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ABSTRACT

The United States has experienced an unprecedented crisis related to the misuse of and addiction to opioids. As of 2018, 128 Americans die each day of an opioid overdose, and total economic costs associated with opioid misuse are estimated to be more than $500 billion annually. The crisis has evolved in three phases, starting in the 1990s and continuing through 2010 with a massive increase in use of prescribed opioids associated with lax prescribing regulations and aggressive marketing efforts by the pharmaceutical industry. A second phase included tightening restrictions on prescribed opioids, reformulation of some commonly misused prescription medications, and a shift to heroin consumption over the period 2010 to 2013. Since 2013, the third phase of the crisis has included a movement towards synthetic opioids, especially fentanyl, and a continued tightening of opioid prescribing regulations, along with the growth of both harm reduction and addiction treatment access policies.

Economic research, using innovative frameworks, causal methods, and rich data, has added to our understanding of the causes and consequences of the crisis. This body of research also identifies intended and unintended impacts of policies designed to address the crisis. Although there is general agreement that the causes of the crisis include a combination of supply- and demand-side factors, and interactions between them, there is less consensus regarding the relative importance of each. Studies show that regulations can reduce opioid prescribing but may have less impact on root causes of the crisis and, in some cases, have spillover effects resulting in greater use of more harmful substances obtained in illicit markets, where regulation is less possible. There are effective opioid use disorder treatments available, but access, stigma, and cost hurdles have stifled utilization, resulting in a large degree of under-treatment in the U.S.

How challenges brought about by the COVID-19 pandemic may intersect with the opioid crisis is unclear. Emerging areas for future research include understanding how societal and healthcare systems disruptions affect opioid use, as well as which regulations and policies most effectively reduce potentially inappropriate prescription opioid use and illicit opioid sources without unintended negative consequences.

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1 Introduction

The opioid crisis in the United States imposes challenges to population health, and a range of social and economic outcomes. An argument can be made that the misuse of opioids reflects one of the most substantial public health crises that the U.S. has faced in modern times. While the origins of the crisis are reasonably well understood, there are competing theories on why an initial period of opioid misuse developed into a crisis that has persisted for over two decades, has lead to more deaths than any previous drug epidemic, and shows no signs of abating. Moreover, the policy efforts to address the crisis have achieved only mixed success to date. In 2020, public health attention in the U.S. and elsewhere shifted abruptly to the COVID-19 pandemic, but as a grim reminder that the opioid crisis has not become any less severe, preliminary evidence indicates increasing rates of opioid mortality. According to the Centers for Disease Control and Prevention, 12-month counts of drug overdose deaths rose 9.1 percent from March 2019 to March 2020 or 67,726 to 73,860 (Ahmad, 2020).

During the last decade, a sizable body of economic research has emerged studying the origins of the opioid crisis, the factors that shaped its transformation from prescription to illicit sources, and the impact of policies and regulations that have been implemented. Our review focuses on economic studies that we located through searches of standard sources and soliciting feedback from economists working on opioid-related issues. These studies add to large literatures outside of economics that have made, and continue to make, contributions of utmost importance to understanding the opioid crisis.[1] Further, this review mainly examines the opioid crisis within the U.S. We note that opioids have imposed substantial costs on other countries, however the U.S. – to date – has arguably been hardest hit by the opioid crisis. For this reason, we predominantly examine the U.S. experience. Future work could more closely review how this crisis has developed in other countries.

Four broad conclusions emerge from the economic literature to date. (1) Estimates of economic costs of opioids on society are high, but the estimates of costs vary widely, largely depending on how lost life is factored into the calculations. (2) Labor markets are both affected by the opioid crisis and may play a role in explaining its origins. Most evidence indicates that worse economic times are associated with higher opioid use, although some studies suggest that this relationship may be spurious (resulting from confounding factors) and or with reverse causation (where increased opioid use depresses employment and labor force participation). Origins of the opioid crisis are likely to have roots in both supply-side

[1] See Barry and Frank (2019) for an eloquent discussion of the importance of incorporating evidence from fields beyond economics.

and demand-side factors, but with feedback loops and many different mechanisms at play in the complicated relationship between opioids and economic climate. Regardless, collectively the economic studies to date imply that labor market factors explain at most a small portion of the opioid crisis. (3) Healthcare providers and the pharmaceutical industry played a critically important role in the origins of the crisis. In particular, aggressive marketing of new prescription opioids with high potential for addiction towards physicians pre-disposed to liberal prescribing of medications provided an ideal setting for the emergence of a crisis. Indeed, the literature suggests that the healthcare sector played a larger role contributing to the crisis than economic factors. This finding implies a more direct route for policies designed to mitigate the crisis than if the primary origins of the crisis resulted from the economic climate and changes in social institutions. However, policies that simply 'turn off' the supply of prescription opioids, without addressing existing addiction to these drugs, risk failure by driving substitution towards other, difficult to regulate, and riskier substances. (4) Supply-side policies that restrict access to prescription opioids have been aggressively adopted by governments, and on the demand-side there has substantial movement towards increasing treatment access, through relaxing regulations and insurance expansions. Some economists have also emphasized marijuana legalization as a policy that may have benefits in the form of reducing opioid use.

Going forward, research is needed to resolve remaining uncertainty on the effectiveness of existing policies, to evaluate policies that are only beginning to be implemented such as those focusing on harm reduction rather than abstinence, and to better understand interactions between the opioid crisis and other types of substance use disorder harms, such as the recent and rapid increase in deaths involving stimulants.

2 Three Waves of the Opioid Crisis

The ongoing opioid crisis in the U.S. can be viewed as having occurred in three waves. The first stage reflected massive increases in the use of prescribed opioids and dates from the mid-1990s through 2010. This wave occurred during a period of loosening restrictions on the prescribing of opioid painkillers and extensive marketing of them to both healthcare providers and consumers. The second wave, from 2010 to 2013, was distinguished by extensive growth in heroin use and associated deaths, although problems related to prescribed opioids remained substantial during this period. The current wave (through the time of writing), beginning in 2013, has been characterized by surging deaths and problems related to the use of synthetic opioids, particularly fentanyl and its analogs.

The first wave of the opioid crisis is thought to have begun shortly after the 1996 approval and release of Purdue Pharma's soon-to-be blockbuster drug OxyContin. Prior to the mid-1990s, opioid prescribing was surrounded by a culture of 'opia-phobia,' as opioid painkillers have a long history of misuse in the U.S. reaching back to the Civil War (Macy, 2018). Through most of the 20th century, physicians were reluctant to prescribe opioids for pain management, even to cancer patients and to the terminally ill (Quinones, 2016; Hill Jr, 1993; Paice et al., 1998; Weissman, 1993). In 1996, Purdue Pharma introduced a new generation of opioids with the launch of OxyContin, an oxycodone product with an extended-release mechanism that was originally designed to reduce addiction. Purdue Pharma's marketing approach was remarkable: the firm's promotional budget was magnitudes larger than those of competitor firms, and far higher than any previous opioid marketing campaign. In addition, the campaign specifically targeted healthcare providers who already displayed high rates of opioid prescribing despite the prevailing culture of opia-phobia (Alpert et al., 2019).

To further change prescribers' attitudes, Purdue Pharma and other opioid manufacturers funded the American Pain Society, which lobbied the Joint Commission to prioritize the treatment of pain (McGreal, 2018). The Joint Commission is a non-profit accreditation organization whose certification is used by the Centers for Medicare and Medicaid Services (CMS) to determine the reimbursement status of medical facilities nationwide. In 2001, the Joint Commission implemented a pain scale, with pain being assessed as the 'fifth vital sign,' along with pulse, temperature, respiration rate, and blood pressure. More specifically, healthcare providers were required to incorporate pain into patient assessments and, where appropriate, encouraged to treat pain symptoms medically, including through the use of prescription opioids. These actions played an important role in the emerging lax culture of opioid prescribing that characterized the first decade of the 2000s: by 2012, 259 million prescriptions for opioids were dispensed and approximately one in four Americans were prescribed an opioid medication each year (Kilby, 2016; Mallatt, 2019).

