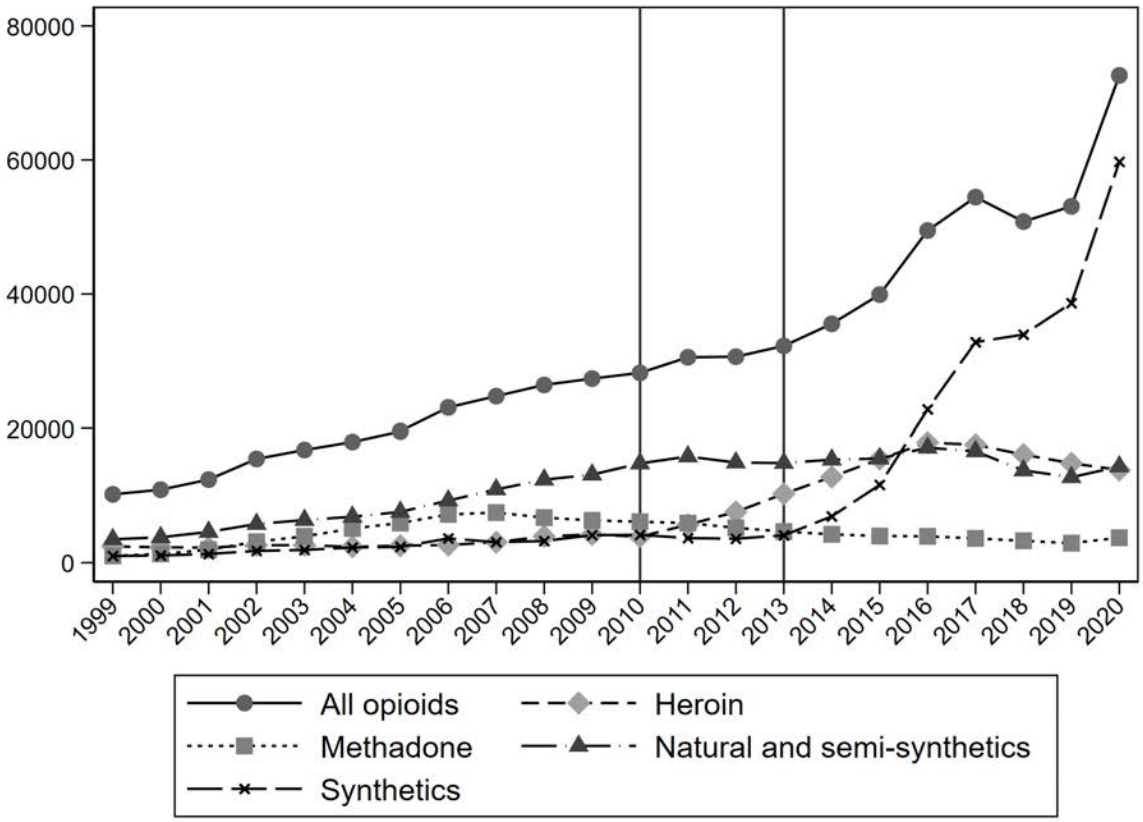
A review of the history of the opioid epidemic, beginning in the 1990s and continuing through to today, demonstrates that the crisis is not static but rather changes over time in response to altered economic and social factors. For example, the nature of primary opioids consumed has swiched from the first to the third wave, from primarily prescription opioids to fully synthetic opioids, and the model consumer has similarly changed from disproportionately less educated Whites initially to to a broader and more diverse swath of the U.S. population more recently. The literature shows that policies that monitor opioid consumption among groups at elevated risk are more effective at improving health outcomes.

The ongoing COVID-19 pandemic has intersected with the opioid crisis. As with the COVID-19 pandemic's health impacts, the opioid crisis has created widening racial gaps; in 2020, provisonal CDC data showed the Black overdose mortality rate surpassed that of Whites for the first time since 1999 (Friedman and Hansen, 2022). While the literature is in its infancy at the time of writing, COVID-19 has massive implications for access to healthcare, supply of opioids, financial stability of both individuals and governments, social isolation, and overall mental and physical health. How these factors interact with the opioid crisis, in both in the short- and long-term, is not yet clear. Early studies raise concerns that the two ongoing crises will interact in ways that worsen public health overall. Jacka et al. (2021) find that during COVID-19, opioid use disorder patients being treated with medications reported increased problems accessing treatment and harm reduction services (e.g., syringe exchange services). Nguyen et al. (2021) show that in the beginning of the COVID-19 pandemic, buprenorphine prescribing faced an abrupt slowdown; Currie et al. (2021a) indicate that prescriptions for opioid pain medications also declined at the start of the pandemic, but both opioids for pain and bupronorphine prescriptions rebounded quickly. Using unique data from Ohio, Currie et al. (2021b) show that opioid overdoses spiked during the beginning of the pandemic and, more recently, Ruhm (2021a) has found that there were more than 20,000 excess deaths attributed to drugs during the first year of the pandemic. These findings suggest that COVID-19 may have worsened access to treatment but also reduced the ability to obtain opioids for misuse.

