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Investigating the complexity of naloxone distribution: Which policies matter for pharmacies and potential recipients

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Abstract

Despite efforts to expand naloxone access, opioid-related overdoses remain a significant contributor to mortality. We study state efforts to expand naloxone distribution through pharmacies by reducing the non-monetary costs to prescribers, dispensers, and/or potential recipients of naloxone. We find that laws that only address liability costs have small and insignificant effects on the volume of naloxone dispensed through pharmacies. In contrast, we estimate large effects of laws removing the need for patients to obtain prescriptions from traditional prescribers (e.g., primary care physicians): laws authorizing non-patient-specific prescription distribution and laws granting pharmacists prescriptive authority. We test whether areas designated as primary care shortage areas—where it would be costlier to obtain a prescription—were disproportionately impacted. Shortage areas experienced sharper growth in pharmacy naloxone dispensing in states adopting prescriptive authority policies. These gains were primarily due to those facing low out-of-pocket costs, suggesting that price barriers also must be addressed to increase naloxone purchases.

Keywords

Opioid crisis; Naloxone; Pharmacy distribution; Prescriptive authority; Harm reduction; H75; I18; K32

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Declaration of competing interest

The authors declare that they have no conflict of interest.

CRediT authorship contribution statement

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Supplementary materials

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1. Introduction

Improved access to naloxone is one of the central pillars of federal, state, and local policy responses to the opioid overdose crisis (Smart et al., 2021). In 2022, over 109,000 people died from a drug overdose, most of which involved opioids (Tanz et al., 2024). Naloxone, a non-addictive medication with minimal side effects, can reverse the effects of an opioid overdose if administered in time (Cawley and Dragone, 2023; Chamberlain and Klein, 1994). While naloxone is increasingly carried by first responders (Smart et al., 2022) and local community groups (Clark et al., 2014; Wheeler et al., 2015), improving naloxone distribution to laypeople has been found to be an especially cost-effective mechanism to reduce overdose deaths (Townsend et al., 2020). Continued gaps in naloxone availability prompted policy interest in improving naloxone access for bystanders through pharmacies (ASPE, 2021; CDC, 2019; Guy et al., 2019). To facilitate access to this lifesaving medication, every state had adopted some type of naloxone access law (NAL) to remove barriers to obtaining naloxone through pharmacies by 2018 (Smart et al., 2021).

There is mixed evidence regarding the impacts of these state NALs on fatal overdoses.[1] Potential explanations for these mixed findings are that NALs vary in how they reduce the costs of obtaining naloxone (Smart et al., 2021; Davis and Carr, 2015). Differences in how past studies have categorized the laws in analyses may have contributed to the mixed findings in addition to differences in study timeframes, which result in a disparate set of states and laws contributing to identification. Furthermore, there is limited work assessing how NALs affect naloxone dispensing from retail pharmacies—a first-order outcome targeted by these policies. A body of implementation research has raised questions about the extent to which NALs are capable of increasing such dispensing given lack of knowledge among pharmacists about their state NALs (Thakur et al., 2020) and failure to stock naloxone in pharmacies (Abbas et al., 2021; Eldridge et al., 2020; Graves et al., 2019; Meyerson et al., 2018; Spivey et al., 2020).

This paper evaluates how NALs influence this first-order outcome of pharmacy-based naloxone dispensing. We distinguish between different types of NALs that we theorize differentially affect costs to the prescribers, dispensers, and recipients of naloxone. “Traditional-prescription NALs” primarily aim to reduce potential liability costs associated with the prescribing or dispensing of naloxone, but they retain a traditional prescription model whereby an individual seeking naloxone from a pharmacy must first obtain a prescription from a healthcare provider. We contrast traditional-prescription NALs with two types of “pharmacy-access NALs” that instead aim to reduce consumer costs associated with obtaining a naloxone prescription prior to visiting a pharmacy: (1) non-patient-specific (NPS) prescription dispensing models, which allow pharmacists to dispense naloxone to any individual who meets certain criteria specified by a designated non-pharmacist prescriber or medical licensing board (these include most standing orders or protocol orders); and (2) pharmacist prescriptive authority laws, which grant pharmacists the ability to prescribe

