Pharmaceutical promotion, physician response, and opioid abuse: Identifying the role of physicians in the opioid crisis

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Abstract

This paper investigates the role of physicians and their prescriptions in the opioid epidemic. In order to disentangle the supply behaviour of doctors from the demand behaviour of patients, I leverage the staggered introduction of Medicaid expansion across states to exogenously shift opioid supply. Crucially, I argue that Medicaid expansion is composed of two distinct periods. The first is the pre-expansion announcement period. I argue that during the pre-expansion period, because eligible individuals have yet to receive their coverage there is no change in patient demand or disease burden. However, once the policy is announced, physicians and pharmaceutical firms may change their supply-side behaviour in anticipation of future profits from Medicaid expansion. The second period captures the de-facto expansion of health insurance, which is likely to affect patient demand for pharmaceutical products. Focusing my analysis on the announcement period, I show that pharmaceutical firms respond in advance of policy implementation, increasing the number and value of promotions of opioid products to physicians. These effects are driven by counties with the largest program-eligible population. Using difference-in-differences, I identify an increase in prescription opioid sales over this same period. I also find that increased promotions and prescriptions are associated with an increase in opioid-related deaths in the short-run, which do not appear to be persistent 1 year post-announcement.

Keywords: Opioid epidemic, pharmaceutical promotion, prescribing

JEL Codes: I10, I12, I13

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1 Introduction

The opioid epidemic has had devastating effects globally and in the United States. Between 1999 and 2019, the U.S. has seen nearly half a million deaths attributed to opioids, a statistic that masks a larger number of close-calls due to overdoses and the suffering associated with living with addiction. While commonly prescribed opioids no longer make up the majority share of these opioid deaths as of 2015 (Mattson et al., 2021), they nevertheless still play an important role in drug initiation. Indeed, evidence suggests that between 8% and 12% of those who use prescription opioids for chronic pain go on to develop an opioid use disorder (Jones et al., 2015). This is of particular concern to health policy experts, given that prescription opioids continue to make up an important form of medical treatment, with 35% of Americans having received at least one prescription for opioids in 2017.

While these startling statistics clearly point to the need to study the continuing importance of prescription opioids, they also offer a compelling case study to understand the market for prescriptions more generally. Understanding the market for prescriptions is difficult, however, in part because it accommodates three types of agents: patients, physicians, and pharmaceutical firms. These three agents engage with one another in order to produce a prescription, but crucially each of them has private information. In this context, physicians must act as the intermediary between patient demand for prescription opioids and the pharmaceutical industry. This role makes them uniquely important for understanding the market for prescriptions, and the downstream consequences on patients. However, as an intermediary, their behaviour is influenced by both demand and supply side forces.

In this paper, I disentangle the supply behaviour of doctors from the demand responses of patients. I first study the causal effect of pharmaceutical promotion to physicians on prescriptions written for opioids. To the extent that these promotions serve as either information transfer from firms to physicians, or simply persuasion, I argue it is not obvious that physicians will necessarily respond by increasing prescription of the promoted drug. I then investigate the extent to which this additional prescribing has downstream consequences on patient outcomes and whether these additional promotion-induced prescriptions contribute meaningfully to opioid overdose deaths.

To address these questions, I leverage the staggered introduction of Medicaid expansion in the United States between 2013 and 2016. This state-level policy extended public health insurance to prime-age adults earning within 138% of the federal poverty line. A key feature of this policy that I exploit is the presence of a period following a state's announcement of expansion where the policy roll-out is perfectly anticipated but has yet to occur. I argue that during this period

pharmaceutical firms are able to anticipate a growth in the market for their products and show that they react strategically by increasing their promotions to physicians. Leaning on evidence from Alpert et al. (2015) and Alpert (2016), I argue that patient demand remains unchanged during the period prior to implementation of the policy. I focus the analysis on this announcement period, and identify reduced form effects on promotions, prescriptions and opioid deaths using difference-in-differences strategy.

Combining a number of rich datasets, I link the anticipation of Medicaid expansion to a host of outcomes. Data on pharmaceutical promotion comes from Open Payments, a national disclosure program hosting data on the universe of promotional transactions between pharmaceutical firms and physicians. Data on prescription opioid sales comes from the Drug Enforcement Agency's (DEA) Automation of Reports and Consolidated Orders System (ACROS). Data on mortality (both opioid-related, and other causes) comes from the National Vital Statistics' Underlying Cause of Death data. I combine these three primary datasets, along with a number of supporting datasets detailed below, with information collected on the timing of the announcement and implementation of Medicaid expansion.

My paper presents three main findings: (i) pharmaceutical firms increase promotions to physicians in anticipation of local Medicaid expansion, (ii) physicians, in turn, increase prescribing for opioids, and (iii) opioid overdose deaths increased, but this effect was not persistent.

First, in response to the announcement of Medicaid expansion, I find that pharmaceutical firms strategically responded in advance of the policy roll-out with promotional activity to physicians increasing broadly for all prescription drugs. These results are true both at the intensive and extensive margins: firms increase promotions to a growing network of physicians, as well as the value of these promotional visits. I show these effects were more pronounced for the promotion of opioids specifically, with a 47% increase in the value of promotions made following the announcement, but prior to the implementation of Medicaid expansion.[1] I argue that pharmaceutical firms increase these promotions in order to build networks with physicians in markets that are most likely to be affected by the policy (and thus offer the largest profit opportunities). Indeed, the effects on promotional activity are driven entirely by counties with larger than median Medicaid-eligible population.[2] I argue that these changes in promotional behaviour are uncorrelated with patient demand side responses, but might affect physician prescribing behaviour.

[1]The fact that opioid producing firms appear to respond more strongly to the announcement could be an indication of the ability for those firms to quickly mobilize the necessary promotional funds.

[2]Medicaid eligibility under the expanded policy was extended to all adults under the age of 65 who earned less than 138% of the federal poverty line.

Second, in order to determine whether physician behaviour is affected by this change in promotional behaviour, I investigate the effects on opioid prescriptions. I find that sales of prescription opioids during this announcement period increased. Because patient demand is assumed to be unchanged in the absence of insurance roll-out, this is suggestive of a promotion-induced change in prescribing behaviour to existing patients, rather than an underlying change in disease burden or drug-seeking behaviour.

Finally, I discuss the consequences of this promotional behaviour on patient outcomes. Given the dual role of this pharmaceutical promotion as both informative and persuasive, the effect of these additional prescriptions on opioid deaths is not necessarily obvious. To the extent that pharmaceutical firms are simply providing physicians (who may have limited time or attention to devote to changing treatment protocols and clinical guidelines) with additional information about the appropriate use of opioids, we might expect that these promotions serve to reduce opioid-overdose deaths. I find, however, that following the announcement of expansion, opioid deaths in the subsequent 6 months increased modestly. This effect was not persistent, with opioid deaths returning to pre-announcement levels within one year. Likely, this is in part due to the protective effects of the Medicaid expansion itself, which included coverage for both prescription drugs as well as substance and opioid abuse treatment. I argue that because during this period physicians are nudged into prescribing by the initial pharmaceutical promotional response, these results represent the down-stream effects of a marginal prescription. I provide evidence that these results do not appear to be driven by changes in underlying mortality trends, using cancer deaths as a placebo which is unlikely to be affected by the change in access to medical care or the promotional behaviour of pharmaceutical firms in the short term.

This work contributes first to the growing literature on the origins of the opioid epidemic and the relative importance of supply-side factors (Alpert et al., 2019, 2018; Schnell and Currie, 2018; Schnell, 2017; Powell et al., 2020; Arteaga and Barone, 2021; Finkelstein et al., 2018; Evans et al., 2019; Eichmeyer and Zhang, 2020; Buchmueller and Carey, 2018; Buchmueller et al., 2019). I build on Alpert et al. (2019) and Arteaga and Barone (2021), who investigate the long-term consequences of Purdue Pharma's extensive marketing following the launch of OxyContin in 1996. I argue that unlike these earlier promotional campaigns, which were tied explicitly to the ease of physician prescribing (as in Alpert et al. (2019)) and the potential market demand (as in Arteaga and Barone (2021)), the announcement of Medicaid expansion serves to hold constant demand side responses in the short term. I additionally focus on a later stage of the opioid epidemic, during which time physicians had increasingly improved clinical knowledge about the

risks associated with opioid prescribing (Gray et al., 2021). Drawing on variation induced by Medicaid expansion legislation, I am able to speak to the unintended consequences of this policy roll out on opioid deaths, following Averett et al. (2019); Sharp et al. (2018); Wettstein (2019).

This paper also contributes to the broader literature on the market for pharmaceutical prescriptions (Rizzo, 1999; Alpert et al., 2015; Mizik and Jacobson, 2004; Ching and Ishihara, 2012; Carey et al., 2021; Spurling et al., 2010). To the best of my knowledge, it is the first to identify evidence of strategic pharmaceutical promotion in advance of a policy roll-out. The rich detail of promotional data and policy context allow me to address concerns about selection of payments to physicians. Carey et al. (2021) similarly investigate the impact of pharmaceutical promotion on a subset of physicians serving Medicare Part D patients. In an event-study approach, they find that following a promotional payment, physicians increase both the number and duration of prescriptions. Notably, however, it is unclear in this context why pharmaceutical firms change their promotional behaviour to these physicians to begin with. Finally, with increasing awareness that the aggressive marketing of Purdue Pharma played an important role in the opioid crisis (Quinones, 2015), the impacts of these promotions on physicians have likely changed in recent years, and thus my estimates better reflect the changing influence of pharmaceutical promotion on physicians.

The remainder of this paper is organized as follows. Section 2 provides background on the opioid epidemic and Medicaid expansion. Section 4 explains my identification strategy, and section 3 describes the data used. Section 5 provides results and robustness, and section 7 concludes.

2 Background

2.1 The Origins of the Opioid Epidemic

Since 1999, the U.S has seen a startling growth in the number of opioid-related deaths. Throughout this period, the epidemic has evolved across three main phases, not only moving from predominantly rural to urban areas, but perhaps more importantly transitioning from natural and semi-synthetic opioids, such as OxyContin and Oxycodone (and the illegal heroin), to Fentanyl and other synthetics. There have been a number of hypotheses about the underlying cause of the epidemic, alternately identifying the importance of either (patient) demand or (physician) supply forces.

One prominent demand-side argument is that of Case and Deaton (2015, 2017), who argue

that opioid deaths together with other conditions indicative of "despair" (such as alcoholism and suicidality) were triggered largely by prolonged economic decline and the feeling of falling behind. While this argument is consistent with the rural origins of the epidemic, Ruhm (2018) notes that these economic effects are overshadowed by the availability and use of drugs, suggesting an increased role of supply-side forces. Alpert et al. (2019) similarly argue that wide-spread availability of opioids was accelerated following the introduction of OxyContin into a local market. Specifically focusing on states without limits on prescriptions, Purdue Pharma (the makers of OxyContin) engaged in aggressive promotional tactics to physicians following the launch of the drug. These promotional changes were coupled with an increasing recognition on the part of the medical community of the importance of pain in the treatment of patients (Tompkins et al., 2017). Alpert et al. (2019) argue that these promotional activities can explain a substantial share of subsequent opioid death growth over the period.[3]

The resultant growth in deaths in the early 2000s caused increased scrutiny from policy-makers, who implemented a number of demand and supply side policies to curb opioid abuse. Supply side policies frequently targeted physician prescribing behaviour, which by some estimates explain up to 30% of the variation in opioid overdose deaths (Finkelstein et al., 2019). Among these are Prescription Drug Monitoring Programs (PDMPs), which are designed to increase the information available to physicians about their patient's prescription history in order to prevent abuse (Meara et al., 2016; Buchmueller and Carey, 2018; Bao et al., 2016; Nguyen et al., 2019). Pain Management Clinic Laws target supply by imposing prescribing restrictions on pain management clinics, with the goal of reducing high-volume prescribing (Ziedan and Kaestner, 2020; Chang et al., 2016). Similarly, some states have passed laws imposing explicit limits on the length of initial prescriptions. Unlike PDMPs and PCLs, these laws appear to act against their underlying intent and actually increase the over number opioids prescribed (Sacks et al., 2021). Finally, harm reduction policies such as Naloxone Access Laws (NAL) and Good Samaritan Laws (SAL) are designed to explicitly reduce fatal overdoses and misuse by providing medication to reverse overdoses and providing legal immunity to anyone assisting in an overdose (Rees et al., 2019).[4] While the research on the impacts of all of these policies is mixed, and varies substantially based on the specific context, policies designed to restrict use and abuse are largely effective.

[3] Arteaga and Barone (2021) exploit an alternate feature of Purdue's marketing strategy, which explicitly targeted high-cancer incidence regions. In areas with this high underlying demand for opioids and high growth potential, they find promotion of opioids to physicians caused a large increase in both opioid prescriptions and deaths.

[4] Although other work by Doleac and Mukherjee (2019) suggest the potential for Naloxone to introduce moral-hazard incentives.

Understanding the specific mechanisms behind these individual programs, however, remains difficult. In part, this is because while the administrative burden of a program may fall entirely on one side of this market (either the patient demand or physician supply), it does not necessarily account for general equilibrium responses. In the case of PDMPs, for example the administrative burden falls on physicians, who must consult patient directories to verify that there are no existing prescriptions made for opioids prior to dispensing a new script. However, these policies are similarly salient for patients, who might adjust drug-seeking behaviour in light of the increased oversight by physicians (Ali et al., 2017).