There were an estimated 3,442 deaths involving prescription opioid poisoning (not counting synthetic opioids or heroin) in 1999; this number increased to approximately 15,000 overdoses at the beginning of the second wave of the crisis in 2011.[2] Similarly, rates of substance use disorder (SUD) grew by a factor of six between 1999 and 2009 (Paulozzi et al., 2011). Opioid prescribing peaked between 2010 and 2012 (Pacula and Powell, 2018a; Schuchat et al., 2017).

The crisis then evolved to a second wave where deaths and other adverse consequences

[2]All figures on drug deaths cited in this chapter are based on information contained on death certificates. These certificates understate the actual death numbers by 20 to 25 percent because of incomplete reporting of drug involvement (Ruhm, 2018).

associated with heroin use dramatically increased. Alpert et al. (2018), and Evans et al. (2018) show that this transition was, in part, fueled by a reformulation of OxyContin in August of 2010. The reformulated medication was crush-resistant and therefore harder to snort or inject. Additional government policies targeting the supply of opioid prescriptions (discussed below) also led to rising heroin use (Mallatt, 2020b). Heroin overdoses tripled between 2010 and 2013, whereas prescription opioid overdoses not involving heroin plateaued or subsided slightly. The overall effect of these market and policy changes was to increase the total number of fatal opioid overdoses.

There are differences across the U.S. in terms of the source of heroin. This heterogeneity in source has important implications for policy efforts aimed at curbing use of this substance, and suggests that there are disparities in the type, and potentially harmfulness, of heroin consumed across the country. On the East coast, heroin has historically been imported in white powder form from South Asia while consumers on the West coast generally obtained black tar heroin sourced from Mexico (Abouk et al., 2019). Cutting agents and fentanyl are more easily incorporated into powdered heroin in the East and are more dangerous than pure heroin. Subsequently the East coast has suffered disproportionately from a large spike in synthetic opioid overdoses beginning in 2014. While the source of heroin has remained relatively stable on the West Coast over the various stages of the crisis, East Coast consumers experienced a change in the source of heroin in 2015 when Mexican cartels became the major suppliers of heroin in this area, effectively pushing South Asian suppliers out of the market (United States Department of Justice, 2018b).

In 2013, during the third wave which witnessed the shift towards fentanyl, the U.S. Drug Enforcement Agency (DEA) began reporting the presence of this substance and its analogues in seized heroin.[3] Fentanyl is an extremely potent synthetic opioid that offers several advantages over heroin to suppliers. In particular, fentanyl is relatively cheap to produce, and easier to transport and smuggle since smaller quantities are required. The production of heroin necessitates the relatively expensive, time-intensive, and conspicuous growth of opium poppies. In contrast, fentanyl and its chemical analogues are completely synthesized from ingredients in a lab. Many input components are imported from China to Mexico, where the drug is then synthesized in labs and smuggled across the U.S. border (United States Department of Justice, 2018b). An experienced opioid user may require one or two grams of heroin per day (depending on purity), but equivalent dosages of fentanyl are measured in micrograms (mcg), which saves distributors the costs and detection risks of

[3]There was a spike in fentanyl deaths between 2005 and 2007 in Chicago, Detroit, and Philadelphia related to a single lab in Mexico that was shutdown in 2006 (Pardo et al., 2019).

transporting many kilograms of heroin through border checkpoints.

Data from the 'darknet' (i.e., the non-trackable internet) suggest that the wholesale price of fentanyl and its analogues is much lower than heroin, with a 100 mcg dose costing about four cents in a wholesale setting. A wholesale kilogram of heroin (typically 50 percent pure at this stage in the production process) costs between $33,000 and $100,000 (United States Department of Justice, 2018a), while an equivalent ten grams of fentanyl costs approximately $8,060 to $10,400 online, with prices falling rapidly from 2014 to 2016 (Miller, 2020). Distributors began cutting relatively expensive heroin with relatively cheap fentanyl to lower production costs. Anecdotal evidence suggests that early-adopting dealers temporarily captured market share, after which other dealers also began adding fentanyl to their product to remain competitive. According to the DEA the addition of fentanyl to heroin poses '...a higher risk of overdose to even the most experienced opioid users.' Fentanyl is also available in diverted prescription form (such as Actiq and Duragesic), but is relatively expensive and thus rarely a source of illicitly traded fentanyl (Lamy et al., 2020).

Fentanyl was involved in 5,544 overdose deaths in 2014; compared with 9,580 and 19,410 deaths in 2015 and 2016 respectively. By 2017 this drug was associated with 28,466 deaths. The fentanyl fatal overdose rate temporarily plateaued at around that level over the period 2018 to 2019, but rose again in the early months of 2020 suggesting that the crisis continues to worsen (Centers for Disease Control and Prevention, 2020b).

3 Background on the Opioid Crisis: Costs and Causes

3.1 Overall Prevalence and Costs

Data from the National Survey of Drug Use and Health (NSDUH) – the official government source for substance use statistics in the U.S. – indicate that in 2018, 1.7 million Americans met diagnostic criteria for prescription opioid use disorder (OUD) and over 500,000 for heroin-related OUD (McCance-Katz, 2018). These numbers represent a lower bound on the true prevalence of OUD as individuals are likely to under-report this condition in survey settings and since the NSDUH excludes groups likely to have disproportionately high rates of OUD (e.g., institutionalized and homeless individuals). Between 1999 and 2018, nearly 450,000 Americans died from an opioid overdose (McCance-Katz, 2020). Opioid misuse and overdoses impose additional costs on the healthcare system in the form of emergency department visits, direct treatment costs, and expenses associated with neonatal abstinence syndrome (NAS). Nonmedical costs include those related to the criminal justice system, lost

worker productivity, and many others. Economists have studied ways to estimate total costs, using insights from economic cost studies in other contexts. Total societal costs of opioid misuse had been calculated at $55 billion in 2007 and $78 billion in 2013 (Birnbaum et al., 2011; Florence et al., 2016), but these estimates exclude the costs of premature mortality. Taking premature mortality into account, as well as some other costs, yields much higher estimates of $504 billion in 2015 from the Council of Economic Advisers (White House Council of Economic Advisers, 2017), $179 billion in 2018 from the Society of Actuaries (Davenport et al., 2019) and, most recently, over $1 trillion in 2017 (Florence et al., 2020).

3.2 Demographic Trends in Overdose Mortality

The opioid crisis has not affected socioeconomic and demographic groups equally. Here we summarize some broad patterns related to gender, race, and age. Overall drug overdose death rates are higher among men than women; about two thirds of opioid overdoses occur among males. However, women are relatively more heavily represented among prescription opioid deaths, with men making up only 59 percent of these fatalities. Non-Hispanic white Americans suffer disproportionately from prescription overdoses, with a death rate of 17.5 deaths per 100,000 population in 2016 (Scholl et al., 2019). American Indians and Alaska Natives have the second highest rate of opioid overdose deaths, but data on these demographic groups are sparse (Scholl et al., 2019; Rudd et al., 2014). Black and Hispanic Americans have traditionally been somewhat less affected by the crisis, perhaps due to under-treatment of pain within these groups, which may have inadvertently protected them from opioid initiation and overuse (Alexander et al., 2018; Frankt and Monkovic, 2019). However, fatal overdose rates are rising among Blacks in more recent years as fentanyl is increasingly concentrated in urban areas, where Black Americans are disproportionately likely to reside. From 2015 to 2017, opioid mortality rates rose especially quickly among Blacks aged 45 to 64 years in large metro areas (Lippold, 2019). From 2011 to 2016, the age-adjusted rate of overdose deaths involving fentanyl grew the most in the Black population, reaching 140.6 percent per year, while this rate rose 108.8 and 118.3 percent annually for non-Hispanic whites and Hispanics (Spencer et al., 2019).[4] Older populations report far less opioid misuse (McCance-Katz, 2018) and lower rates of opioid overdose deaths corroborate these survey responses, whereas individuals aged 18 to 59 suffer relatively higher opioid fatality rates (Centers for Disease Control and Prevention, 2020a).