[1]See Abouk et al. (2019), Doleac and Mukherjee (2022), Erfanian et al. (2019), Lee et al. (2021), Cataife et al. (2021), McClellan et al. (2018), Rees et al. (2019), and Rudolph et al. (2022) for a subset of these studies.

naloxone directly to patients. Both types of pharmacy-access NALs obviate the need for individuals seeking naloxone to obtain a prescription prior to visiting a pharmacy; however, the two types disparately affect the procedures required of pharmacies and pharmacists in ways that may differentially shape their expected costs and therefore the willingness of pharmacies to stock and dispense naloxone. In this paper, we evaluate the effects of these "pharmacy-access NALs" on pharmacy naloxone dispensing.

All states now have at least one of these pharmacy-access NALs in place, and it is important to understand their effectiveness in promoting naloxone purchases for at least two reasons. First, the FDA recently approved nalmefene hydrochloride nasal spray (Opvee), an opioid antagonist with similar properties as naloxone but purportedly more effective against potent illicitly manufactured fentanyl. Opvee currently requires a prescription, which will potentially limit its distribution due to the additional barriers faced by consumers. The lessons from NALs will be important for informing future policy related to Opvee. Second, the model of distributing drugs through pharmacies via NPS prescription models or pharmacist prescriptive authority has been applied to a range of other pharmaceutical drugs and medical products (Hilts et al., 2022; Lott et al., 2021; Qato et al., 2020; Rodriguez et al 2020; Sachdev et al., 2020), highlighting the need to understand the broader effectiveness of these distribution mechanisms.

For all analyses, we use a difference-in-differences framework, leveraging the staggered adoption of these different policies. We rely primarily on event study analyses to test for pre-existing trends and to study the timing of the effects since we might expect that these policies alter naloxone access with a lag. We explicitly consider dimensions across which we expect pharmacy-access NALs to have heterogeneous impacts. First, we examine effects based on county Health Professional Shortage Area (HPSA) designation, anticipating that pharmacy-access NALs may be particularly effective in areas with lower access to traditional prescribers of naloxone (i.e., primary care physicians [Smart et al., 2020]). In addition, we examine effects based on naloxone recipient insurance status, recognizing that pharmacy-access laws reduce some non-monetary costs to consumers but do not directly address the price of the medication, which varies by insurance status.

Our paper makes three main contributions. First, it is rare in the NAL literature to use rich pharmacy data which cover dispensing regardless of insurance status. Prior studies have often relied on Medicaid claims data or studied downstream outcomes without testing whether naloxone access itself improved (e.g., Rees et al., 2019; Abouk et al., 2019). We use all-payer pharmacy data and directly test assumptions made throughout this literature on the effectiveness of these laws. We show that traditional-prescription NALs have little impact on pharmacy dispensing, consistent with the assumption that they fail to address many of the barriers or costs consumers face in obtaining a prescription. While we examine the specific context of naloxone, distinguishing between different legal mechanisms aimed at expanding the pharmacist's role as healthcare provider points to broader insights on the complex and interactive role that prescriber, dispenser, and consumer costs play in shaping prescription drug distribution.

Second, we assess whether pharmacy-access NALs disparately impact naloxone access for different geographic areas and by insurance status. The analysis of sub-state heterogeneity is new to this literature, which has typically estimated aggregate effects with little focus on heterogeneity. Pharmacy-access NALs are designed to eliminate the requirement to obtain a patient-specific prescription, suggesting that areas in which it is harder to see a physician should experience disproportionate effects of these policies. Using HPSA designations as a proxy for these difficulties, we find especially large effects of prescriptive authority policies in shortage areas. NPS prescription law effects show smaller effects in shortage areas, which may reflect that these models often still require collaboration between pharmacists and traditional naloxone prescribers, even if patients no longer need to obtain a patient-specific prescription from their provider. In addition, we study the differential impacts of these policies by insurance status given the substantial variation in out-of-pocket costs faced by consumers even when these legal barriers have been substantially reduced. We estimate especially large effects for the Medicare and Medicaid populations. While there are several reasons that these groups may disproportionately benefit from pharmacy-access NALs, it is notable that they face low cost-sharing during this time period (Peet et al., 2022), consistent with the importance of cost as an additional and interactive barrier to naloxone access