2.2 Opioids and the Role of Insurance Coverage

While the scientific literature on the opioid crisis (both in economics and in other disciplines) is vast, relatively little attention has been given to the role of insurance. This is particularly important as its consequences to overdose deaths and health are not immediately obvious.

Evidence has shown that increased access to health insurance coverage improves health care utilization. Currie and Gruber (1996), Finkelstein et al. (2012), Dafny and Gruber (2005), and Furzer et al. (2021) among others, find access to public health insurance significantly increases health care utilization and lowers out-of-pocket medical expenditures and medical debt. Similar to private insurance, Medicaid also covers most categories of major medical intervention, including pharmacological therapy. Indeed, Ghosh et al. (2017) find that in the first 15 months following expansion, prescription drug use increased 19% in states which expanded Medicaid, compared to those that did not. Interestingly, they do not observe any effect of the Medicaid expansion on private insurance or Medicare prescription utilization, suggesting a lack of crowd out of private prescription drug use, and a potential net growth in demand for prescription drugs.

Investigations into the impact of Medicaid expansions on opioid deaths more specifically do not yield such conclusive results. In a state-level difference-in-difference (and event study) framework, Averett et al. (2019) find no detectable effect of Medicaid expansion on opioid deaths, arguing that perhaps the unit of analysis is insufficiently detailed to disentangle potentially opposing treatment effects. On the other hand, using detailed enrollment and reimbursement data Sharp et al. (2018) find that although the expansion enrolled individuals no more likely to be prescribed opioids, it did increase uptake of two medically assisted treatments for opioid dependence/abuse. Finally, focusing specifically on young adults, Wettstein (2019) finds that increasing coverage leads to large decreases in mortality for that age group.

Perhaps one of the drivers of these inconclusive or mixed effects on opioid deaths, is the compelling evidence that treatment of opioid use disorder (OUD) is increasing among those newly covered by Medicaid expansion. Meinhofer and Witman (2018) find that admission to medically assisted treatment facilities increased 113% by Medicaid beneficiaries, without crowding out admissions from those with other insurance types. This is just one example of policy intentionally designed to reduce and manage opioid addiction and use disorders. A comprehensive review of the broad range of public health policy targeting the opioid epidemic is available in Maclean et al. (2020). Broadly, however these policies are developed to address either the demand for and use of opioids, or their supply by physicians.

Beyond this, evidence shows that the coverage effects may spillover onto unintended subgroups. Powell et al. (2020) find that increase coverage due to Medicare Part D, which provides public insurance for those 65 years and older, increased mortality and substance abuse age groups for those in younger age-groups who were not eligible for the coverage, with a 10% increase in opioid supply lead to a 7% increase in opioid deaths among the ineligible. They suggest that the underlying mechanism driving these effects is diversion; older individuals are prescribed more (unnecessary) opioids under the increased coverage, which are diverted into the illegal market.

2.3 Pharmaceutical Promotion

Prescription drug spending in the U.S has been the fastest growing component of national health expenditures in recent years (National Center for Health Statistics, 2017). Keeping pace, pharmaceutical promotional spending has also grown substantially from $11.4 billion in 1996 (Donohue et al., 2007) to $29.3 billion in 2011 (Datta and Dave, 2017) and is concentrated among patented drugs across two different promotional markets.[5] The first of these is the consumer market, with Direct-to-Consumer advertising (DTCA) through print and media.[6] The majority of promotional spending, however, is Direct-to-Physician promotion (DTPP).[7] These physician promotions frequently involve personalized visits by the sales representative to the physicians' office with the explicit goal of encouraging them to increase prescribing of the promoted drug. Sales representatives can make offers of anything from samples of the drug in question, informa-

[5]The fluctuations in industry promotional spending are, in fact, heavily influenced by the patent expiration of major drugs (Datta and Dave, 2017)

[6]The United States and New Zealand are currently the only two countries which allow direct-to-consumer advertising that includes product claims (Ventola, 2011).

[7]By some estimates, pharmaceutical promotional budgets allocate up to 80% specifically towards targeting physicians(Datta and Dave, 2017).

tional brochures, paid meals during discussions, or travel and consulting (or speaking) fees paid directly to the physician.

One likely reason for the substantially higher share of direct-to-physician promotion is the nature of the relationship between the physician and their patients, and the underlying information asymmetry between them first alluded to by Arrow (1963).[8] Given the nature of the information asymmetry between doctors and their patients, and the potential for additional hidden actions to be taken in response to pharmaceutical incentives, a growing literature has attempted to assess the impact of this promotional spending on physicians' prescribing behaviours.[9] Public concern centers around whether this interaction may compromise a physicians' prescribing decision towards a more expensive alternative. Recent evidence has shown that this promotion could induce artificial product differentiation among otherwise similar drugs (Ching and Ishihara, 2012). Previous work has clearly established that increased interaction with pharmaceutical representatives is associated with a higher prescribing volume and lower price sensitivity on the part of the physician (Mizik and Jacobson, 2004; Rizzo, 1999; Spurling et al., 2010; Carey et al., 2021).[10] Importantly, Agha and Zeltzer (2019) demonstrate estimates of the impact of promotion on prescribing are likely a lower bound of the true effect. This is, in part, due to the important (although indirect) role of spillovers across the peer network of the physician initially promoted to.

2.4 Medicaid Expansion

The Affordable Care Act (ACA) of 2010 introduced numerous provisions to address the widespread need in the United States for health care reform. Among these provisions, three emerge as being pivotal to the Act. The first was the public insurance expansions, which are state decisions on whether or not to take up Medicaid expansions. The Individual Mandate was the second key provision and created tax penalties for all U.S residents who were not covered by some form of health insurance (and was applied federally). Finally, the ACA overhauled private health insurance market regulations by removing penalties for pre-existing conditions, banning medical underwriting and eliminating annual and lifetime benefit limits (Frean et al., 2017). These three provisions have substantially reduced rates of uninsurance in the United States (Frean et al.

[8] McGuire (2000) offers an excellent overview of the physician agency literature.

[9] One such example is Inderst and Ottaviani (2012), who develop a model of physician agency and demonstrate that an advisor will recommend a product for which he has been paid a commission if the expected payoff is larger than the expected cost to doing so, arguing that a larger commission would satisfy this condition more frequently. They further suggest that commissions would be higher the less the physician is concerned with the accuracy or suitability of their recommendation.

[10] An excellent meta-analysis is provided in Kremer et al. (2008).

(2017), Cohen and Martinez (2014), Sommers et al. (2015)) and evidence suggests that they have actively increased both public and private coverage rates (Kaestner et al. (2017), Courtemanche et al. (2016)). While the focus of this paper is the Medicaid expansion provision of the ACA, I also discuss, where appropriate, the potential implications of the other two provisions.

Medicaid expansion provisions provided health insurance to low-income adults without children who were not disabled or elderly (Moffitt, 2016, p.24). Coverage was extended to adults under the age of 65 earning 138% of the federal poverty line (FPL). Crucially, this expansion was not designed to significantly effect state budgets at the outset and included a higher federal match on fees for newly eligible adults (100% until 2016, phasing down to 90% in 2020 and onward (ACA, 2010). However, a 2012 Supreme Court ruling found Medicaid expansion unconstitutionally coercive, in essence making expansion voluntary at the state level (Musumeci, 2012). It is important to note that, as a result of this Supreme Court ruling, there is significant variation in the timing of expansion across those states which approved the reform, both in when the required bill was signed by state legislature and in the effective date of expansion. While states may have signed into law the provisions necessary for Medicaid expansion, since initial funding for the program came solely from the Federal government, it was not until January 1, 2014 that those who were eligible in the earliest expansion states could enroll for coverage. Those states that legislated expansion after this deadline faced similar bureaucratic lags prior to coverage.[11] I refer to this period, between the legislation of expansion and the effective expansion[12] as the anticipatory, or announcement period. A description of states which chose to expand Medicaid, and the timing of expansion is given in Table A.1.

A crucial component of Medicaid is it's in role insuring both health care services and pharmaceutical treatment. While there is substantial variation across states, Medicaid is designed to provide beneficiaries with a low-cost prescription drug coverage. Federal limits on co-pays range between $4 and $8 depending on the drug type, although not all states impose these co-pays, and some allow for exemptions for specific beneficiary groups.[13]

As of January 1, 2017, 31 states and Washington D.C have elected to expand Medicaid, and research shows an increase in the number of individuals enrolled in the program of over 26% compared to 2013 levels (Ghosh et al., 2017). Frean et al. (2017) find that approximately 60% of ACA coverage gains were due to Medicaid expansions alone. In the remaining states, consumers are not eligible for expanded Medicaid coverage, however, have access to federally regulated

[11] On average, states experience a 7.5-month gap in between legislation and expansion of coverage.
[12] The effective expansion date is the first day of federal funding for expanded Medicaid program.
[13] https://www.kff.org/medicaid/issue-brief/understanding-the-medicaid-prescription-drug-rebate-program/

Health Insurance Marketplaces. Despite this, states which chose not to expand Medicaid saw their enrollment grow by approximately 7%. This has widely been interpreted as a "welcome mat" effect (Moffitt, 2016), or the "woodwork" effect (Frean et al., 2017), whereby the law may have increased awareness about the program among adults who were previously eligible but not enrolled.[14] Importantly, this growth in Medicaid enrollment has not been shown to crowd out private insurance enrollments (Ghosh et al. (2017), Frean et al. (2017)). The demonstrated lack of crowd out of other insurance types reinforces the idea of a growth in the consumer market which could be accessed by a pharmaceutical firm.

3 Data

To understand the role of health care reform on the opioid epidemic, and separate the demand and supply components, I use three main datasets. These data identify pharmaceutical promotion, prescription opioid distribution, and county level opioid deaths, which I describe in detail below. I supplement my analysis with a number of supporting data sets, providing information on Medicaid announcement and expansion timing, county-level characteristics, as well as the drug and policy environment.

3.1 Pharmaceutical Promotion

Pharmaceutical promotion data is obtained from the Centers for Medicare and Medicaid Services' (CMS) Open Payments Data. This data was first collected under the Physician Payment Sunshine Act (2010) and was made publicly available through a national program which legally mandates that manufacturers disclose payments and other transfers of value to physicians. The reporting data is rich, indicating the type of payment provided,[15] the full name of the physician receiving the payment, their primary specialty, as well as location of primary practice, the man-

[14] I argue that these woodwork effects are not a cause for concern in my setting for two reasons. Firstly, as individuals are myopic in their consumption of healthcare goods (Einav et al., 2015), it is unlikely that this spillover occurs in anticipation of policy roll-out. Second, to the extent, that it does, this would bias my estimates towards 0.

[15] Payments can fall into one of 15 broad categories: consulting fees, compensation for services other than consulting (including serving as a faculty or as a speaker at an event other than a continuing education program), honoraria, gift, entertainment, food and beverage, travel and lodging, education, research, charitable contributions, royalty or license, current or prospective ownership or investment interest, compensation for serving as a faculty or as a speaker for an unaccredited and non-certified (or accredited or certified) continuing education program, grant, or space rental or facility fees.

ufacturer as well as the specific product being promoted. Importantly, any payment or transfer of value must legally be reported, even in the event that, for example, the physician requests the money be transferred to charity or a to a family member.[16] The data spans August 2013 (the first available period of reporting) to December 2016, during which time there were a total of over 26.5 million observations.[17]

Because my main outcome of interest is county-level mortality, I aggregate the promotional data to the county-month level, measuring the number of individual physicians visited by an opioid-manufacturer in any given county-month, as well as the total number of visits and the total value of these visits (in dollars). In doing so, I am able to measure both the intensive-margin response by firms (for example, a change in the value of promotions being made), as well as the extensive-margin (for example, an increase in the number of physicians being contacted). These various margins of response allow for a more comprehensive understanding of the strategic promotional behaviour of pharmaceutical firms in response to, or in anticipation of, policy changes. Finally, in order to identify whether the drug promoted is an opioid (since initial data releases do not include classifications of drug types), I merge the promotions data with the CMS Drug Category Lists, which contains a list of all generic and branded opioids. This allows me to identify whether a visit was made to specifically promote an opioid product.

Table A.2 provides information on the top 10 promoting firms (by promotional dollar value spent) in this data, the value of their promotions, and their most commonly promoted (brand-name) drug and its common use. Perhaps unsurprisingly, the most commonly promoted medications are used to treat some of the most common physical ailments suffered in the United States. I also provide details for the highest value opioid promoting firm, Purdue Pharma's promotion of OxyContin. Notably, OxyContin does not appear to be the most frequently promoted opioid, as evidenced in Table A.3, suggesting that individual visits for OxyContin are more lucrative for physicians than for more commonly promoted opioids.

[16] Transfers under $10 in value do not need to be reported, unless the annual total of these transfers exceeds $100. Any ownership or investment interests held by a physician's immediate family members must also be disclosed. For additional information see https://www.cms.gov/OpenPayments/About/Open-Payments-Data-in-Context

[17] This can be seen as a lower-bound on the number of promotional visits/reimbursements made, as some reports include a grouping of multiple payments. Indeed, individual physicians frequently have multiple observations in the same day of the data, frequently representing promotional relationships with multiple firms.