The risk of opioid overdose is also positively correlated with a myriad of other demographic

[4]For further studies on age and race dimensions of the crisis, please see Rudd et al. (2014), Martins et al. (2015), Ihongbe and Masho (2016), Hedegaard et al. (2017), Pouget et al. (2018), and Scholl et al. (2019).

characteristics, including being disabled, unmarried or widowed, unemployed, uninsured, incarcerated, having low education, being a citizen (in comparison to a non-citizen), renting rather than owning a home, residing in a non-rural area, and having a low income. Residents of South Atlantic states and Mountain states have relatively high rates of overdose.[5] This heterogeneity in prevalence rates across population subgroups provides important context for understanding hypotheses related to origins of the crisis and potential impacts of policies.

3.3 Labor Market Impacts

In theory, opioids could improve labor markets through better management of chronic pain symptoms and, in turn, enhanced work capacity. However, labor market outcomes could worsen if addiction or other prescription opioid-related problems – for example dizziness, nausea, and sedation – reduce work capacity. Most studies to date indicate that, on net, expanded use of opioids worsens labor market outcomes in the form of lowered labor force participation and additional expenses for employers. Opioid use also raises health insurance costs due to direct expenditures on prescriptions for this medication, and other (indirect) increases in healthcare costs. In this section, we review studies where the direction of causality operates from the overuse of opioids to labor market outcomes; later in discussing the origins of the crisis, we review studies where causation runs in the opposite direction.

The labor force participation rate for prime working aged men (25 to 54 years) has been declining since the 1970s, and opioids have potentially exacerbated this trend. Nearly half of prime working aged men who are out of the labor force report using pain medication on any given day, and about one third take prescription opioids (Krueger, 2017). Several studies using aggregate measures corroborate the finding that opioid misuse causes labor market problems. Harris et al (2020) show that the prevalence of high rates of opioid prescribing decrease labor force participation rates, while Deiana and Giua (2018) show that restricting access to opioids has the potential to increase them. Similarly, Aliprantis et al. (2019) find that higher prescribing rates predict lower labor force participation for prime working aged men and women, with particularly large reductions for persons without a four-year college degree. Beheshti (2019b) shows that restrictions on hydrocodone prescribing, implemented in 2014, led to improvements in labor market outcomes. Park and Powell (2020) find that the crisis's transition to illicit opioids led to reduced labor market engagement, and to rising rates of disability applications and enrollment. Rietveld and Patel (2020) demonstrate that additional opioid exposure is negatively associated with measures of entrepreneurship and small business

[5]Relative risk factors are taken from Altekruse et al. (2020).

formation. However, Currie et al. (2018) uncover a positive relationship between prescribing and employment-to-population rates among women, but no association among men.

Studies using individual-level data yield more mixed results. Using firm-worker matched data from Denmark, Laird and Nielsen (2017) find that additional opioid prescribing decreases labor force participation and income. Similarly, Savych et al. (2018) demonstrate that longer-term opioid prescribing increases the duration of temporary disability spells among those receiving Workers Compensation benefits in the U.S. However, some analyses of survey data on individuals indicate that SUDs are not associated with transitions from full- to part-time work, or with on-the-job problems with coworkers, or financial strain (Baldwin and Marcus, 2014; Maclean et al., 2015). Evidence from Norway suggests that treatment using Cox-2 Inhibitors decreased sickness days among workers with joint pain (Bütikofer and Skira, 2018) and, in the U.S., Garthwaite (2012) finds that removal of Vioxx (a particularly effective Cox-2 Inhibitor) from the market in 2004 led to a 0.35 percentage point reduction in overall labor force participation and $19 billion in lost wages in the year following removal. These findings point to a possibility that proper use of opioids for pain treatment may help workers remain on the job or return to work. Insuring individuals with opioid use disorder is also expensive, costing employers an extra $10,000 per a year in medical expenses and $1,200 annually in work losses (Rice et al., 2014).

3.4 Costs to Families

There is also evidence of the opioid crisis imposing costs in the sphere of family structure and child well-being. The number of children living with an adult with an opioid use disorder increased 30 percent, and those with an adult using heroin rose 200 percent, between 2002 and 2017 (Bullinger and Wing, 2019). Buckles et al. (2020) find that as a result of the opioid crisis, the fraction of children living away from a parent and in a household headed by a grandparent increased. Gihleb et al. (2020), and Gihleb et al. (2019b) document rising rates of child removals and NAS over the course of the opioid crisis. From 2000 to 2015, the number of foster care cases related to drug misuse increased 66 percent, and foster care costs rose by $20,000 per case. The rate of NAS, where infants experience opioid withdrawal symptoms due to in-utero exposure to opioids, has grown by 500 percent since 1999. The U.S. spends $1.5 billion in treating NAS-related complications each year. Evans et al. (2019) illustrate rising rates of child maltreatment cases due to increased opioid misuse.

3.5 Crime

The opioid crisis seems to be less associated with crime, in the popular press, than the heroin crisis of the 1970s, the crack and cocaine crisis of the 1980s and early 1990s (Fryer et al., 2005; Pollack and Reuter, 2014), or the methamphetamine crisis that occurred in the 2000s (Dobkin and Nicosia, 2009; Plüddemann et al., 2010). Nevertheless, there is evidence linking both violent and property crimes with opioid prescriptions (some of which are diverted to other users) and heroin use. In line with this hypothesis, Bondurant et al. (2018) and Wen et al. (2017) find that expanding access to SUD treatment during the opioid crisis decreases both violent and financially-motivated crimes.[6] Dave et al. (2018) document that reducing the supply of prescription opioids decreases violent crime.

3.6 Origins of the Crisis

Famously documented in Case and Deaton (2015), 'deaths of despair' – i.e. deaths from drug overdoses, suicides, and chronic liver disease (often inaccurately referred to as alcohol deaths)–drove a surprising reversal in the decline of mid-life mortality among non-Hispanic white Americans in the early 21st century. White mortality patterns began to reverse (from a declining trend to an increasing trend) around the year 2000. This pattern is unique to the U.S., as other Organisation for Economic Co-operation and Development (OECD) countries continued to experience midlife mortality rate reductions during the same time period. Drug deaths are by far the most important contributor relative to suicides and liver disease, accounting for at least three-quarters of the overall effect. Among white men aged 25 to 55 years without a college education, the death rate from drugs, suicides, and chronic liver disease was 125 to 150 deaths per 100,000 population in 2017, a 250 percent increase over 1992 rates (Leonhardt and Thompson, 2020).

In the past 40 years, the U.S. experienced wage stagnation among less educated workers due to automation, import competition, outsourcing, weakening unions, increased market concentration, and productivity clusters in abstract tasks which benefit cities and the highly educated, while posing a disadvantage to less connected geographies and the less educated. The U.S. has also seen declines in the labor force participation rate, increases in mental illness, disability, and chronic pain, as well as falling family and community engagement. Some scholars contend that these changing economic factors have negatively impacted specific groups of society, leaving them without hope of re-gaining economic stability and their position in society. In response, members of these groups have turned to substances as a

[6] Swensen (2015) shows that fatal drug overdoses also decrease as treatment access increases.

means to self-medicate their pain. Deaton argued in his 2017 testimony to Congress: '[Deaths of despair] respond more to prolonged economic conditions than to short-term fluctuations, and especially to the social dysfunctions, such as loss of meaning in the interconnected worlds of work and family life, that come with prolonged economic distress' (Deaton, 2020).