Finally, this study is the first in the NAL literature to address concerns about bias due to the staggered implementation of these policies (Goodman-Bacon, 2021), despite substantive concerns about policy effect heterogeneity due to variation in the development of the opioid crisis, differences in the specific policies that comprise states' NALs, and evidence of implementation lags in pharmacy responses to policy changes. We address these issues by implementing and extending an approach that imputes counterfactual "untreated" outcomes for treated observations to estimate treatment effects (Gardner, 2022). Much of the emerging "new" difference-in-differences literature is difficult to apply to a setting with multiple types of policies. In our context, the two pharmacy-access NALs can be modeled as non-overlapping, which simplifies some of the complexities of jointly estimating two difference-in-differences models and permits use of the imputation approach. We introduce a straightforward extension to estimate average treatment effects for such contexts.

Given the ongoing surge in drug-involved fatalities, driven now by synthetic opioids, a clearer understanding of the specific mechanisms through which naloxone policies work to increase pharmacy distribution of naloxone is critical. There is considerable interest in understanding what types of harm reductions policies work and who they help (Cawley and Dragone, 2023). These questions remain relevant even with the most recent FDA decision to allow Narcan and RiVive, two formulations of naloxone, to be sold over the counter, as they speak to the potential effects of reducing cost-related barriers for naloxone dispensers (e.g., information and time costs) and patients (e.g., monetary and time costs) through retail channels. Furthermore, our findings emphasize the importance of attending to pre-existing state NAL environments as likely moderators of the impacts of the FDA decision. We provide important evidence to help inform the contribution of various types of NALs toward expanding naloxone pharmacy access and to better conceptualize the likely implications of federal changes in naloxone laws. More broadly, pharmacist prescriptive authority is a policy option that is used for other pharmaceutical and medical products and there is interest in understanding the consequences of expanding the scope of practice for pharmacists,

especially as a way to address healthcare shortages. Our analysis speaks to this issue by studying differential effects in HPSAs.

We provide additional background and a conceptual framework in the next section. Section 3 discusses the data, while Section 4 introduces the difference-in-differences strategy and extensions for jointly studying multiple policies. We present the results in Section 5. Section 6 concludes.

2. Background on naloxone access laws and a conceptual framework

2.1. Background

In 2001, New Mexico became the first state to adopt a naloxone access law (NAL) aimed at increasing naloxone availability to individuals who are at increased risk of experiencing or witnessing an opioid overdose. The timing of this state law coincided with the launch of the first large-scale take-home naloxone prescription program in the United States, implemented in a rural New Mexico county that had the highest heroin overdose mortality rate in the country (Burris et al., 2001). Over the next decade, five more states passed similar legislation. Most of these early NALs removed potential liability for prescribing, dispensing, or administering naloxone (Davis and Lieberman, 2021). While these protections from civil or criminal liability in theory reduce the legal costs associated with providing or using naloxone, the actual liability risk of prescribing or dispensing naloxone in accordance with state law is minimal (Davis and Carr, 2017). These early laws did little to reduce the non-monetary costs incurred by individuals seeking to obtain naloxone since individuals still had to obtain their own patient-specific prescriptions. This may represent a serious barrier to individuals who use opioids, particularly for individuals who have limited access to traditional health care systems due to, for example, inadequate availability of healthcare providers, stigma or structural barriers, or lack of health insurance coverage.