3.2 Opioid Retail Sales

The second main component of my data are measures of opioids retail sales. This data comes from the Drug Enforcement Agency's (DEA) Automation of Reports and Consolidated Orders System (ACROS) and was provided to the Washington Post following a court order.[18] Unlike the publicly available ACROS reports, which provide quarterly aggregates for the 3-digit zip code level, the Washington Post data has more granular detail in both time and geographic dimensions. These data provide information on all shipments of opioids from manufacturers and distributors to pharmacies and practitioners between 2006 and 2014, during which time there were over 500 million transactions. I argue that this is a reasonable proxy for the volume of prescriptions written by physicians in a region. I use the county-month level aggregates, which consists of data on the dosage-equivalent number of Oxycodone and Hydrocodone pills sold, as well as the number of shipments to retailers and practitioners. The data focus on these to particular opioid types as they make up three quarters of all shipments.

3.3 Opioid-Related Mortality

The final main component of my data measures publicly available county-month level mortality from the National Vital Statistics Systems' (NVSS) Multiple Cause of Death data from 2010 to 2016. These data capture all deaths with at least one underlying cause attributed to (any) opioids.[19] I follow coding convention used by the Center for Disease Control (CDC) and the broader literature[20], which designate opioid-related deaths using ICD-10 codes X40-X44, X60-X64, X85, Y10-Y14. This broad categorization serves to additionally alleviate concerns over missing opioid-related designations for drug-related deaths raised in Ruhm (2018). Figure 1 demonstrates the large geographic variation in opioid deaths which has been growing over time. I present deaths due to opioids for 1999, for comparison with earlier work in this area, as well as for 2010 and 2016, the start and end years of my sample.

To further understand whether these underlying dynamics are truly driven in part by the promotional relationship and changes in insurance status, I include two additional placebo causes of death in the analysis - cancer and external causes of death. Because of the typically slow disease

[18] For more information: https://www.washingtonpost.com/graphics/2019/investigations/dea-pain-pill-database/

[19] Because my data relies on publicly available mortality data, it unfortunately suffers from small-sample suppression. In county-month bins which experienced fewer than 10 opioid related deaths, the NVSS suppresses the true count. I conservatively impose that these suppressed bins are set to 0 in my sample.

[20] See for example Alpert et al. (2019)

progression of cancer, I expect that mortality would be significantly less responsive to insurance coverage in the short and medium term. Similarly, the relatively more "random" nature of external causes[21], will allow me to ensure that Medicaid expansion is not correlated with other factors which may change a county's ability to provide a constant quality of care.

3.4 Medicaid Timing and Controls

Data on the timing of announcement and expansion of Medicaid come from two sources (and are outlined in detail in Table A.1. Timing of the legislation and announcement of expansion was hand collected.[22] Data on the timing of Medicaid expansion implementation comes from the Kaiser Family Foundation's data on the status of state Medicaid expansion decisions.[23] Figure 2 plots the number of states that have announced medicaid expansion (the red dashed line) as well as the number of states that have implemented the policy (the blue solid line) over time. The two lines are not perfectly parallel because of a unique feature of the Supreme Court mandate, after which implantation for the earliest round of adopters was scheduled to begin on January 1, 2014. All states which had legislated expansion prior to that period all received expanded coverage at the same time.

A number of supporting datasets are also necessary to complete the analysis. Data on annual county population comes from the Census Bureau's Annual Estimates of the Resident Population for Counties in the United States between 2006 and 2016. County level poverty estimates come from the Census Bureau's Small Area Income and Poverty Estimates. Unemployment measures are taken from the Bureau of Labor Statistics. Data on state-level prescription drug monitoring program timing and intensity come from Horwitz et al. (2018).[24] Finally, data on insurance coverage rates comes from the Census Bureau's Small Area Health Insurance Estimates using the American Community Survey.[25]

[21] These external causes of death are categorized into methods such as suffocation, drowning, fire/heat, motor-vehicle accidents, firearms, cuts/piercings, and other similar types of causes not driven by illness.

[22] Source material for this data is available from the author upon request.

[23] Available at https://www.kff.org/medicaid/issue-brief/status-of-state-medicaid-expansion-decisions-interactive-map/

[24] I use the Modern system Operation Date provided in Horwitz et al. (2018) as the date of PDMP implementation, which represents the date which any authorized user is able to access and query the database.

[25] https://www.census.gov/data/datasets/time-series/demo/sahie/estimates-acs.html

4 Empirical Strategy

In order to understand the specific role of physician prescriptions in the opioid epidemic, this paper leverages the staggered introduction of Medicaid expansion across states. To mitigate the effect of patient response, my analysis differs from the conventional two-way fixed effect (TWFE) set-up by focusing specifically on the period during which this expansion is anticipated.

I argue that explicitly accounting for this anticipation is crucial disentangling the two sides of the market for opioids. I support this argument by taking first the naive TWFE set-up without the anticipatory period.

$$Y_{cst} = \alpha + \beta Implement_{st} + \gamma X_{cst} + S_s + T_t + \epsilon_{cst} \tag{1}$$

Equation 1 estimates the average effect of the implementation Medicaid expansion, exploiting across-state variation in the timing of the expansions. $Implement_{st}$ takes the value of one in each period t following the implementation of Medicaid expansion. The coefficient of interest β, thus, captures the effect of state s expanding Medicaid at time t. X_{cst} is a vector of time-varying county characteristics, such as population, unemployment, and poverty rates. Despite these controls, there is nevertheless the possibility of time-varying state policies which may be correlated with the outcome of interest. Additional specifications attempt to control for this directly by including measures such as timing of Medical Marijuana Laws[26], and mandatory Prescription Drug Monitoring Program legislation. These will capture state initiatives to combat the opioid epidemic. Further, geographic variation in income and poverty within states implies that different counties will have different population sizes eligible for the expansion of Medicaid. As a result, we may expect that these effects also vary within state, and more specifically based on the proportion of the population that falls below the Federal Poverty Line (FPL), which acts as a reasonable proxy for the proportion eligible. To capture this variation, I also estimate Equation 1 for the top and bottom deciles of poverty counties.

This difference-in-differences estimation strategy, however, is only valid under the assumption of parallel trends in the treatment and control groups, and further masks potential heterogeneous effects across time. Given the large body of evidence demonstrating the persuasive role of pharmaceutical promotional, we may be concerned that this treatment effect captures both a

[26]This may be particularly relevant given evidence that marijuana and opioids can act as substitutes in pain relief (Powell et al., 2018; Shover et al., 2019; McMichael et al., 2020; Bachhuber et al., 2014; Anderson and Rees, 2021).

demand-side response on the part of newly insured individuals, as well as a supply-side response of physicians or distributors. This may be particularly problematic if, as literature suggests, physicians' prescribing practices are influenced by the promotional visits of pharmaceutical sales representatives (Alpert et al., 2019), and these representatives increase these visits strategically in advance of the expansion. In this case, the parallel trends assumption necessary for the validity of the difference-in-differences estimates may be violated.

To understand the extent to which this anticipatory response is occurring, Equation 2 proposes an alternative specification, which attempts to naively capture strategic behaviour on the part of pharmaceutical firms. To do this, I estimate the time-varying effect of the announcement (rather than implementation) of Medicaid expansion. In this specification, $Announce_{st}$ takes the value of 1 for all periods t following the legislation and announcement of Medicaid Expansion. Following Equation 1, I impose that the only treatment occurring in a state is the announcement of expansion, without flexibly accounting for the subsequent potential response following implementation.

$$Y_{cst} = \alpha + \delta Announce_{st} + \gamma X_{cst} + S_s + T_t + \epsilon_{cst} \tag{2}$$

Finally, in Equation 3, I flexibly incorporate both periods of the policy, arguing that this allows me to disentangle supply and demand side responses. This specification exploits the timing in between the announcement of expansion and the de-facto legislation, $Announce_{st}(1 - Implement_{st})$. Thus the coefficient δ measures the effect following the legislation and announcement of Medicaid expansion, but in advance of any actual changes in coverage. The coefficient β will capture the effects of the implementation itself.[27]

$$Y_{cst} = \alpha + \delta Announce_{st}(1 - Implement_{st}) + \beta Implement_{st} + \gamma X_{cst} + S_s + T_t + \epsilon_{cst} \tag{3}$$

I argue that the coefficient δ in Equation 3 captures the effect of a supply-side response to the announcement of Medicaid expansion in advance of policy roll out. Underlying this argument is the assumption that during this period patient demand and disease burden remain unchanged. I assume that in advance of any policy, patients in expansion and non-expansion

[27] During this period, we might expect both patients, and physicians and pharmaceutical firms to respond to the policy. Identifying the response of physicians alone, thus comes through δ.

states experience no differential changes to their underlying insurance coverage or health care needs. To support this assumption, I offer a number of arguments, supported by evidence in the literature on consumer responses to insurance. First, I argue that demand-side anticipation is not a cause for concern. That is, we should not expect those eligible for the policy to begin consumption smoothing (and purchasing necessary prescriptions) in advance of coverage. In fact, evidence suggests that in response to reductions in future price as a result of increased insurance coverage, patients reduce their contemporaneous use of chronic drugs. In a study of Medicaid-eligible adults, Alpert (2016) finds that announcement of eligibility increased coverage caused eligible patients to defer their use of treatment for chronic conditions until coverage was received. These patients, however, did not exhibit any such patterns in the use of acute medication (used in the treatment of illnesses requiring immediate attention, such as antibiotics).

That this lack of consumption smoothing on the part of patients can result from well-documented myopia in healthcare decisions. Evidence from a number of different insurance expansion experiments (including notably the Oregon Health Insurance Experiment) find that both public and private insurance holders spend more in the final months of an insurance enrollment year (Einav et al., 2015; Aron-Dine et al., 2015; Lin and Sacks, 2019). Beyond this, however, I argue that the eligibility requirements for this expanded Medicaid target the most financially constrained subset of the population. At the start of 2013, the federal poverty line for a household of one set income thresholds at $11,490.[28] Given these severe constraints, I argue it is unlikely that the Medicaid eligible population was able to begin out-of-pocket consumption prior to coverage.

The above described (lack of) patient behaviour also supports the assumption that pharmaceutical firms are not likely to attempt to induce changes in demand directly by increasing Direct-to-Consumer promotion. This type of spending typically makes up a small portion of pharmaceutical promotional budgets (Datta and Dave, 2017), but may nevertheless cause concern if it occurs. Because patients are myopic, however, I argue that the incentives for pharmaceutical firms to spend finite promotional resources are lower than directing them towards physicians. To this end, in an analysis of direct-to-consumer promotion following the announcement of Medicare Part D expansion, Alpert et al. (2015) finds no evidence of anticipatory responses by pharmaceutical firms in this dimension.

One final concern, however, may be that because of the nature of the expansions, as well as the "individual mandate" expansions of the ACA, changes in Medicaid enrollment may also

[28] https://aspe.hhs.gov/2013-poverty-guidelines

be due to those who were previously eligible for Medicaid prior to the expansion; Frean et al. (2017) identify this as the "woodworking" effect. To the extent that this is occurring, I expect it to do so across both treatment and control states.[29] For these reasons, I argue the coefficients of interest in Equation 3 measure changes in pharmaceutical promotional behaviour in response to the announcement of future increased coverage, and subsequent response following the extension of this coverage.

To next determine whether this change in promotional activity can be linked to a change in physician prescribing, I estimate Equation 3, where the outcome of interest becomes the opioid pill-dosage equivalent sold to retail pharmacies and practitioners in a county-month. I argue that this is reduced-form evidence of a down-stream effect of pharmaceutical promotion on physician prescribing patterns.[30]

I use specification Equation 3 in a reduced-form way to first understand the effects on pharmaceutical promotion of opioids, as well as other drugs more broadly. To determine whether these promotions affect the prescribing behaviour of physicians, I next look at aggregate county-level opioid retail sales at pharmacies and legal providers. Finally, to understand the potential downstream impacts of pharmaceutical promotion on opioid deaths, I look at the effect of Medicaid announcement and implementation on opioid deaths per 100,000 in the population. In all specifications, standard errors are clustered at the state level and population weights are applied.

4.1 Event Study

To understand the heterogeneous effects of this policy announcement over time, Equation 4 estimates an event study specification. Letting $Announce_s$ be month that Medicaid expansion was announced in state s, and $D^m_{s,t} = \mathbb{1}\{m = t - Announce_s\}$ indicates treatment of state s in the m periods relative to announcement time t. The event study equation can thus be expressed as follows.

[29] I note however, that there is the possibility that this learning happens disproportionately following the announcement of expansion in treated states. However, I argue that, demand side effects are no doubt tempered by the bureaucratic wait times to actually receive coverage. Indeed, if wait times for the Children's Health Insurance Program (administered through Medicaid), are any indication, expansion states had a wait time roughly twice as long as non-expansion states, averaging approximately 4.5 months.

[30] Current data limitations prevent me from estimating this directly in an instrumental-variables approach. Data overlap in timing between the pharmaceutical promotions and prescriptions prevent an implementation of instrumental variables. Future iteration of this work, will however incorporate longer time-frames of prescriptions data, and allow for a direct test of this hypothesis. This would allow for the announcement of expansion would act as an exogenous shock to promotional behaviour in the first stage, allowing for a causal estimation of the subsequent impact of these promotional behaviours on physician prescribing.

$$Y_{cst} = \alpha + \sum_{j=-p}^{-2} \beta_j D_{s,t}^m + \sum_{j=0}^{k} \beta_j D_{s,t}^m + S_s + T_t + \gamma X_{cst} + \epsilon_{cst} \tag{4}$$

The coefficients of interest in this specification are β_j, which estimate the within-state change in the outcome Y_{cst} in the j periods following treatment, relative to never-treated states. I omit the indicator for the period prior to the period of treatment following convention, and use this as the base period of comparison.