Recent research supports the hypothesis that economic factors have an impact on opioid overdoses. Declines in local manufacturing employment depress wages and employment, and increase opioid overdose deaths (Charles et al., 2019). Trade liberalization with China has caused higher rates by suicide and fatal drug overdoses, especially among white males (Pierce and Schott, 2020). Opioid overdoses are also impacted by short-term labor market shocks such as a rise in the unemployment rate and plant closures: a worsening economic climate appears to increase overdoses (Hollingsworth et al., 2017; Venkataramani et al., 2020). Maclean et al. (2020) show that heroin-related admissions to SUD treatment decline during economic downturns, but the authors find no evidence that prescription opioid-related treatment admissions vary with changes in the business cycle. Minimum wage policies have been shown to reduce suicides, although there is less clear evidence for opioids (Dow et al., 2020). Similarly, counties that experience growth in industries that employ white males experience fewer opioid overdoses, implying protective effects of industry-specific growth for them. Dow et al. (2020) find that increases in the federal minimum wage and increases in the Earned Income Tax Credit (EITC) decrease rates of suicide (but not fatal drug overdose) among Americans without a college education, implying that economic assistance may assuage some forms of despair. Although multiple studies indicate a role for economic indicators in determining adverse opioid outcomes, the magnitudes of the predicted effects are small relative to the overall increases in opioid prescribing and overdoses, and are therefore unlikely to be key determinants of the crisis.

Few studies examine how changes in culture or social cohesion affect opioid outcomes, which implies an substantial gap in the literature. In large part, the paucity of research on these conceptually important factors may reflect the difficulty in obtaining detailed and well-measured data on them. Identification using standard econometric methods may be challenging. In particular, since measurements of both economic and cultural well-being have deteriorated for some groups since the early 1970s, separating the causal effects of each may be difficult. In addition, underlying forces may influence both economic and cultural factors, further raising the difficulty of isolating causal effects from spurious correlations. Finally, there is plausible endogeneity in the relationship of worsening economic conditions, declining family stability, and decreasing civic engagement for whites without a college degree. These phenomena have no single clear cause, but econometric identification requires that researchers

use believably exogenous shocks to well-measured variables. Research identifying the effect of economic change using small temporary economic shocks (typically by including time fixed effects that account for macro trends) and the resulting local average treatment effects may not be capturing the pervasive influence of these more opaque generational trends.[7]

While several studies, mentioned above, suggest a causal relationship between economic conditions and opioid overdoses, other research indicates that economic factors have only limited effects on drug, suicide, and chronic liver disease deaths. Although counties that experience relative economic decline also had higher growth in drug mortality, Ruhm (2019a) finds that the relationship is greatly mitigated (sometimes to zero) by controlling for confounding factors and for allowing for selection on unobservables.

In other words, economic conditions are correlated with population patterns of behavior, and short-run and medium-run economic woes alone do not explain the bulk of the variation in opioid overdose across the U.S. Similarly, Currie et al. (2018) argue that there is little or mixed connection between counties' employment-to-population ratio and opioid prescriptions. In particular, the authors find a weak link among women and no relationship among men. Currie and Schwandt (2020) further illustrate that current labor market opportunities do not explain a substantial part of the opioid crisis, and urge attention towards policies aimed at addressing the opioid epidemic itself.

Other research finds results that run contrary to the hypothesis that poor economic outcomes cause more opioid misuse or other negative health outcomes. Metcalf and Wang (2019) show that mining employment is actually positively correlated with opioid misuse – that is, counties realizing a decrease in this type of employment experience lower rates of opioid overdose than those that are also reliant on mining but do not experience the negative economic shock. Evidence from Denmark shows that industry export growth increases on-the-job injury and elevates stress levels and rates of depression, heart attacks, and strokes (Hummels et al., 2016); this finding conforms with other evidence of health benefits during economic downturns (Ruhm, 2000). Furthermore, workers in more injury-prone industries which experience employment growth receive more opioid prescriptions as their industry expands (Musse, 2020). Therefore, even industries that gain from trade in the form of export or overall economic growth more generally may see increased rates of opioid use through the channel of rising rates of injury or illness incurred while working.

To summarize, the opioid crisis can be viewed through an economic lens as resulting from an interaction between supply-side and demand-side factors, and feedback between the two.

[7]See Case and Deaton (2020) for a detailed discussion of these issues and for their arguments for why they believe that declines in social capital are the key factor explaining increases in 'deaths of despair.'

At the most fundamental level, supply-side factors related to the increased production and marketing of opioids, combined with changes in prescribing patterns and policies (e.g., the Joint Commission listing pain as the fifth vital sign) were the proximate cause. These factors explain why the crisis began, fairly suddenly, in the late 1990s, after the approval of OxyContin and pharmaceutical industry efforts to normalize the prescribing of opioids. Conversely, demand-side factors such as skill-biased technological change and import competition are unable to account for the timing of the increase in opioid prescriptions and the resulting adverse consequences. However, demand-side factors play an important role (albeit abetted by the pharmaceutical industry's targeted marketing efforts to healthcare providers most likely to prescribe opioids on the part of suppliers) in determining who was most affected. Moreover, the mutually reinforcing relationships between economic conditions and opioid use may create a feedback loop of economic and personal despair. In this regard, the crisis can usefully be viewed as a cyclical, reinforcing model of despair and self-medication through opioid misuse which was acted upon by outside forces from public policy, the changing prescribing culture, and possibly other factors that have not yet been examined in the literature.

3.7 Healthcare Institutions

Particularly important are the effects of additional exposure to opioids and to physicians who prescribe opioids more aggressively. Finkelstein et al. (2019) study those who move between U.S. counties to assess the effect of the local prescribing environment on opioid use. The authors show that moving from a county that has a relatively low rate of top-prescribing physicians to one with a relatively high rate is associated with additional overdoses for migrating individuals. The results imply that 30 percent of the variation in opioid deaths across counties is explained by place-specific effects, namely physician prescribing behavior. More directly, Schnell and Currie (2018) find that physician education plays a role in opioid prescribing styles. In particular, those physicians with medical degrees from low-ranked schools prescribe at higher rates than otherwise similar physicians. Schnell (2018)'s finding that physicians differ dramatically in their response to the reformulation of OxyContin further serves to underline the role played by physician prescribing in the crisis. Opioid marketing to doctors also has an impact on how different states experience the opioid crisis. Alpert et al. (2019), and Nguyen et al. (2019a) find that pharmaceutical company marketing efforts increased prescribing by physicians. More generally, Lin et al. (2020) demonstrate that geographic area variations in the intensity of medical care provided are positively associated with opioid death rates.

4 Policy Responses to Prescription Opioid Misuse

Governments at all levels have undertaken a range of policy approaches in attempts to curb the opioid crisis. The nature of these policies has changed over time, corresponding to some extent with the types of opioids targeted, and as the character of the crisis has shifted from prescription to illicit opioids. While some localities have departed from the general trend, early policies tended to focus on interventions designed to curtail the supply of prescription opioids, or raise the financial or time costs of accessing these substances. More recent policies have typically emphasized demand-side factors, such as the ability to obtain prescriptions from multiple healthcare providers, and harm reduction efforts, such as naloxone access laws. Which type of policy response is more likely to be more effective is unclear *ex ante*. There are also potentially synergies between policies, suggesting gains to implementing multiple complementary efforts.