More broadly, while the opioid crisis is unprecedented in its scope, the U.S. has experienced drug epidemics previously. These include a heroin epidemic in the 1970s, a cocaine epidemic

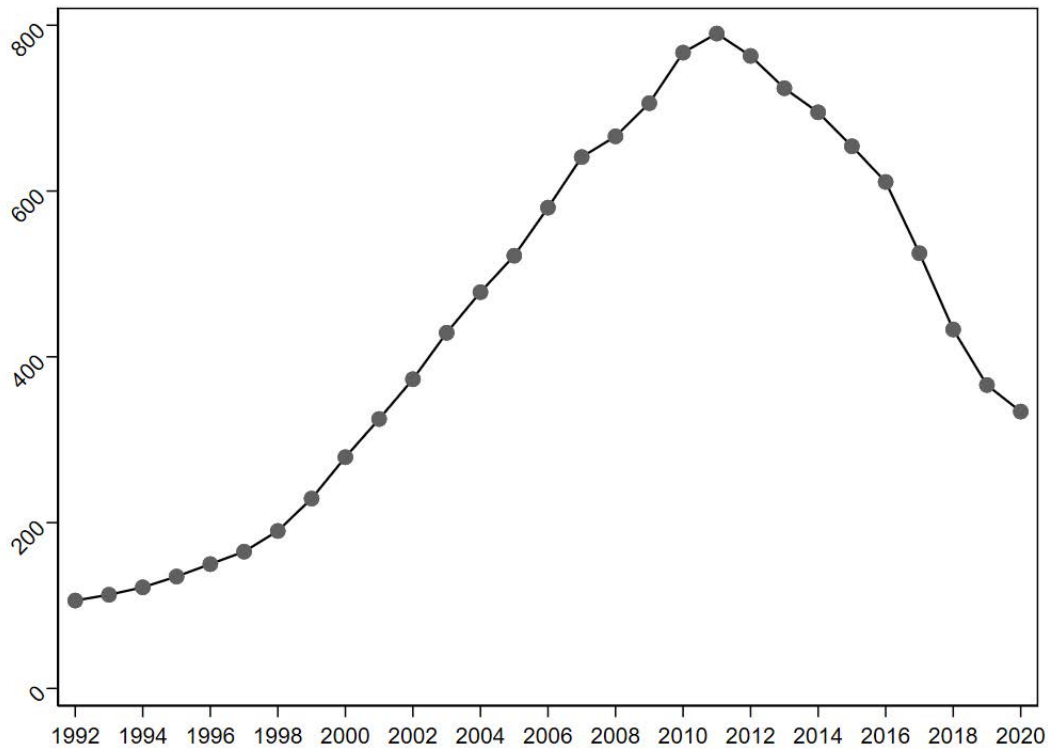
in the 1980s, and a methamphetamine crisis in the 1990s and early 2000s. Examination of these earlier drug epidemics and the factors and policies that are viewed as abating them may be useful to policymakers (Moore and Pacula, 2020). Currently deaths from cocaine and stimulant use are rapidly rising in the U.S. (Hedegaard et al., 2020; Ciccarone, 2021; Kariisa et al., 2021). Approximately 16,000 people died from a cocaine overdose in 2019, an eight percent increase over 2018 (Kariisa et al., 2021). Between 2012 and 2018 the psychostimulant fatal overdose rate increased nearly five-fold (Hedegaard et al., 2020). These trends suggest that public health attention should address a broad set of addictive substances. Further, each year 93,296 people in the United States die from alcohol use Esser et al. (2020). The reviewed literature has shown that both policies and medical infrastructure have in some cases reduced and effectively treated substance misuse. In addition, changing social norms (in particular stigma among patients, providers, and society generally regarding the nature of substance use disorders) may be an effective strategy to address underlying addiction within the U.S. However, mixed results of existing research reveal that policy design is not likely simple or inexpensive, and instead will require sincere and sustained efforts by various stakeholders.