Following recent growing literature discussing the validity of two-way fixed effects estimates, I note that these β_j parameters estimate average treatment effects under a number of assumptions. The first requires parallel trends; that is the potential outcomes in the absence of treatment, between treated and never-treated groups are the same. This assumption would be violated if the announcement of Medicaid expansion was influenced by specific supply-side behaviour of opioid producers and physicians. I argue this is not unlikely the case given the scale of the Medicaid program (and its breadth of coverage), and particularly in light of the legislative process involved in mandating coverage. It is unlikely, therefore that the specific timing of announcements was influenced by supply-side responses. Empirical evidence provided below supports this assumption.

The second important assumption requires no anticipation of the treatment prior to initiation. In this specific context, I argue that if the treatment were defined as the de-facto implementation of Medicaid, this assumption would not be satisfied (and provide evidence of this below). As argued earlier, this results from the anticipatory response of pharmaceutical firms to the growth in potential market size and future profits. However, I argue that the announcement of this legislation, and in particular its specific timing is unanticipated by pharmaceutical firms and patients.

Finally, a third assumption underlying these estimates is homogeneous treatment effects. Sun and Abraham (2020) note that in order to obtain unbiased estimates of β_j, there must be homogeneity in the treatment effect across treated cohorts. In my context, this assumption may not necessarily hold, particularly if there are concerns that earlier expanding states had larger health-care needs, and higher underlying patient demand. To address this, I follow the adjustments suggested in Sun and Abraham (2020), using never treated units as a control group (rather than imposing comparisons between early and late treated states).[31]

[31] Estimates of the variance-based decomposition weights of TWFE difference-in-differences estimates proposed by Goodman-Bacon (2021) suggest that the results driven largely by comparisons between ever- and never-treated

I note that because there is substantial variation in the length of the period between announcement and expansion across states, these event-study estimates do not present a direct comparison to the TWFE difference-in-differences estimations described above. While, the event-study specification in Equation 4 include an indicator for periods following the implementation of Medicaid, the specification is not able to separately identify the response following announcement prior to implementation. In this respect, the TWFE estimates are complementary to the event study specifications.

5 Results

5.1 Pharmaceutical Promotion

I present TWFE estimates of Equation 1, Equation 2, and Equation 3 in Table 1 for measures of logged opioid promotional spending (columns 1 through 3) and logged average spending per visit (columns 4 through 6).

Columns (1) and (4) present the naive specification in Equation 1, reporting the effect of the expansion on logged total promotional spending (in a county month) and logged average transaction value.[32] In each of these specifications, the coefficient of interest on $Implement_{st}$, β, is negative and statistically significant, suggesting perhaps counter-intuitively that pharmaceutical firms *reduced* promotion along both the intensive and extensive margins, by reducing the dollar amounts transferred, and the number of visits and physicians, following the expansion of public health insurance.

I argue however, that this estimate is liked biased as a result of strategic behaviour on the part of pharmaceutical firms. More specifically, because the decision to expand is legislated by the state, firms are aware that the expansion will occur with certainty following the announcement and may begin promotion in anticipation of the expansion. This is further suggested by the results presented in columns (2) and (5), which present the results of the estimate the effect of the announcement that a state has legislated expansion from Equation 2. I find that in this case, the results are reversed, and the point estimate on the coefficient of interest switches signs. While these results are not consistently statistically significant, they suggest that firms are indeed behaving strategically, and begin their promotions to physicians in advance of expanded

units.

[32] I use logged outcome variables because of the left-skewed nature of the data. Nevertheless, results for outcome variables in levels are consistent, and available in Table A.4.

Medicaid coverage being available to their patients.

As a result of this break in the parallel-trends assumption, estimates of the Medicaid effect itself are biased downward. Finally, columns (3) and (6) present results for the interacted model, which able to capture the interim period between announcement and expansion, as well as the final expansion effect. I find that following the announcement of Medicaid legislation, pharmaceutical firms increase the value of promotions to a county in a given month by approximately 47%. This change, however, appears to be transitory, with no further detectable effect once Medicaid is expanded. This increase is similarly seen when investigating the effects on the average value of a promotional visits. While these results are slightly more muted than the total spending effects, they follow a similar pattern. This result provides insight into the strategic response of pharmaceutical firms, suggesting that the announcement of the policy caused changes at both the intensive and extensive margins of spending.

Table 2 turns next to an alternate strategic response of pharmaceutical firms, investigating the effects on the logged number of visits to physicians made by pharmaceutical sales representatives (in columns 1 through 3), and the logged number of individual physicians visited in a county-month. In measuring these responses, I am able to speak to trade-offs these firms make across the limited resources of sales representative time and budget. I note first that the naive specifications in columns 1, 2, 4, and 5 demonstrate a pattern consistent with the promotional spending outcomes. While the number of individual visits made by pharmaceutical sales representatives does not appear to respond to the announcement of Medicaid (in column 3), sales representatives appear instead to be reallocating their time across physicians in a dynamic way.

It is important to note that there is no reason to expect this phenomenon of strategic behaviour to occur exclusively among opioid-producing firms. Indeed, the market conditions which create incentives for opioid producers are likely to similarly affect manufacturers of other drug types (which are similarly covered by the insurance expansion. Table 3 presents the analogous results to Table 1, investigating the value of non-opioid related promotions.[33] Table 4 reports the point estimates for the logged number of non-opioid visits and logged physicians promoted to. The same general pattern of response is visible in non-opioid promotion as with opioid promotion. This is not surprising, as pharmaceutical coverage under Medicaid is not limited to opioids. However, the increase in the amount of promotional spending in a county-month is more muted for non-opioid drugs; in the period between legislation and expansion, $Announce_{st}(1-Implement_{st})$, counties saw an almost 27% increase in non-opioid promotion, substantially smaller than the ef-

[33]This includes promotions for any other non-opioid drug. I note that the data also includes information on promotions for medical devices, which I exclude from my analysis.

fects for opioids. This suggests that relative to the broader market, opioid-producing firms are perhaps better able to mobilize the necessary promotional funds and sales representatives to capitalize on strategic opportunities.

To further explore the dynamics of these behavioural responses, and to confirm that there are no further pre-trends in the data, Figure 3 plots the event study estimates of Equation 4. Figure 4 similarly plots these event study estimates, implementing the Sun and Abraham (2020) corrections. Two facts are immediately apparent; first, pharmaceutical firms appear to react quite quickly, with the effect peaking before the fifth month following the announcement of Medicaid expansion. This is consistent with the TWFE results, particularly in light of the fact that the average duration in between a state announcement and expansion of Medicaid is approximately 7.5 months. Second, while the point estimates of β_j in the pre-treatment period are not statistically significant (or jointly significant), I cannot definitively rule out the possibility that pharmaceutical firms anticipate even the announcement of Medicaid expansion. Between 1999 and 2018, the industry spent over $4.7 billion lobbying at the federal level alone (Wouters, 2020), thus it may not be unreasonable to expect that the industry has insider knowledge about upcoming legislation. [34] To the extent that this is occurring, it would bias my estimates towards zero.

5.2 Opioid Retail Sales

I next investigate the reduced form effects of this promotion (operating through the effect of the Medicaid expansion) on opioid prescriptions.[35] Table 5 presents these results in a format analogous to previous tables. The first three columns report the results for the outcome measuring the number of opioid shipments in a county month; this is a measure of the number of retailers and distributors making orders for OxyCodone and Hydrocodone, as well as the number of times in a county-month these retailers make these orders. Columns (4) through (6) present the results for doses per 1000 in the population. This dose metric is calculated by the DEA and is meant to be comparable across the various formulations and strengths ordered by these retailers. Finally columns (7) through (9) present the linear probability model results for any shipments in a given county-month. Largely, the results mirror those for pharmaceutical promotion, with a few

[34] Future iterations of this work will attempt to press further on these dynamics by estimating the effects using the date the expansion bills were proposed in legislature (rather than the date on which they passed).

[35] The current version of this draft is unable to estimate this directly in an instrumental variables framework as the publicly available data for promotions and prescriptions do not have common support over time.

exceptions. I again find that, if I impose (and assume) no anticipatory effects to the Medicaid expansion, as in columns (1), (4), and (7), the estimated effects of the expansion are small or negative and imprecisely estimated. I find large effects of announcement, which appear to be driven almost entirely by the period in between the announcement and the actual implementation. My results imply an increase of over 200 additional opioid orders in a county-month (an over 27% increase from the mean). I find similarly large effects on dose per 1000 people, the announcement was associated with an increase of 54 units per 1000 (an increase of 17% from the mean). Importantly, because I argue that patient demand over this period remains unchanged, I think of these responses as promotional spillovers onto existing patients (for whom coverage is not discontinuously changing) rather than for newly eligible individuals. The long-term effects, following the expansion ($Implement_{st}$) are similarly large, as may be expected, given that individuals gain access to the coverage which allows them to purchase prescriptions. They are, however, imprecisely estimated, perhaps given the data ends in 2014 and shortens the available post period window. Finally, I find no effects on the likelihood that a county has at least one opioid order in a month. This is perhaps unsurprising, given that this occurs with, on average, probability 1.

Figure 5 presents the event study estimates for the effect on doses per 1000 people. While noisier than the estimates for promotional effects, these results tell a similar story. The peak in additional doses, however, is after the 10th month following promotion. This is consistent with the longer-term effects suggested by the difference-in-differences result. I argue that this offers suggestive evidence of an increase in prescription opioids in a county following an increase in promotional visits, which I argue are exogenously induced by state-level Medicaid expansion policy. Crucially, I rely on the underlying assumption there is no actual change in insurance status or health burden, implying that this is a pure supply shock, induced by pharmaceutical promotion to physicians.

5.3 Deaths

The results until this point have demonstrated compelling evidence of a strategic pharmaceutical response to a policy announcement. I show that pharmaceutical firms increase their opioid specific promotional spending on physicians, and that this strategy appears to generate additional prescriptions for those who I argue are unaffected by the policy. However, these relationships are not necessarily malicious or detrimental. Indeed, Ching and Ishihara (2012) note the important role of pharmaceutical promotion in providing new clinical information to physicians with limited

time. This motivation is coupled with one of persuasion and the desire to induce the physician to prescribe the pharmaceutical firm's particular brand or product. As a result, it is important to understand the downstream consequences of these firm-physician relationships on patients.

Table 6 investigates this directly, using the cumulative logged opioid deaths over the 6, 9 and 12 months following the announcement of Medicaid expansion. I focus my analysis on logged cumulative deaths over this period, as understanding the precise timing of deaths, and the underlying mechanisms between a prescription and a patient outcome are complex. Indeed, while physical opioid dependence can manifest in as little as one week of consistent use (Rieder, 2019), the timeline for more severe physiological responses is less clear. To the extent that physicians are prescribing these additional opioids to their existing patients (who, I argue experience no discontinuous change in disease burden), I consider them to be the marginal opioid patient. That is, physicians were nudged into prescribing opioids for these patients as a result of the promotional activity, and would not have otherwise done so in the absence. As a result, an additional mechanism for negative outcomes could be diversion from these marginal patients into the black market.[36] In this case, the direct recipient of the prescription remains unharmed, but the prescription might nevertheless result in a harmful outcome.

Results reported in Table 6 suggest that in the 6 months following the announcement of Medicaid expansion, there was a small increase in logged cumulative opioid deaths. Under the assumption of no discontinuous demand changes, I argue that these results are driven by increased promotional activity, which induces physicians to increase opioid prescriptions. Coefficient estimates for the subsequent 9 and 12 months, however, suggest that these results are not persistent. On possible explanation for this fade-out is the protective effects of the insurance coverage itself. Evidence from Meinhofer and Witman (2018) suggests that admissions to treatment for opioid use disorders increased substantially following the implementation of Medicaid expansion. Beyond this, given the pervasiveness of opioid-determent policies over this period, an additional cause for concern might be that these other policies in some way affect patient outcomes. I show in subsection 6.2 that this is not likely to be the case.

[36] An excellent discussion of this is available in Alpert (2016) and Schnell (2017).

6 Robustness

6.1 Medicaid Eligibility

I have argued that my empirical focus the announcement of Medicaid expansion allows me to tease out the strategic response of pharmaceutical firms and subsequent physician responses. I argue that this is because pharmaceutical firms, as rational agents, are able to understand the changing market forces and demand-side factors for their products. However, concerns may remain that these responses are, instead, to other market forces that are correlated with the timing of policy announcement.

To address these concerns, Table 7 presents estimates of pharmaceutical response to the announcement of policy, splitting the sample to capture variation in Medicaid eligibility across counties. The top panel presents estimates for counties with a below median share of their population living below the Federal Poverty Line. As eligibility for the expansion was determined by an income that was below 138% of the FPL, this top panel presents the estimates for counties with a below median share of the population eligible for the program. If pharmaceutical firms are indeed promoting in anticipation of a growing market share, we would not expect to see large changes in their promotional behaviours in these counties. This is confirmed by the point estimates presented in column 3 of the top panel. Following the announcement of Medicaid expansion, there was a (statistically insignificant) reduction in logged promotional spending in these regions. Looking instead at counties with an above median share of individuals below the FPL (in the lower panel of Table 7), I argue that positive changes in pharmaceutical promotions would be consistent with strategic behaviour. I find that the results are entirely driven by these poorer counties.