A rapidly growing literature in economics and policy evaluates several of these regulations. This research suggests the desirability of both supply-side and demand-side policies, as well as the importance of considering relevant local factors that may interact with both types of policies; e.g., see Pacula and Powell (2018b), and Saloner and Barry (2018) for an excellent discussion on this topic, and Barry and Frank (2019), Mauri et al. (2020), and Schuler et al. (2020) for comprehensive recent reviews of state and federal policy studies related to opioid outcomes. Of note, most supply-side policies to date have focused on reducing opioid prescribing, opening the door to possible substitution towards illicit drugs (such as heroin) that are harder to regulate and, arguably, more harmful. Conversely, demand-side policies often address outcomes that may impact underlying addiction to opioids. For example, OUD treatment access (discussed later in this chapter).

4.1 Prescription Drug Monitoring Programs

One of the earliest policies implemented by states, and currently by far the most common, is the prescription drug monitoring program (PDMP). PDMPs were adopted as early as 1939, in California, and were designed to reduce the misuse of prescription medications generally, not specifically opioids (Holmgren et al., 2020). A PDMP is a centralized database containing patient scheduled prescription medications. PDMPs are designed to increase information available to healthcare providers related to patients' history with medically-obtained prescription opioids. By 2017, all states had a PDMP in operation (Holmgren

et al., 2020).[8] Conceptually, healthcare providers (e.g., physicians who prescribe medications and pharmacists who dispense them) enter information into the database when patients are prescribed or dispensed prescription medications, including opioids. Healthcare providers then have the ability to access the patient's historical use of opioids and other controlled substances. The hope is that healthcare providers will then identify individuals who are potentially misusing opioids and limit access of the drugs to these individuals, thereby curbing misuse without reducing access to medications for legitimate patients. For example, doctor shopping can be identified and prevented by reviewing patient histories. Similarly, and ideally, implementation of a PDMP should not curtail access to prescription opioids for patients who use the medication appropriately (e.g., to manage acute pain).

For PDMPs to reduce opioid misuse, healthcare providers must actually use the database, both by entering information after they prescribe or dispense controlled substances and by checking the patient's history before doing so. Several features of the earliest PDMPs may have stifled their effectiveness. Importantly, these PDMPs were voluntary: pharmacists were required to enter controlled substance histories into the centralized database but healthcare providers were not required to check the database at the time of prescribing or dispensing medications. Since many healthcare providers contend that the act of checking or entering information in the database is burdensome, prescribing providers often did not engage with PDMPs. Early PDMPs were not electronic, adding to the administrative burden of using the system. Given this backdrop, some healthcare providers have pushed back on PDMP adoption because of the hassle of utilizing them, such as difficulty in obtaining logins, the database not being accessible (i.e., the platform being 'down'), and incomplete data (Haffajee et al., 2015; Young et al., 2017; Lin et al., 2017). Beginning in 2007, several states adopted arguably stronger PDMPs. In particular, this more robust policy approach often involved adding 'mandatory access' provisions requiring prescribers to use the database. Conceptually, such mandatory access PDMPs should have more impact than voluntary systems as healthcare providers are legally bound to query the system.

A number of economic studies have examined the impact of PDMPs on opioid misuse. Those examining broad measures of a PDMP, that do not distinguish between voluntary and mandatory access programs, generally suggest they have a limited impact. For example, using a sample of disabled non-elderly Medicare beneficiaries, Meara et al. (2016) do not observe changes in various opioid misuse outcomes following adoption of a PDMP. Similarly, Buchmueller and Carey (2018) find that among Medicare enrollees, voluntary PDMPs are

[8]Missouri was the last state to implement a PDMP, and the law has been contested since its effective date, so many studies consider Missouri to not have an operating PDMP.

not effective in reducing patterns of harmful opioid behavior, whereas mandatory-access PDMPs are effective. However, Kilby (2016) shows a 12 percent reduction in opioid-related mortality post-PDMP, and a 10 percent decline in prescribing among patients with employer-sponsored insurance. Other studies, suggest that optional-use PDMPs have larger effects on the Medicaid population (Bao et al., 2016) and on users with previous patterns of behavior indicative of opioid misuse (Mallatt, 2019). The limited impact of many voluntary PDMPs is not surprising as database use is often relatively infrequent among healthcare providers. For example, in states where PDMP use is not mandatory, roughly 14 to 25 percent of healthcare providers utilize the system (Alexander et al., 2015).

More recent studies distinguish between voluntary and mandatory access PDMPs, and provide more definitive evidence that the latter reduced prescription opioid misuse (Ali et al., 2017; Buchmueller and Carey, 2018; Deiana and Giua, 2018; Bao et al., 2018; Grecu et al., 2019; Mallatt, 2019, 2020b; Kaestner and Ziedan, 2019; Wen et al., 2019; Ziedan and Kaestner, 2020). For example, Grecu et al. (2019) show that, following adoption of a mandatory PDMP, the number of admissions to substance use disorder treatment related to opioid use decreases by 20 to 25 percent, although reductions only emerge two years post-policy. The authors also document an age-gradient in the estimated treatment effects with admissions rates decreasing by 32, 17, and 12 percent among those aged 18 to 24, 25 to 44, and 45 years or older.

In addition to changes in direct effects on opioid use, recent research suggests that mandatory PDMPs reduce crime (Dave et al., 2018; Deiana and Giua, 2018), improve children's birth outcomes and decrease NAS (Gihleb et al., 2020; Ziedan and Kaestner, 2020), and reduce foster care admissions (Gihleb et al., 2019a). The assumed mechanism is that reduced opioid use leads to these improvements. A full consensus has not yet been reached, with some studies showing opposing findings. For example, Mallatt (2018) finds that PDMP adoption leads to increased heroin-related crime in counties with high rates of opioid use.

There may be a feedback loop induced by PDMPs whereby pharmaceutical companies reduce prescription opioid promotions following a mandatory PDMP which, in turn, lowers demand for these medications (Nguyen et al., 2019b). PDMPs also appear to directly decrease healthcare provider prescribing of opioids. Using rich health insurance claims data, Sacks et al. (2019) show that opioids dispensed to opioid-naive users decline post-PDMP. Since the databases will contain relatively little information on new users, these results suggest that PDMPs instead reduce prescribing for other reasons, the most likely being hassle costs of using the system (Bachhuber et al., 2018).[9] Using unique data from Kentucky, Alpert

[9]Note, however that some states are able to provide risk scores of all patients in PDMPs; e.g., see https://apprisshealth.com/solutions/narxcare/ (last accessed November 9th, 2020).

et al. (2020) similarly suggest that reductions in physician opioid prescribing may be at least partially attributable to the hassle costs associated with using the PDMP. Using claims data, Mallatt (2019) shows that PDMPs target users displaying signs of opioid misuse.

While studies establish that mandatory PDMPs reduce prescription opioid use and improve some associated outcomes, there could be positive or negative spillover effects on the use of other prescription medications, addictive substances, or non-drug pain therapies. For instance, if prescription opioids and other addictive substances are economic complements, then PDMP-attributable reductions in opioid prescribing should decrease the use of other substances.[10] However, if prescription opioids and other drugs instead are instead economic substitutes, then consumers will switch to the substitute drug as new obstacles to obtaining prescription opioids emerge. Cawley and Ruhm (2011) provide a careful discussion of the relationships between substances. Whether substitution improves or worsens public health will be determined by the relative harms of the involved drugs. Several studies provide evidence of such substitution. For example, Grecu et al. (2019) show that opioid-related admissions to SUD treatment programs decline following adoption of a mandatory PDMP, and that there are also decreases in admissions for cocaine and marijuana use, which could be economic complements to opioids. However, Mallatt (2020b) finds that consumers substitute to heroin following the establishment of PDMPs, with particularly strong evidence in localities with high prior levels of prescription opioid use. This result is concerning if heroin use is more harmful than the consumption of prescription opioids; we may expect heroin to be more dangerous because of the method of consumption (e.g., injection rather than swallowing pills) or if users are less able to monitor the potency of the dose they are ingesting.