Figure 1: Trends in fatal opioid overdoses: 1999 to 2020



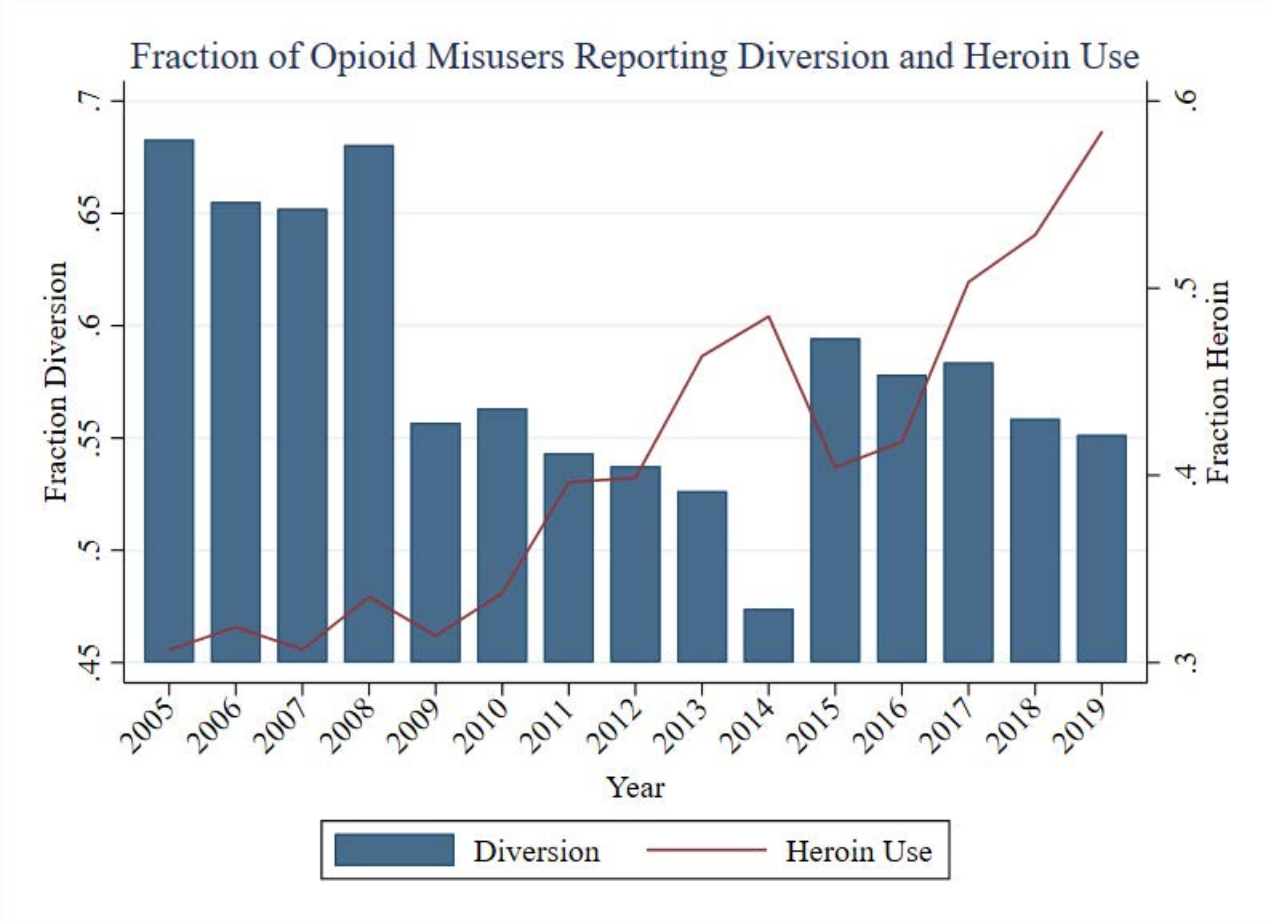
Notes: Data are drawn from the Centers for Disease Control and Prevention. See text for details.

Figure 2: Trends in the rate of opioid prescriptions filled at retail pharmacies in morphine milligram equivalents per capita: 1992 to 2020



Notes: Data are obtained from the IQVIA Institute (2020).

Figure 3: Trends in the faction of opioid users reporting diversion and heroin use: 2006 to 2019



Notes: Data are drawn from the National Survey on Drug Use and Health. See text for details.

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