I next investigate these distributional effects on the physician response to promotion, in Figure 6. These event-study results plot the log dosage of opioids sold in counties in the highest decile (in black) and lowest decile (in purple) of poverty. Unlike the pharmaceutical response, which is concentrated almost exclusively in high-eligibility counties, the results for the top and bottom decile counties follow each other quite closely. There are a number of reasons why this could be. First, promotional nudges made by pharmaceutical firms may have spill-over effects across physician networks. This is consistent with evidence in Agha and Zeltzer (2019). Second, while the DEA data provide incredibly rich geographic data on the location pharmacies and the intensity of opioid sales, one limitation of these data is the inability to link them directly with physicians receiving promotions. As such, these data serve as an approximation of the changes

in prescribing in a region. Despite these limitations however, I argue that these similar effects across poverty deciles might further support the underlying assumption that patient demand remained unchanged during the announcement period. To the extent that physicians respond to promotional behaviour by prescribing to their existing patients, rather than newly eligible individuals, I would not expect these results to similarly be concentrated in high-poverty counties. As these existing patients are likely more socioeconomically diverse than the newly eligible population, these results would be consistent with a constant patient demand.

Finally, I note that while the Federal Poverty Level thresholds for eligibility are federally mandated, individual states are able to adjust these threshold (to be either more or less demanding than federal cut-offs).[37]. I adjust for these differences in Table 9 and find that this does not appear to affect the results in a meaningful way.

6.2 Alternate Opioid Control Policies

Unlike prior literature investigating the impacts of pharmaceutical promotion of opioids on downstream consequences for patients, my time period of study is one where the risks and dangers of opioid largely commonly known. From 2010 onward, over half of states had enacted some form of prescription drug monitoring program (PDMP) or recreational marijuana laws (see Table A.1). While PDMPs explicitly place administrative burden on physicians in an effort to reduce unnecessary prescribing, they might nevertheless also affect patient demand behaviour. Recent survey evidence from Ali et al. (2017) suggest that the implementation of a PDMP is associated with a reduction in doctor shopping behaviour.[38] Recreational marijuana laws, on the other hand, may serve to reduce the profitability of opioid markets for pharmaceutical firms, as evidence suggests that cannabis and opioids may be substitutes in the treatment of pain (Powell et al., 2018).

In order to address concerns that these alternate opioid control policies may be correlated with the announcement or implementation of Medicaid expansion (or affect patient behaviour through some other mechanism), Table 10 incorporates identifiers for the implementation of PDMPs and medical marijuana laws. The results are robust to the inclusion of these alternate policies

[37] Data on state-level thresholds, and changes to these cutoffs over time are available through the Kaiser Family Foundation. https://www.kff.org/medicaid/state-indicator/medicaid-income-eligibility-limits-for-other-non-disabled-adults/

[38] Doctor shopping occurs when drug-seeking patients consult with a number of physicians (sometimes across geographic boundaries), in order to obtain a prescription dose that may be larger than any individual physician may feel is appropriate to prescribe (Quinones, 2015).

6.3 Changes in Underlying Health

In subsection 6.2, I argue that there is little cause for concern that my results are driven by changes in demand for opioid products. One lingering concern, however, might be that the estimated changes in opioid-specific mortality are correlated with broader issues in healthcare provision or underlying population health. I address this in two ways. To the extent that the announcement of Medicaid expansion is correlated with poor underlying health in the population more generally, I address by first controlling for a lagged measure of county-level all-cause mortality in all of my main results.

I further attempt a placebo exercise to alleviate any lingering concerns about correlated shocks to underlying health and the timing of Medicaid expansion. Because of the broader impacts of promotion to non-opioid drug markets, as demonstrated in Table 3 and Table 4, it is not unreasonable to expect that similar pathways might exist for other disease and illness categories. For example, because two of the three top promoted drugs are devoted to cardiac health, we might reasonably expect that these promotional relationships may also have downstream consequences for this disease category. As such, identifying a reasonable placebo cause of death requires identifying a condition that is unlikely to be affected (either positively or otherwise), by changes to prescription medication induced by promotion.

One candidate placebo condition is cancer deaths. To the extent that promotional responses also change for pharmaceutical firms producing cancer-treatment drugs, we might reasonably expect the health consequences of changes to treatment to be slow-moving. To ensure this, I focus on the broad class of all neoplasms (rather than on a particular type of cancer which may respond to changes in treatment more quickly).

Results are presented in Table 8, and suggest that unlike opioid deaths, cancer mortality was unaffected by the announcement of Medicaid expansion. This further suggests that underlying changes to health care provision, or population health more broadly are unlikely to be driving the results for opioid mortality.

7 Conclusion

This paper disentangles supply and demand forces in order to understand their relative importance in the opioid epidemic. Given the unprecedented death toll of opioids in the United States, better understanding the underlying mechanisms that contribute to the epidemic are crucial. Beyond this, opioids provide a useful lens through which to view the market for prescription

drugs more generally, in order to understand how agents in this market interact to generate a prescription. I focus specifically on understanding the role of physicians as the crucial intermediary between patients (who demand pharmaceutical products) and the pharmaceutical firms that produce them.

I leverage a unique natural experiment, capitalizing on the staggered introduction of Medicaid expansion in the United States. Focusing specifically on the period following a state's announcement of expansion, but prior to implementation, I argue that pharmaceutical firms motivated by the future growth in the market for their products, respond strategically in advance of the policy. I argue that during this time, patient demand for opioids remains unchanged, and thus this policy is able to disentangle the often simultaneous responses of demand and supply for opioids.

This paper presents three main findings. First, I show that pharmaceutical firms increase promotion to physicians in anticipation of local insurance expansion. This is true at both the intensive and extensive margins, with a larger total and average value of promotions for opioids directed to physicians. Pharmaceutical firms additionally expanded their physician network over this period, targeting a higher number of individual physicians with promotions. These effects were driven almost entirely by counties with a higher than median Medicaid-eligible population, suggesting that pharmaceutical firms targeted their promotions where they might be most fruitful long-term.

Second, I offer evidence that these promotional relationships affect physician prescribing patterns. Following the announcement of this expansion, I find that sales of prescription opioids increase. I attribute these responses to the effect of promotions, arguing that patient demand and disease burden remains unchanged over the period.

Finally, I discuss the consequences of these relationships for patient outcomes, finding that in the 6 months following the announcement of expansion, opioid overdose deaths saw a modest increase which was not persistent one year out. I provide evidence that these results are unlikely to be driven by changes in underlying mortality trends.

It is important to consider these results in the context of the current policy environment. Promotion continues to be a persuasive tool for pharmaceutical firms, despite policy designed explicitly to curb this type of behaviour. Indeed, The Sunshine Act (2010), which mandated the collection and public release of the very promotional data exploited in this paper is one such example. While prescription opioids have long ceased to be the primary driver of overdose deaths, they nevertheless allow for the persistent danger of initiating patients into the use of

opioids.

References

ACA (2010). Patient protection and affordable care. 9

Agha, L. and Zeltzer, D. (2019). Drug diffusion through peer networks: The influence of industry payments. Technical report, National Bureau of Economic Research. 8, 24

Ali, M. M., Dowd, W. N., Classen, T., Mutter, R., and Novak, S. P. (2017). Prescription drug monitoring programs, nonmedical use of prescription drugs, and heroin use: Evidence from the national survey of drug use and health. *Addictive behaviors*, 69:65–77. 6, 25

Alpert, A. (2016). The anticipatory effects of medicare part d on drug utilization. *Journal of health economics*, 49:28–45. 2, 16, 23

Alpert, A., Lakdawalla, D., and Sood, N. (2015). Prescription drug advertising and drug utilization: The role of medicare part d. Technical report, National Bureau of Economic Research. 2, 4, 16

Alpert, A., Powell, D., and Pacula, R. L. (2018). Supply-side drug policy in the presence of substitutes: Evidence from the introduction of abuse-deterrent opioids. *American Economic Journal: Economic Policy*, 10(4):1–35. 3

Alpert, A. E., Evans, W. N., Lieber, E. M., and Powell, D. (2019). Origins of the opioid crisis and its enduring impacts. Working Paper 26500, National Bureau of Economic Research. 3, 5, 12, 15

Anderson, D. M. and Rees, D. I. (2021). The public health effects of legalizing marijuana. Working Paper 28647, National Bureau of Economic Research. 14

Aron-Dine, A., Einav, L., Finkelstein, A., and Cullen, M. (2015). Moral hazard in health insurance: do dynamic incentives matter? *Review of Economics and Statistics*, 97(4):725–741. 16

Arrow, K. J. (1963). Uncertainty and the welfare economics of medical-care. *American economic review*, 53(5):941–973. 8

Arteaga, C. and Barone, V. (2021). The opioid epidemic: Causes and consequences. 3, 5

Averett, S. L., Smith, J. K., and Wang, Y. (2019). Medicaid expansion and opioid deaths. *Health economics*, 28(12):1491–1496. 4, 6

Bachhuber, M. A., Saloner, B., Cunningham, C. O., and Barry, C. L. (2014). Medical cannabis laws and opioid analgesic overdose mortality in the united states, 1999-2010. *JAMA internal medicine*, 174(10):1668–1673. 14

Bao, Y., Pan, Y., Taylor, A., Radakrishnan, S., Luo, F., Pincus, H. A., and Schackman, B. R. (2016). Prescription drug monitoring programs are associated with sustained reductions in opioid prescribing by physicians. *Health Affairs*, 35(6):1045–1051. 5

Buchmueller, T. C. and Carey, C. (2018). The effect of prescription drug monitoring programs on opioid utilization in medicare. *American Economic Journal: Economic Policy*, 10(1):77–112. 3, 5

Buchmueller, T. C., Carey, C. M., and Meille, G. (2019). How well do doctors know their patients? evidence from a mandatory access prescription drug monitoring program. Working Paper 26159, National Bureau of Economic Research. 3

Carey, C., Lieber, E. M., and Miller, S. (2021). Drug firms' payments and physicians' prescribing behavior in medicare part d. *Journal of Public Economics*, 197:104402. 4, 8

Case, A. and Deaton, A. (2015). Rising morbidity and mortality in midlife among white non-hispanic americans in the 21st century. *Proceedings of the National Academy of Sciences*, 112(49):15078–15083. 4

Case, A. and Deaton, A. (2017). Mortality and morbidity in the 21st century. *Brookings papers on economic activity*, 2017:397. 4

Chang, H.-Y., Lyapustina, T., Rutkow, L., Daubresse, M., Richey, M., Faul, M., Stuart, E. A., and Alexander, G. C. (2016). Impact of prescription drug monitoring programs and pill mill laws on high-risk opioid prescribers: a comparative interrupted time series analysis. *Drug and alcohol dependence*, 165:1–8. 5

Ching, A. T. and Ishihara, M. (2012). Measuring the informative and persuasive roles of detailing on prescribing decisions. *Management Science*, 58(7):1374–1387. 4, 8, 22

Cohen, R. A. and Martinez, M. E. (2014). Health insurance coverage: early release of estimates from the national health interview survey, january–march 2014. *National Center for Health Statistics, Centers for Disease Control and Prevention*. 9

Courtemanche, C., Marton, J., Ukert, B., Yelowitz, A., and Zapata, D. (2016). Early impacts of the affordable care act on health insurance coverage in medicaid expansion and non-expansion states. *Journal of Policy Analysis and Management*. 9

Currie, J. and Gruber, J. (1996). Health insurance eligibility, utilization of medical care, and child health. *The Quarterly Journal of Economics*. 6

Dafny, L. and Gruber, J. (2005). Public insurance and child hospitalizations: access and efficiency effects. *Journal of Public Economics*, 89(1):109–129. 6

Datta, A. and Dave, D. (2017). Effects of physician-directed pharmaceutical promotion on prescription behaviors: Longitudinal evidence. *Health economics*, 26(4):450–468. 7, 16

Doleac, J. L. and Mukherjee, A. (2019). The moral hazard of lifesaving innovations: naloxone access, opioid abuse, and crime. *Opioid Abuse, and Crime (March 31, 2019)*. 5

Donohue, J. M., Cevasco, M., and Rosenthal, M. B. (2007). A decade of direct-to-consumer advertising of prescription drugs. *New England Journal of Medicine*, 2007(357):673–681. 7

Eichmeyer, S. and Zhang, J. (2020). Can a single opioid prescription make a difference? evidence from physician prescribing variation in emergency departments. Technical report, Working paper. 3

Einav, L., Finkelstein, A., and Schrimpf, P. (2015). The response of drug expenditure to non-linear contract design: Evidence from medicare part d. *The quarterly journal of economics*, 130(2):841–899. 10, 16

Evans, W. N., Lieber, E. M., and Power, P. (2019). How the reformulation of oxycontin ignited the heroin epidemic. *Review of Economics and Statistics*, 101(1):1–15. 3

Finkelstein, A., Gentzkow, M., and Williams, H. (2018). What drives prescription opioid abuse? evidence from migration. *Stanford Institute for Economic Policy Research Working Paper*, pages 18–028. 3

Finkelstein, A., Gentzkow, M., and Williams, H. L. (2019). Place-based drivers of mortality: Evidence from migration. Technical report, National Bureau of Economic Research. 5