Some researchers argue that PDMPs need not be mandatory to reduce prescription opioid use. Wang (2020) shows that PDMPs (whether voluntary or mandatory) reduce opioid misuse when they are adopted in combination with a state-level health integration technology policy that promotes the sharing of health records electronically. Kaestner and Ziedan (2019) find that adoption of a mandatory PDMP reduces sales of scheduled prescription drugs. However, when also controlling for whether the PDMP is electronic, the authors find that the coefficient estimate on the mandatory PDMP variable becomes statistically indistinguishable from zero. They interpret these results to imply that the salient feature of the PDMP is whether the database is electronic, not whether healthcare providers are mandated to check it.

Overall, we note that while there are many studies on PDMPs, the literature has not yet reached full consensus on the importance of PDMP implementation and design, leaving

[10]The PDMP may also have a direct effect by reducing the prescribing of other scheduled drugs, such as sedatives or stimulants.

scope for future work in this area. There is also opportunity for new research studying how supply-side restrictions affect substitution towards other non-drug medical therapies and and how to ensure that policies do not pose undue burdens on underrepresented minority populations (Substance Abuse and Mental Health Services Administration, 2020).

4.2 Other Supply-side Policies

There are a number of less studied state-level supply-side interventions. One important category is pain management clinics laws (PMCL), which establish minimum requirements that pain management clinics must meet in order to dispense prescription drugs. Broadly, PMCLs are organized to prevent the emergence or operation of 'pill mills' – medical clinics that knowingly and willingly dispense prescription drugs, including to illegitimate consumers. Pill mills were especially notorious in Florida, which was considered the epicenter of the opioid crisis in the early 2000s. By preventing the ability of nefarious clinics from emerging or allowing authorities to shutter such clinics, the PMCLs reduce both the overall supply of prescription opioids and the extent of diversion to illegitimate users.

PMCLs involve many separate requirements for clinics and doctors' offices, with variation in the specific stipulations across states. Each set of laws specifies which facilities are classified as pain management clinics, typically citing prescribing patterns or advertising practices that are characteristic of pill mills. The packages of laws then add more requirements aimed at reducing prescribing within these clinics or shutting them down altogether.

Twelve states have passed legislation targeting pill mills. These policies appear to be effective in reducing prescription opioid use. Using government data on sales of scheduled prescription medications, Ziedan and Kaestner (2020) document 15 to 50 percent declines in prescription opioid sales after implementation of a PMCL. Early evidence from Florida and Texas suggest these targeted efforts are effective at curbing prescribing and reducing harmful secondary outcomes like overdoses (Chang et al., 2016; Lyapustina et al., 2016; Mallatt, 2020b; Meinhofer, 2016; Rutkow et al., 2015). Meinhofer (2016) shows that the substantial crackdown in Florida caused the number of active pain clinic licenses to fall from 988 in 2010 to 407 in 2012. Additionally, quantities of prescribed opioids decreased by 59 percent, opioid-related admissions to drug treatment facilities increased by 33 percent and overdose rates declined. Florida was also unique in that the DEA arrested many offending prescribers during that state's crackdown on pain clinics, whereas pill mill laws in other states did not include a substantial law enforcement component.

Chang et al. (2016) find that, prior to the pill mill legislation, the top four percent of

opioid prescribers in Florida were responsible for 67 percent of total opioid prescriptions in the state. After the pill mill legislation and law enforcement efforts were implemented, the high risk providers saw fewer patients and prescribed fewer opioids. Lyapustina et al. (2016) indicate that the Texas pill mill law reduced opioid prescribing by between eight and 24 percent. Using nationwide data on business establishment counts, Mallatt (2020a) shows that the laws cause ten to 15 percent of establishments within a certain class of specialty clinics (including pain clinics) to exit, equivalent to 23 fewer pain clinics for each treated state. These studies reveal that pill mill laws operate at both the extensive margin, driving pain clinics to exit treated counties and states, as well as on the intensive margin, as top prescribers prescribe fewer opioids and see fewer patients.

PMCL adoption appaers to have positive spillovers to labor market and crime outcomes. Kaestner and Ziedan (2019) find that employment and earnings improve modestly post-law, while Deiana and Giua (2018) demonstrate that labor market participation rates increase and unemployment rates decline. Further, Mallatt (2020b) shows that PMCLs are negatively associated with crime rates related to heroin possession and dealing.

Many states have recently passed laws limiting the length of initial prescriptions for opioids (typically to seven days). In considering the impact of these policies, Sacks et al. (2019) unexpectedly show that such policies increase the overall amount of opioids prescribed to new users. This contrary result is driven by the reduction in the length of prescriptions that is more than offset by increases in the frequency of short prescriptions. Determining whether the net effect is harmful or beneficial depends on the relative risks of growth at the extensive margin (frequency of prescriptions) versus reductions at the intensive margin (length of prescriptions).

An important private policy that substantially altered the supply of prescription opioids within the U.S. was the August 2010 reformation of OxyContin by Purdue Pharma. From its introduction to the market in 1996 through early August 2010, OxyContin, an extended release version of oxycodone that was often prescribed in high doses, was one of the most commonly misused prescription opioids (Cicero et al., 2005). One problem with the original formulation was that consumers often crushed or dissolved the pills and then inhaled or injected the drug an a more intoxicating form, thereby circumventing the extended release mechanism occurring with oral ingestion. Under pressure from the Food and Drug Administration, Purdue Pharma released a re-formulated version of Oxycontin that was more difficult to crush or dissolve. The company also quickly (within days) discontinued the original version, thereby abruptly shutting off access to the previous, easy-to-abuse formulation of OxyContin. There were high hopes for the potential of misuse-deterrent reformulations to reduce the injection, snorting,

crushing, or chewing of prescription opioids (White et al., 2009).

However, the Oxycontin reformulation had unintended spillovers into markets for illicit drugs. While the exogenous and sudden supply shock markedly reduced the use of this opioid, there was substantial and rapid substitution to heroin by consumers. Alpert et al. (2018) conclude that areas with high underlying rates of OxyContin misuse realized large increases in heroin deaths after the reformulation, and that the reformulation explains up to 80 percent of the rise in fatal heroin overdoses after 2010. Similarly Evans et al. (2018) find that each foregone prescription overdose death prevented by the OxyContin reformulation was offset by an additional death from heroin overdose. Further, because heroin is commonly injected and consumers often share needles, this drug-to-drug substitution led to increased transmission of hepatitis B and C (Powell et al., 2019; Beheshti, 2019a). Evans et al. (2020) find additional negative spillovers taking the form of increased child removals in areas with worse opioid outcomes, and Park and Powell (2020) find negative spillovers to labor force participation, finding increases in disability claiming.

The longer-term effects of these policies are not yet well understood. For instance, new initiation into medications for opioid use disorder might decline such that, in steady state, there would be fewer individuals who misuse opioids under the reformulation than there would have been in its absence. However, recent research by Powell and Pacula (2020) suggests the opposite outcome. In particular, the authors uncover evidence of more deleterious effects in the long-run because the reformulation spurred development of illicit drug markets.

States and the federal government have also used the Controlled Substance Act (CSA) as a tool for addressing the opioid crisis.[11] Two changes in CSA, targeting rival products and introduced separately, have allowed economists to study whether there are competitive spillovers to prescription products when one but not another product is regulated. In August 2014, the U.S. federal government added tramadol, the second most popular opioid medication at the time, to the CSA (entering this medication at level V, which involves restrictions on refills). Twelve states implemented the identical policy prior to federal action, providing an opportunity to compare effectiveness of the same opioid policy at state versus federal levels. Seven weeks after tramadol's scheduling, the leading opioid form on the market, hydrocodone combination products, was moved from level III to the more restricted level II (where no refills are allowed). Gupta et al. (2020) find that the tightening of these prescribing restrictions decreased their use, but also caused some increases in prescriptions of close competitors. As a result, there was no statistically detectable short-run reduction in total number of opioid prescriptions. In addition to supply-side policies, states adopted doctor-shopping laws (DSL)

[11] This represents one of the few policies that have been used at a federal level.

requiring patients to report to their healthcare professional previous prescriptions and, in a broad manner, prohibiting patients from obtaining medications through fraud, deceit or misrepresentation. Popovici et al. (2018) show that DSLs reduce opioid overdose deaths and opioid-related admissions to SUD treatment.

Prescription opioids and marijuana may be substitutes along at least some dimensions. For instance, marijuana may sometimes serve as an alternative treatment for chronic pain. Several studies suggest that patients substitute marijuana for opioids following the adoption of a state medical marijuana law (MML). In particular, these studies use health insurance claims data and show that prescriptions for opioids decline post-law (Bradford and Bradford (2017, 2018); Bradford et al. (2018); McMichael et al. (2020)). Recent work suggests that recreational marijuana laws (RMLs) may have a similar impact on the utilization of prescription opoids (Wen and Hockenberry, 2018). Moreover, reported chronic pain among older adults (Nicholas and Maclean, 2019), and both health-related work absences (Ullman, 2017) and Workers' Compensation benefit receipt (Ghimire and Maclean, 2020) decline (chronic pain is a common ailment among those receiving Workers Compensation benefits), suggesting that the use of marijuana may sometimes be effective in reducing chronic pain and other work-impeding ailments. Dispensaries, venues in which consumers can legally purchase marijuana, appear to be particularly important in the relationship between marijuana and opioids. Powell et al. (2018) show that the opening of legal medical marijuana dispensaries reduces opioid-related admissions to SUD treatment facilities by 15 percent and opioid fatalities by 16 percent. Similarly, Smith (2020) indicates that deaths from prescription opioid overdose fall 11 percent after a medical marijuana dispensary opens. These effects are concentrated among non-Hispanic white males.

However, the benefits of expanded access to marijuana through state laws on chronic pain do not appear to extend to all populations. For example, Maclean et al. (2020) show that applications for Social Security Disability Income and Supplemental Security Income increase following adoption of an MML or RML. The authors hypothesize that individuals applying for disability post-law may have weak labor market attachment or marginal disabilities that are not improved by marijuana use.

4.3 Enforcement of Illicit Drug Prohibitions

Now that the crisis has transitioned towards illicit drugs such as heroin and fentanyl, a discussion of the literature on law enforcement crackdowns during past illicit drug crises is potentially useful. A 2014 review by Pollack and Reuter (2014) summarizes many studies

of the effect of such enforcement efforts on drug prices; they do not find solid evidence that raising the risk of arrest or the increasing the length of drug sentences affects street prices. Cunningham and Finlay (2016), and Dobkin and Nicosia (2009) examine the effects of government efforts to make the precursors of methamphetamine less available. Both studies find only temporary effects on price, purity, and harmful outcomes, each outcome returning to its pre-intervention level within a few months to two years. Reuter (1986) similarly finds that cracking down on the importation and high level distribution of cocaine and marijuana in the 1980s had little effect on street-level drug prices.

In contrast, a study of Australia's 2001 effort to reduce the importation of heroin uncovers a large impact on both purity and price (Moore and Schnepel, 2019). The authors also find a short-term increase in violent and financially-motivated crime, as well as longer-lasting decreases in overdoses and property crime. Australia may present a unique case for the enforcement of illegal heroin shipments due to its island geography, which allows greater success in targeting suppliers. Applying Australia's approach to the U.S. may therefore not realize the same efficacy, as the land border with Mexico is more porous and there is evidence that fentanyl is often shipped to the U.S. by mail.[12]

Using web scrapes of darknet drug markets from 2014 to 2016, Miller (2020) documents that wholesale fentanyl is priced 90 percent below equivalent doses of heroin on the black market. Moreover, as fentanyl became more prevalent over this period, its price fell. In 2014, the international law enforcement initiative 'Operation Onymous' shut down darknet drug markets and resulted in the arrests of darknet market administrators, sellers, and customers. However, this intervention caused only a small and temporary price increase in fentanyl which was overwhelmed by the general downward trend during the same time period. Miller (2020) shows that while Chinese efforts to limit the illegal manufacture and export of various fentanyl analogues did flatten the downward time trend in fentanyl prices, the resulting prices remained strikingly low at the wholesale level. On the other hand, Mulligan (2020) argues that reduced law enforcement efforts after 2013, due to the 'Holder memo,' played an important role in the emergence of illicit fentanyl.[13]

[12]See Griswold et al. (2018), and Peiper et al. (2019) for examples of fentanyl precursors sourced abroad and mailed to the U.S.

[13]In the Holder memo, then Attorney General Eric Holder directed federal lawyers to stop prosecuting nonviolent drug crimes. However, the reformulation of Oxycontin and other regulatory measures, noted above, over this time period may preclude clean identification of Holder memo effects.

4.4 Harm Reduction Policies

Since there is little evidence that intensifying enforcement has significant potential for decreasing misuse or raising street prices of illicit or diverted drugs, much of the recent policy response emphasizes harm reduction strategies aimed at reducing fatal overdoses and other problems related to the misuse of opioids. Harm reduction policies include, but are not limited to, naloxone access laws (NALs), Good Samaritan Laws (GSL), and syringe exchange programs (SEP). NALs provide legal immunity to healthcare providers prescribing or administering naloxone, a medication used to reverse opioid overdoses;[14] GSLs grant immunity or mitigated sentencing to individuals who call 911 in the case of an overdose; and SEPs simplify the act of obtaining new, clean syringes for injection drug users, and may include the availability of supervised injection sites or other safety measures (e.g., test strips used to determine if heroin contains fentanyl).[15]

Evidence on the effectiveness of NALs is mixed. Doleac and Mukherjee (2018), emphasizing concerns about possible moral hazard, find that online searches for naloxone increase by seven percent and for opioid-treatment fall one percent post-NAL; opioid-related possession arrests, sales, and emergency department visits increase by 17 percent, 27 percent, and 15 percent, respectively, with no change in opioid-related mortality. Conversely, Rees et al. (2019) show that NAL adoption leads to a nine to ten percent reduction in opioid-related mortality and with consistently negative, but less statistically significant, reductions associated with the passage of GSLs. Abouk et al. (2019) highlight the importance of the specific features of NALs, finding that those granting direct authority to pharmacists to distribute naloxone reduce fatal overdoses, whereas other types of NALs do not. An important challenge for all research on this topic is that the enactment of NALs has occurred over a short time period that coincides with the explosion of fentanyl. This confluence of rapid policy adoption and changes in substances used implies that uncovering causal effects using standard quasi-experimental methods is difficult, and even more so if the exact timing of when these policies become effective (which may differ from formally legislated dates) is not well understood.