Finkelstein, A., Taubman, S., Wright, B., Bernstein, M., Gruber, J., Newhouse, J. P., Allen, H., and Baicker, K. (2012). The oregon health insurance experiment: Evidence from the first year. *The Quarterly Journal of Economics*, 127(3):1057–1106. 6

Frean, M., Gruber, J., and Sommers, B. D. (2017). Premium subsidies, the mandate, and medicaid expansion: Coverage effects of the affordable care act. *Journal of Health Economics*, 53:72–86. 8, 9, 10, 17

Furzer, J., Isabelle, M., Miloucheva, B., and Laporte, A. (2021). Public drug insurance and children's mental health: Risk-specific responses to lower out- of-pocket treatment costs. Technical report, CIRANO. 6

Ghosh, A., Simon, K., and Sommers, B. D. (2017). The effect of state medicaid expansions on prescription drug use: evidence from the affordable care act. Technical report, National Bureau of Economic Research. 6, 9, 10

Goodman-Bacon, A. (2021). Difference-in-differences with variation in treatment timing. *Journal of Econometrics*. 18

Gray, B. M., Vandergrift, J. L., Weng, W., Lipner, R. S., and Barnett, M. L. (2021). Clinical knowledge and trends in physicians' prescribing of opioids for new onset back pain, 2009-2017. *JAMA Network Open*, 4(7):e2115328–e2115328. 4

Horwitz, J., Davis, C. S., McClelland, L. S., Fordon, R. S., and Meara, E. (2018). The problem of data quality in analyses of opioid regulation: The case of prescription drug monitoring programs. Technical report, National Bureau of Economic Research. 13

Inderst, R. and Ottaviani, M. (2012). Competition through commissions and kickbacks. *The American Economic Review*, 102(2):780–809. 8

Jones, C. M., Logan, J., Gladden, R. M., and Bohm, M. K. (2015). Vital signs: demographic and substance use trends among heroin users—united states, 2002–2013. *MMWR. Morbidity and mortality weekly report*, 64(26):719. 1

Kaestner, R., Garrett, B., Chen, J., Gangopadhyaya, A., and Fleming, C. (2017). Effects of aca medicaid expansions on health insurance coverage and labor supply. *Journal of Policy Analysis and Management*, 36(3):608–642. 9

Kremer, S. T., Bijmolt, T. H., Leeflang, P. S., and Wieringa, J. E. (2008). Generalizations on the effectiveness of pharmaceutical promotional expenditures. *International Journal of Research in Marketing*, 25(4):234–246. 8

Lin, H. and Sacks, D. W. (2019). Intertemporal substitution in health care demand: Evidence from the rand health insurance experiment. *Journal of Public Economics*, 175:29–43. 16

Maclean, C., Mallatt, J., Ruhm, C. J., and Simon, K. I. (2020). Review of economic studies on the opioid crisis. *NBER Working Paper*, (w28067). 7

Mattson, C. L., Tanz, L. J., Quinn, K., Kariisa, M., Patel, P., and Davis, N. L. (2021). Trends and geographic patterns in drug and synthetic opioid overdose deaths—united states, 2013–2019. *Morbidity and Mortality Weekly Report*, 70(6):202. 1

McGuire, T. G. (2000). Physician agency. *Handbook of health economics*, 1:461–536. 8

McMichael, B. J., Van Horn, R. L., and Viscusi, W. K. (2020). The impact of cannabis access laws on opioid prescribing. *Journal of health economics*, 69:102273. 14

Meara, E., Horwitz, J. R., Powell, W., McClelland, L., Zhou, W., O'malley, A. J., and Morden, N. E. (2016). State legal restrictions and prescription-opioid use among disabled adults. *New England Journal of Medicine*, 375(1):44–53. 5

Meinhofer, A. and Witman, A. E. (2018). The role of health insurance on treatment for opioid use disorders: Evidence from the affordable care act medicaid expansion. *Journal of health economics*, 60:177–197. 7, 23

Mizik, N. and Jacobson, R. (2004). Are physicians "easy marks"? quantifying the effects of detailing and sampling on new prescriptions. *Management Science*, 50(12):1704–1715. 4, 8

Moffitt, R. A. (2016). *Economics of Means-Tested Transfer Programs in the United States*, volume 1. University of Chicago Press. 9, 10

Musumeci, M. B. (2012). A guide to the supreme court's decision on the aca's medicaid expansion. *Focus on Health Reform*. 9

National Center for Health Statistics (2017). Health, united states, 2016: With chartbook on long-term trends in health. 7

Nguyen, T. D., Bradford, W. D., and Simon, K. I. (2019). How do opioid prescribing restrictions affect pharmaceutical promotion? lessons from the mandatory access prescription drug monitoring programs. Technical report, National Bureau of Economic Research. 5

Powell, D., Pacula, R. L., and Jacobson, M. (2018). Do medical marijuana laws reduce addictions and deaths related to pain killers? *Journal of health economics*, 58:29–42. 14, 25

Powell, D., Pacula, R. L., and Taylor, E. (2020). How increasing medical access to opioids contributes to the opioid epidemic: evidence from medicare part d. *Journal of health economics*, 71:102286. 3, 7

Quinones, S. (2015). *Dreamland: The true tale of America's opiate epidemic*. Bloomsbury Publishing USA. 4, 25

Rees, D. I., Sabia, J. J., Argys, L. M., Dave, D., and Latshaw, J. (2019). With a little help from my friends: The effects of good samaritan and naloxone access laws on opioid-related deaths. *The Journal of Law and Economics*, 62(1):1–27. 5

Rieder, T. (2019). *In pain: A bioethicist's personal struggle with opioids*. HarperCollins. 23

Rizzo, J. A. (1999). Advertising and competition in the ethical pharmaceutical industry: the case of antihypertensive drugs. *The Journal of Law and Economics*, 42(1):89–116. 4, 8

Ruhm, C. J. (2018). Deaths of despair or drug problems? Technical report, National Bureau of Economic Research. 5, 12

Sacks, D. W., Hollingsworth, A., Nguyen, T., and Simon, K. (2021). Can policy affect initiation of addictive substance use? evidence from opioid prescribing. *Journal of Health Economics*, 76:102397. 5

Schnell, M. (2017). Physician behavior in the presence of a secondary market: The case of prescription opioids. Technical report, Mimeo, University of Princeton. 3, 23

Schnell, M. and Currie, J. (2018). Addressing the opioid epidemic: is there a role for physician education? *American journal of health economics*, 4(3):383–410. 3

Sharp, A., Jones, A., Sherwood, J., Kutsa, O., Honermann, B., and Millett, G. (2018). Impact of medicaid expansion on access to opioid analgesic medications and medication-assisted treatment. *American journal of public health*, 108(5):642–648. 4, 6

Shover, C. L., Davis, C. S., Gordon, S. C., and Humphreys, K. (2019). Association between medical cannabis laws and opioid overdose mortality has reversed over time. *Proceedings of the National Academy of Sciences*, 116(26):12624–12626. 14

Sommers, B. D., Gunja, M. Z., Finegold, K., and Musco, T. (2015). Changes in self-reported insurance coverage, access to care, and health under the affordable care act. *Journal of the American Medical Association*, 314(4):366–374. 9

Spurling, G. K., Mansfield, P. R., Montgomery, B. D., Lexchin, J., Doust, J., Othman, N., and Vitry, A. I. (2010). Information from pharmaceutical companies and the quality, quantity, and cost of physicians' prescribing: a systematic review. *PLoS medicine*, 7(10):1292. 4, 8

Sun, L. and Abraham, S. (2020). Estimating dynamic treatment effects in event studies with heterogeneous treatment effects. *Journal of Econometrics*. 18, 21, 40

Tompkins, D. A., Hobelmann, J. G., and Compton, P. (2017). Providing chronic pain management in the "fifth vital sign" era: Historical and treatment perspectives on a modern-day medical dilemma. *Drug and alcohol dependence*, 173:S11–S21. 5

Ventola, C. L. (2011). Direct-to-consumer pharmaceutical advertising: therapeutic or toxic? *Pharmacy and Therapeutics*, 36(10):669. 7

Wettstein, G. (2019). Health insurance and opioid deaths: Evidence from the affordable care act young adult provision. *Health economics*, 28(5):666–677. 4, 6

Wouters, O. J. (2020). Lobbying expenditures and campaign contributions by the pharmaceutical and health product industry in the united states, 1999-2018. *JAMA internal medicine*, 180(5):688–697. 21

Ziedan, E. and Kaestner, R. (2020). Effect of prescription opioids and prescription opioid control policies on infant health. Technical report, National Bureau of Economic Research. 5

Figures

Figure 1: Geographic Variation in Opioid Deaths Over time

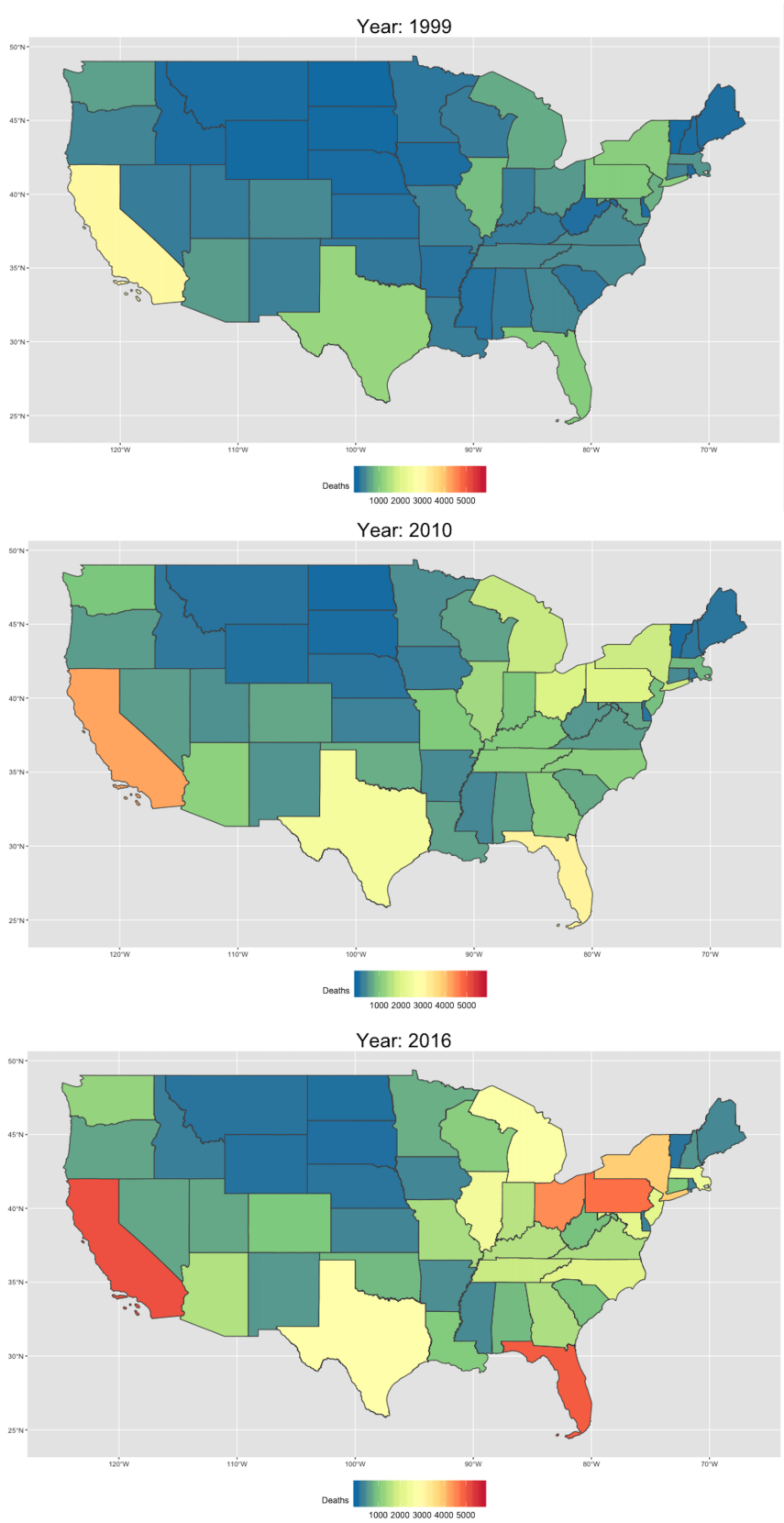


Figure 2: Number of States Treated Over Time

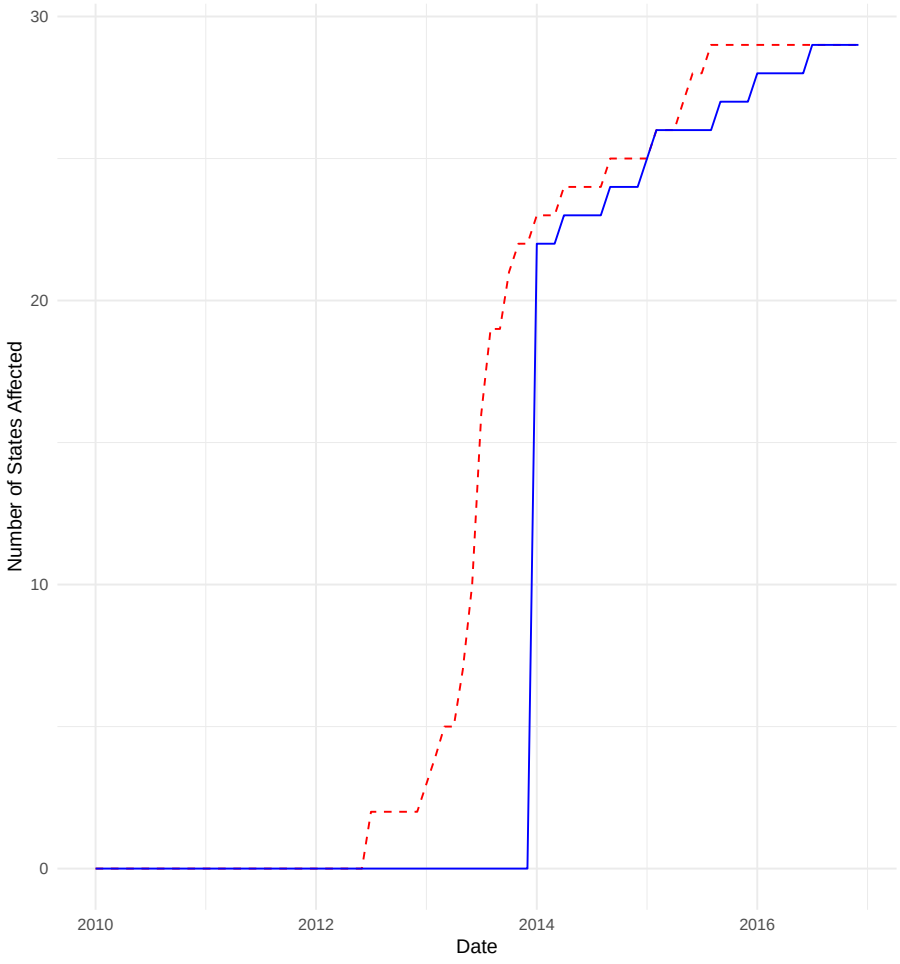


Figure 3: Effect of Medicaid Announcement on Logged Promotional Spending for Opioids

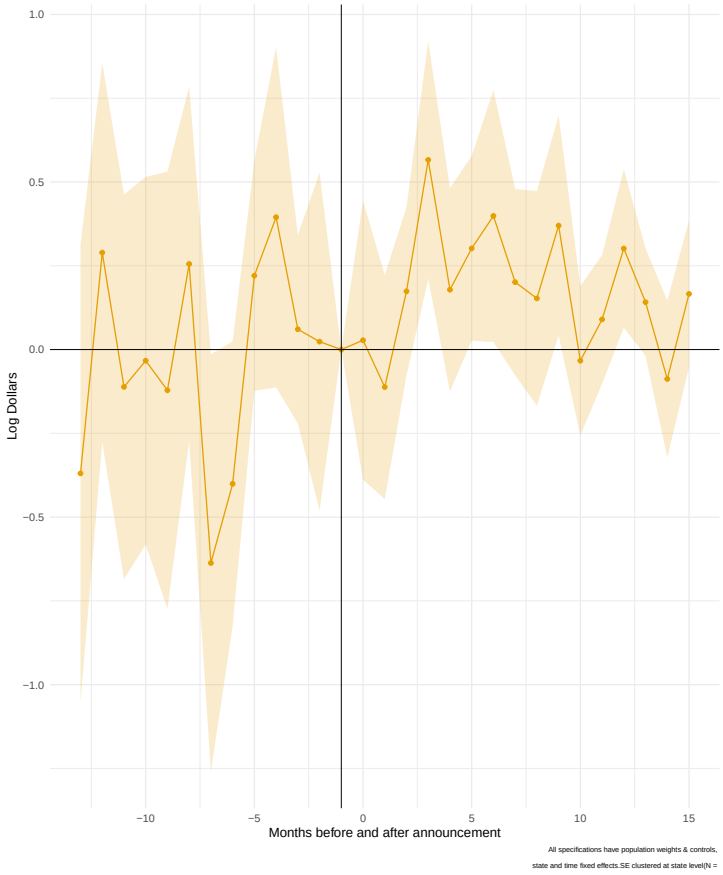
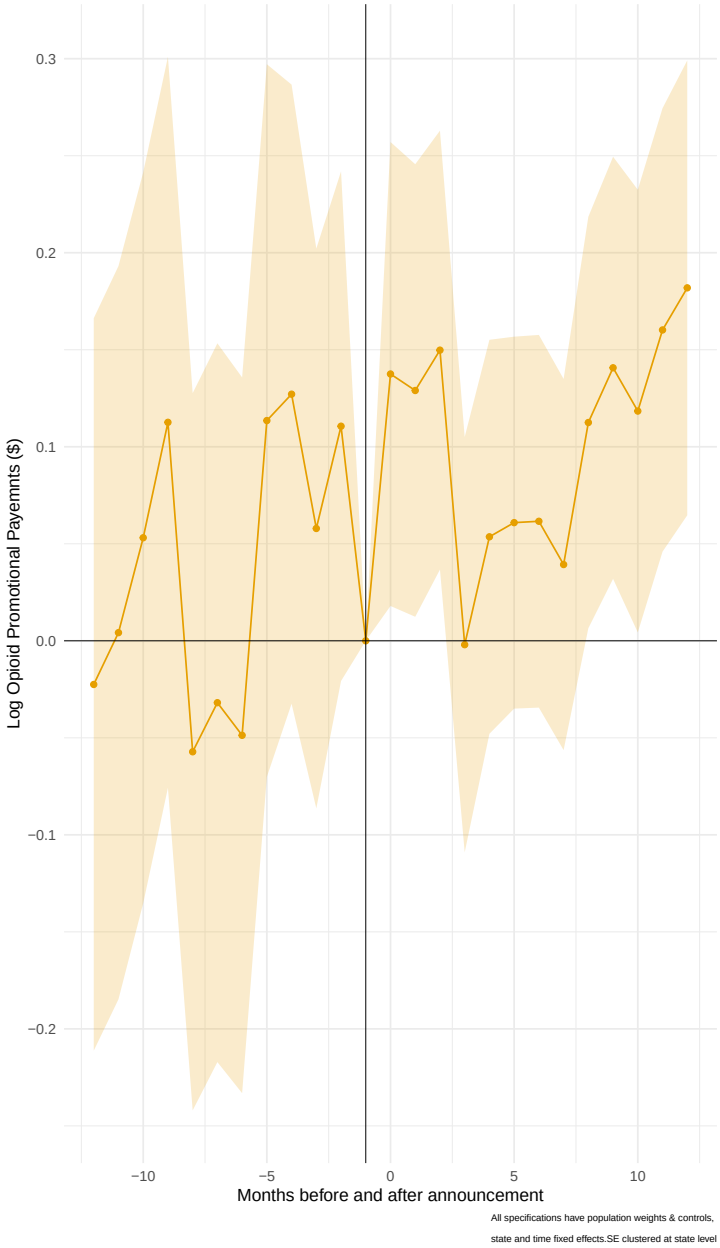


Figure 4: Effect of Medicaid Announcement on Logged Promotional Spending for Opioids (Sun and Abraham (2020) corrected)



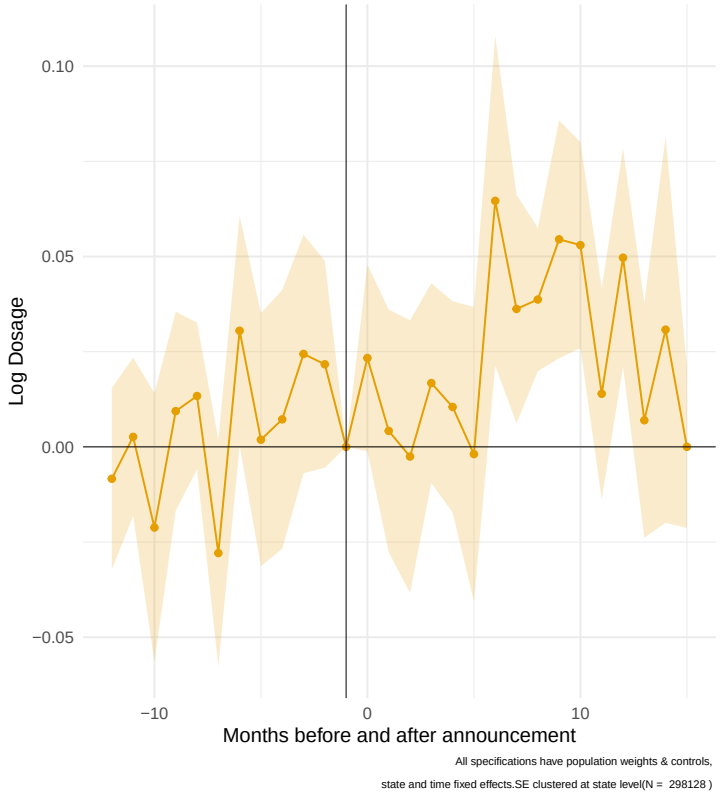


Figure 5: Medicaid Announcement and Logged Opioid Doses Ordered by Retailers

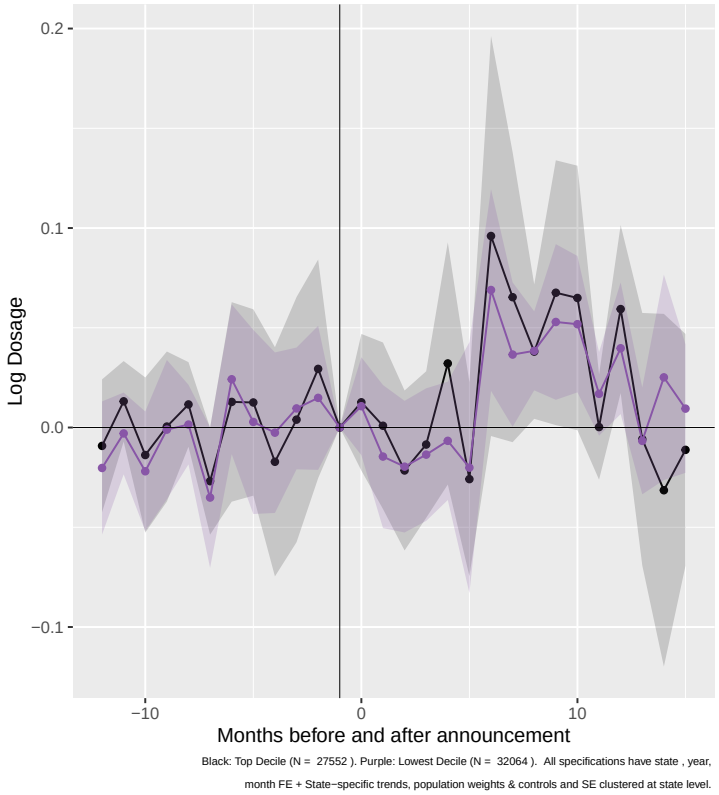
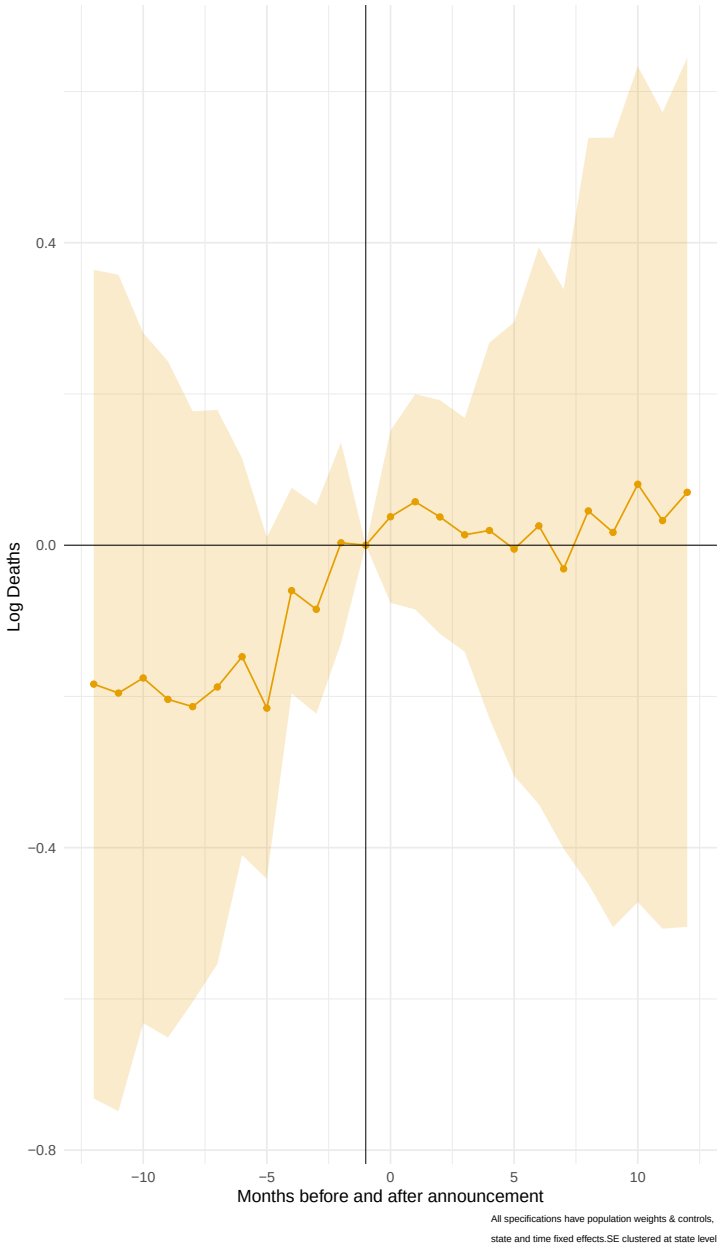