4.5 Price Elasticities, Health Insurance, and Treatment

Even though they are addictive substances, the demand for drugs such as opioids is responsive to economic factors such as time and financial prices (Becker et al., 1991). Therefore, when

[14] See Smart et al. (2020) for a recent review of NALs

[15] Generally, SEPs allow individuals to return used syringes for safe disposal (which also minimizes exposure to discarded 'dirty' syringes for non-users) and receive clean syringes without risk of legal consequences or financial costs.

examining the evolution of the opioid crisis from prescription to primarily illicit drugs, the role of the price elasticity of demand for opioids is important to consider. Factors that reduce the price of opioids, including insurance expansions such as those due to Medicare Part D, could increase their use (Powell et al., 2018). Soni (2019) uses price variations in Medicare Part D to identify important heterogeneity in elasticity of demand for prescription opioids. Focusing on 55 to 74 year olds, she uncovers an overall elasticity of -0.89; however, almost all of the response is concentrated among new users. Soni also presents evidence that non-prescription pain killers are substitutes for prescribed opioids. Einav et al. (2018) use identifying variation from the design of the Medicare Part D 'donut hole' in prescription drug coverage to show that the demand for prescription opioids is rather price inelastic, with an elasticity estimate of -0.04. However, the local average treatment effect is identified off of individuals at the spending margin of the donut hole; these patients are likely sicker than the typical Medicare Part D beneficiary or younger opioid user. Some evidence suggests that heroin may have a relatively high demand elasticity, when compared with other drugs. For example, Saffer and Chaloupka (1999) estimate price elasticities for alcohol, cocaine and heroin of -0.30, -0.28, and -0.94, respectively, although it is unclear how applicable these findings are to the present day. However, a more recent study that combines experimental and longitudinal survey data shows that the conditional demand price elasticity for heroin is -0.80, suggesting that demand for illicit drugs continues to respond to price changes in a manner predicted by economic theory (Olmstead et al., 2015).

A related issue relevant for this discussion is insurance coverage for drug treatment. This coverage is often incorporated with broader changes in the healthcare delivery system, rather than specifically targeting the opioid crisis. While numerous treatment options are available – including medications such as methadone, buprenorphine, and naltrexone, alongside behavioral interventions like counselling (Murphy and Polsky, 2016) – most SUDs, including opioid use disorder, remain untreated. Recent estimates suggest that only one in ten individuals with OUD receive medication for treating it in a given year (Substance Abuse and Mental Health Services Administration, 2019), although there have been recent expansions in availability of DEA-waivered providers of buprenorphine (Dick et al., 2015). While there are many reasons why individuals do not receive treatment – including strong psychological barriers to treatment and stigma – commonly stated causes include inability to pay and lack of insurance coverage (Substance Abuse and Mental Health Services Administration, 2019). Thus, increasing the generosity of insurance, both in terms the number of individuals eligible and the services included in plans, may facilitate treatment uptake and health improvements.

Research on the effects of health insurance on opioid use disorder frequently uses legal

changes resulting from the Affordable Care Act (ACA) as a source of identifying variation. One important modification under the ACA is that SUD treatment (including for OUD) became listed as an essential benefit that must be covered by most plans (McLellan and Woodworth, 2014). In addition, Medicaid, the primarly public health insurance system for low income Americans, jointly funded by the states and federal government, is the largest insurance payer for SUD treatment (McLellan and Woodworth, 2014). Under the ACA, Medicaid coverage was expanded to include all adults with incomes up to 138 percent of the federal poverty line. However, in 2012 the Supreme Court ruled that the federal government could not compel states to expand Medicaid and not all states elected to do so. Several studies have exploited this variation across states to test the impact of expanding Medicaid and show that this had important implications for opioid use disorder treatment access and outcomes.

For instance, Meinhofer and Witman (2018) find that ACA Medicaid expansion increased prescriptions for medications used to treat opioid use disorder by over 100 percent, raised admissions to specialty drug treatment, and increased the probability that opioid use disorder treatment providers accepted Medicaid as a form of payment. Cher et al. (2019) corroborate this finding for OUD treatment medications. This latter finding is particularly important as insurance has historically played a minor role in financing SUD treatment Mark et al. (2016). To date there is limited evidence that this expansion has led to changes in opioid-related deaths (Averett et al., 2019; Abouk et al., 2019). However, the dependent coverage mandate in the ACA (which guarantees that children can remain on their parent's health insurance plans up to age 26) is associated with reductions in opioid fatalities among young adults impacted by the policy (Wettstein, 2019).

A concern with any insurance expansion is its potential to induce moral hazard. In the context of the opioid use crisis, this would take the form of insurance reducing the out-of-pocket prices of prescription opioids, and potentially spurring misuse and opioid use disorder within the population. The research described in the previous paragraph suggests that this concern is largely unwarranted; however, a clear consensus has not yet emerged. For instance, Powell et al. (2020) leverage the plausibly exogenous variation in prescription drug coverage offered by the introduction of Medicare Part D in 2006 and find that a ten percent increase in the supply of medical opioids leads to a seven percent increase opioid deaths among individuals likely ineligible for Medicare. This finding suggests that some of these prescribed opioids are diverted to other users.

5 Conclusions and Directions for Future Research

As the opioid crisis has emerged as a major public health concern, so has a large and rapidly growing body of economic research analyzing this crisis. These studies use the concepts of supply and demand; habit-forming consumption; substitution, complementarity, and spillovers; and interactions with labor markets and family level outcomes. The studies leverage a variety of data sources, with their respective strengths and weaknesses (Smart et al., 2020). Some analyses are purely descriptive; others attempt to determine causal effects. The research has increased our understanding over a variety of important dimensions. For example, supply-side factors (e.g., aggressive pharmaceutical industry promotion of prescription opioids) were a primary cause of the epidemic, but with demands-side factors determining which groups have been most adversely affected. Regulatory and policy approaches have played a role in mitigating these initial harms but have been less successful in addressing the underlying addictions, resulting in spillover effects to the consumption of illicit opioids and the expansion of those markets. Generally, states have played a more active role than the federal government in these policy efforts, although sometimes with federal grant support (e.g., Comprehensive Addiction and Recovery Act of 2016) and advisory statements (e.g., CSA).

Going forward, while PDMPs have been extensively studied, there is room for better understanding the circumstances in which these programs are most beneficial and their long-run impacts. Other policy approaches (e.g., day limits to prescribing, CSA advisories, and most harm reduction policies) have received much less attention. In all opioid policy areas, researchers can benefit from the creation of taxonomies that reduce barriers to studying impacts of the policies (Grant et al., 2020), and from considering the power and appropriateness of the statistical methods chosen (Griffin et al., 2020). There also remains uncertainty about the fundamental causes of the opioid crisis and its relationship with other drug problems, such as the frequency of deaths involving poly-drug use, the rapidly emerging crisis of stimulant use and deaths, and the broader history of rising drug mortality in the U.S. (Ruhm, 2017, 2019b; Jalal et al., 2018). In addition, the rapid changes in circumstances (like the emergence of fentanyl) and policies (such as NAL implementation) provides severe challenges to the standard quasi-experimental methods economists typically use to study these issues. Considerably flexibility and comprehensive understanding of the literatures outside economics will be needed in determining the best approaches to provide credible estimates in future research.

As of this writing, the U.S. and many other countries are in the midst of the COVID-19 pandemic which has lead to over 200,000 American deaths. Although its implications for the

opioid crisis are unclear, preliminary data indicates that COVID-19 is being accompanied by another increase in opioid-related mortality (Centers for Disease Control and Prevention, 2020b). Therefore, assessing the causal toll of the pandemic for opioid use and opioid use disorder will be important. In particular, we need to better understand how opioid problems have been affected by other changes related to COVID-19 such as: reduced willingness to seek healthcare, the growth in telehealth, and other non-medical factors such as isolation, strain, uncertainty, economic recession, a large-scale but short-lived government stimulus package, loss of friends and family members to COVID-19, and general disruptions in daily life. Finally, efforts will be needed to determine the most effective policies to address opioid outcomes in the post-COVID19 setting.

While contributions from many disciplines outside economics play enormous roles in answering the questions addressed above, the particular concerns of economists – in areas such as the roles of incentives, opportunity costs and spillovers, causal identification, and of health as a production process – provide useful complementary insights.

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