Figure 6: Medicaid Announcement and Logged Opioid Doses Ordered (by decile of Medicaid Eligibility)

Figure 7: Effect of Medicaid Announcement on Logged Opioid Deaths



Tables

Table 1: Difference-in-Differences: Medicaid Expansion and the Effect on the Value Opioid Promotion

	Logged Total Spending			Logged Average Spending		
	(1)	(2)	(3)	(4)	(5)	(6)
$Announce_{st}(1 - Implement_{st})$			0.470***			0.371***
			(0.138)			(0.093)
$Implement_{st}$	−0.291***		0.034	−0.151*		0.106
	(0.100)		(0.118)	(0.076)		(0.078)
$Announce_{st}$		0.225			0.222**	
		(0.146)			(0.092)	
Observations	121,958	121,958	121,958	121,958	121,958	121,958
Adjusted R^2	0.496	0.496	0.497	0.343	0.343	0.344

Note: Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 2: Difference-in-Differences: Medicaid Expansion and the Effect on the Frequency Opioid Promotion

	Logged Visits			Logged Doctors Visited		
	(1)	(2)	(3)	(4)	(5)	(6)
$Announce_{st}(1 - Implement_{st})$			0.099			0.083*
			(0.061)			(0.047)
$Implement_{st}$	−0.140***		−0.071	−0.155***		−0.098*
	(0.042)		(0.060)	(0.041)		(0.053)
$Announce_{st}$		0.003			−0.019	
		(0.067)			(0.055)	
Observations	121,958	121,958	121,958	121,958	121,958	121,958
Adjusted R^2	0.566	0.566	0.566	0.583	0.582	0.583

Note: Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 3: Difference-in-Differences: Medicaid Expansion and the Effect on the Value of Non-Opioid Promotion

	Logged Total Spending			Logged Average Spending		
	(1)	(2)	(3)	(4)	(5)	(6)
$Announce_{st}(1 - Implement_{st})$			0.269^{***}			0.056
			(0.096)			(0.055)
$Implement_{st}$	-0.152^{*}		0.034	−0.050		−0.011
	(0.087)		(0.108)	(0.037)		(0.056)
$Announce_{st}$		0.137			0.019	
		(0.110)			(0.056)	
Observations	121,958	121,958	121,958	121,958	121,958	121,958
Adjusted R^2	0.470	0.470	0.470	0.267	0.267	0.268

Note: Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 4: Difference-in-Differences: Medicaid Expansion and the Effect on the Frequency of Non-Opioid Promotion

	Logged Visits			Logged Doctors Visited		
	(1)	(2)	(3)	(4)	(5)	(6)
$Announce_{st}(1 - Implement_{st})$			0.213^{***}			0.175^{***}
			(0.047)			(0.053)
$Implement_{st}$	-0.102^{*}		0.045	-0.106^{**}		0.015
	(0.054)		(0.055)	(0.048)		(0.056)
$Announce_{st}$		0.118^{**}			0.085	
		(0.057)			(0.061)	
Observations	121,958	121,958	121,958	121,958	121,958	121,958
Adjusted R^2	0.527	0.527	0.528	0.550	0.550	0.550

Note: Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 5: Difference-in-Differences: Medicaid Expansion and the Effect on Opioid Prescriptions

	Number of Orders			Dose per 1000			Any Order		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
$Announce_{st}(1 - Implement_{st})$			201.435**			54.083*			0.000
			(93.493)			(29.087)			(0.000)
$Implement_{st}$	−29.739		166.242	27.790		80.408	0.000		0.000*
	(221.930)		(269.947)	(36.319)		(50.740)	(0.000)		(0.000)
$Announce_{st}$		201.364**			54.136*			0.000	
		(93.718)			(29.092)			(0.000)	
Y mean	728.9	728.9	728.9	318.2	318.2	318.2	1	1	1
Observations	148,944	148,944	148,944	148,944	148,944	148,944	148,944	148,944	148,944
Adjusted R^2	0.991	0.991	0.933	0.994	0.994	0.923	0.919	0.919	0.019

Note: Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 6: Difference-in-Differences: Medicaid Expansion and Opioid Overdose Deaths

	Logged Cumulative Opioid Deaths		
	6 months	9 months	12 months
$Announce_{st}(1 - Implement_{st})$	0.064^{***}	0.033^{**}	0.018
	(0.017)	(0.014)	(0.015)
$Implement_{st}$	0.064^{*}	0.035^{**}	-0.015
	(0.032)	(0.014)	(0.017)
Y mean	31.8	38.0	47.9
N	194,700	194,700	194,700
Adj. R^2	0.88	0.904	0.917

Note:Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 7: Total Logged Opioid Promotion Spending by Medicaid Eligibility

	(1)	(2)	(3)
	Below Median < FPL		
$Announce_{st}(1 - Implement_{st})$			−0.017
			(0.049)
$Implement_{st}$	−0.001		−0.010
	(0.056)		(0.058)
$Announce_{st}$		−0.012	
		(0.048)	
Adjusted R^2	0.168	0.168	0.168
	Above Median < FPL		
$Announce_{st}(1 - Implement_{st})$			0.335**
			(0.144)
$Implement_{st}$	−0.185*		0.046
	(0.099)		(0.110)
$Announce_{st}$		0.171	
		(0.127)	
N	64,575	64,575	64,575
Adj. R^2	0.637	0.637	0.637

Note:Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 8: Placebo Outcomes: Medicaid Expansion and Cancer Deaths

	Log Cumulative Cancer Deaths		
	6 months	9 months	12 months
$Announce_{st}(1 - Implement_{st})$	−0.002	−0.000	0.001
	(0.004)	(0.004)	(0.004)
$Implement_{st}$	0.025***	0.004	0.007
	(0.005)	(0.013)	(0.022)
Mean per 100,000	47.0	70.6	94.2
N	194,700	194,700	194,700
Adj. R^2	0.976	0.980	0.982

Note: Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$ level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$

Table 9: Robustness Check: Adjusting for Variation in Eligibility Cutoffs

	(1)	(2)	(3)
	Log Promotional $		
$Announce_{st}(1 - Implement_{st})$			0.268^{*}
			(0.155)
$Implement_{st}$	-0.260^{***}		-0.041
	(0.096)		(0.138)
$Announce_{st}$		0.176	
		(0.141)	
N	120,212	120,212	120,212
Adj. R^2	0.660	0.659	0.660

Note:This table presents TWFE estimates which additionally adjust for the existence of other opioid-specific policy. These include state prescription drug monitoring programs and recreational marijuana laws. Additional controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$ level

Table 10: Robustness Check: Adjusting for Confounding Opioid Policy

	(1)	(2)	(3)
	Log Promotional $		
$Announce_{st}(1 - Implement_{st})$			0.298^{**}
			(0.141)
$Implement_{st}$	-0.192^{**}		0.013
	(0.095)		(0.105)
$Announce_{st}$		0.139	
		(0.120)	
N	120,212	120,212	120,212
Adj. R^2	0.660	0.659	0.660

Note:This table presents TWFE estimates which additionally adjust for varying federal poverty line thresholds across states. Additional controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$ level

Appendix: Supporting Materials

Table A.1: Timing of Legislation, Medicaid Expansion, and Additional Drug Policies

State	Announcement	Expansion	PDMP Mandates	Recreational Marijuana Laws	State	Announcement	Expansion	PDMP Mandates	Recreational Marijuana Laws
Alabama					Montana	4/29/2015	1/1/2016		
Alaska	7/15/2015	9/1/2015		2015	Nebraska				
Arizona	6/17/2013	1/1/2014			Nevada	12/11/2012	1/1/2014	2016	
Arkansas	4/23/2013	1/1/2014	2015		New Hampshire	3/27/2014	8/15/2014	2016	
California	6/27/2013	1/1/2014	2016	2016	New Jersey	6/28/2013	1/1/2014	2015	
Colorado	5/13/2013	1/1/2014		2012	New Mexico	1/9/2013	1/1/2014	2012	
Connecticut	6/2010	1/1/2014	2015		New York	6/28/2012	1/1/2014	2013	
Delaware	7/1/2013	1/1/2014			North Carolina				
District of Columbia	5/13/2010	1/1/2014		2015	North Dakota	4/16/2013	1/1/2014	2014	
Florida					Ohio	10/21/2013	1/1/2014	2011	
Georgia			2018		Oklahoma			2010	
Hawaii	6/21/2013	1/1/2014			Oregon		1/1/2014		2016
Idaho					Pennsylvania	8/28/2014	1/1/2015	2015	
Illinois	7/22/2013	1/1/2014			Rhode Island	7/3/2013	1/1/2014	2016	
Indiana	1/27/2015	2/1/2015			South Carolina				
Iowa	12/12/2013	1/1/2014			South Dakota				
Kansas					Tennessee			2013	
Kentucky	9/3/2013	1/1/2014	2012		Texas				
Louisiana	6/1/2015	7/1/2016	2014		Utah				
Maine					Vermont	07/2012	1/1/2014	2013	
Maryland	5/5/2013	1/1/2014			Virginia			2015	
Massachusetts	7/12/2013	1/1/2014	2014	2015	Washington	6/30/2013	1/1/2014		2012
Michigan	9/16/2013	4/1/2014			West Virginia	5/2/2013	1/1/2014	2012	
Minnesota	2/25/2013	1/1/2014			Wisconsin				
Mississippi					Wyoming				
Missouri									

Note: Announcement dates correspond to date of legislation of Medicaid expansion (sources collected by author from individual state news agencies, and available upon request). Expansion dates from Medicaid's State Profiles (https://www.medicaid.gov/state-overviews/state-profiles/index.html). Recreational Marijuana Laws are from https://marijuana.procon.org/legal-recreational-marijuana-states-and-dc/

Table A.2: Top 10 Pharmaceutical Promotors: Amount Spent

Rank	Manufacturer	Value of Promotions $ (000s)	Share of all Promotions	Most Commonly Promoted Drug	Drug Type/Use
1	Astrazeneca Pharmaceuticals	163558	7.42	SYMBICORT	Asthma Inhaler
2	Janssen pharmaceuticals	161299	7.32	XARELTO	Anticoagulant
3	Novartis Pharmaceuticals	77999	3.54	ENTRESTO	Chronic Heart Failure
4	Allergan inc.	76521	3.47	BOTOX	Botox
5	Merck Sharp & Dohme	70300	3.19	JANUVIA	Diabetes (II)
6	Abbvie	69445	3.15	HUMIRA	Rheumatoid Arthritis
7	Novo Nordisk	66293	3.01	LEVEMIR	Insulin
8	Pfizer	65044	2.95	ELIQUIS	Anticoagulant
9	E.R. Squibb & Sons	64789	2.94	ELIQUIS	Anticoagulant
10	Teva Pharmaceuticals	62345	2.83	NUVIGIL	Excessive Sleepiness
43	Purdue Pharma	10638	0.48	OXYCONTIN	Opioid
	Total	2203578	100.00		

Table A.3: Top 10 Opioids Promoted: Number of Promotions

Drug Type	Number of Promotions	Share of Total
SUBSYS	81055	0.16
NUCYNTA	71398	0.14
OXYCONTIN	66652	0.14
EMBEDA	40886	0.08
HYSINGLA ER	37063	0.08
XARTEMIS XR	36037	0.07
ZOHYDRO ER	27013	0.05
FENTORA	20252	0.04
XTAMPZA ER	19401	0.04
OPANA ER	14682	0.03

Table A.4: Difference-in-Differences: Medicaid Expansion and the Effect on Opioid Promotion

	Total Spending			Average Spending		
	(1)	(2)	(3)	(4)	(5)	(6)
Post Expansion	−234.766		327.437	−11.746*		5.716
	(331.352)		(680.165)	(5.972)		(7.852)
Post Announce		539.159			14.238	
		(677.911)			(8.620)	
Post Announce, Pre Exp			812.196			25.228***
			(677.843)			(9.299)
Y mean	322			14		
Observations	121,958	121,958	121,958	121,958	121,958	121,958
Adjusted R^2	0.609	0.609	0.609	0.129	0.129	0.130

	Visits			Doctors Visited		
	(1)	(2)	(3)	(4)	(5)	(6)
Post Expansion	−0.718		−6.356**	−2.229**		−2.600***
	(3.281)		(2.696)	(1.067)		(0.477)
Post Announce		−7.138**			−2.849**	
		(3.144)			(1.209)	
Post Announce, Pre Exp			−8.146*			−1.927
			(4.796)			(1.174)
Y mean	5			3		
Observations	121,958	121,958	121,958	121,958	121,958	121,958
Adjusted R^2	0.859	0.860	0.860	0.884	0.884	0.884

Note: This table presents two-way fixed effect results measuring the effect of legislation and Medicaid expansion on opioid promotion. Unlike **??**, all outcome variables are measured in levels, rather than logs. Controls include unemployment rate, uninsurance rate, lagged all-cause mortality, proportion with high school, proportion Black and Hispanic, median household income, republican dummies, fixed effects for state, time, state-specific time trends. Standard errors are in parentheses and clustered at the state level. $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.10$