In more recent years, states have adopted NALs aimed at removing this potential access barrier by permitting pharmacists to dispense naloxone through non-patient-specific (NPS) prescription models (e.g., standing orders) or through pharmacist prescriptive authority. Illinois was the first state to adopt a NPS model of naloxone distribution in 2010, implemented via standing order. In April 2014, New Mexico became the first state to grant pharmacists prescriptive authority for naloxone. By the second half of 2018, all states had implemented at least one of these models, with most states allowing for NPS prescription models rather than pharmacist prescriptive authority (see Fig. 1).

2.2. Conceptual framework

While naloxone is increasingly carried by first responders and distributed through overdose education and naloxone distribution (OEND) programs, pharmacies remain an important source of naloxone access for laypersons. Pharmacy dispensing of naloxone is considered a cost-effective means of reducing opioid-related overdose deaths since it targets distribution to a broader set of laypersons (Townsend et al., 2020) by making its distribution more proximal to potential recipients; 90 % of Americans live within five miles of a community pharmacy (Berenbrok et al., 2022).

Naloxone is associated with several costs to the recipient, including the stigma associated with obtaining and carrying it, the legal risk associated with obtaining and carrying it, the monetary and time costs of obtaining a prescription, and the monetary cost of the drug itself. Traditional-prescription NALs seek to address the liability risks associated with prescribing, dispensing of naloxone by selected providers, or the legal and stigma risks associated with obtaining and carrying it by potential consumers or administrators. Traditional-prescription NALs do not necessarily reduce the costs and stigma associated with obtaining a prescription, however. Those costs are more directly addressed through the two types of pharmacy-access laws, which eliminate the requirement to obtain a patient-specific prescription before visiting a pharmacy. From the recipient's perspective, both NPS and pharmacist prescriptive authority laws are functionally equivalent: in both cases, an individual can simply present to the pharmacy and receive the medication (potentially conditional on payment or receipt of training and education).

However, the costs of prescribing and dispensing naloxone that are incurred by pharmacists differ across these different types of pharmacy-access laws. These costs include potential liability risks, informational costs for learning about the new policy, concerns with social or professional disapproval, and time costs for determining patient eligibility and providing training. While some of these costs are presumed to be small (Davis and Carr, 2015), evidence suggests that the perceived risks, administrative burdens, and knowledge gaps may represent substantial barriers among many prescribers and pharmacists (Beletsky, 2007; Thakur et al., 2020).

For example, in states with laws authorizing NPS prescriptions, pharmacists can provide naloxone to any individual who meets certain criteria specified by a non-pharmacist prescriber or medical licensing board. In some states, these laws permit any authorized prescriber to issue a standing order for naloxone distribution, which often requires effort on the part of pharmacies and pharmacists to find a collaborating prescriber (Green et al., 2015); in other states, the laws direct a state government official to issue a standing order or comparable directive that applies to all entities in the state. In both cases, directives can vary in formulations of naloxone authorized, scope of population covered, and training or educational requirements for the pharmacist dispenser or naloxone recipient (see Davis, 2020). Decisions around the specifics of these directives often take time, sometimes leading to notable lags between the effective date of the NPS prescription law and the signing of the order (e.g., see Mozingo, 2018).

Laws granting pharmacists prescriptive authority instead permit pharmacists to prescribe naloxone directly to patients, meaning there is no need to work with a collaborating naloxone prescriber. Additionally, because these laws directly expand pharmacists' scope of practice and commonly impose pharmacist training requirements (Roberts et al., 2019), pharmacists may be more likely to know about their adoption relative to NPS prescription laws. This is a potentially important distinction because several studies of states with NPS prescription laws have shown that a substantial percentage of pharmacists are unaware that they can dispense naloxone without a patient-specific prescription or exhibit inaccurate beliefs about who can be dispensed naloxone under the standing or protocol order (Evoy et al., 2018; Santa et al., 2021; Thakur et al., 2020). Perhaps partially due to these

information barriers, studies in several states with NPS prescription laws have found that a high percentage of pharmacies fail to stock naloxone (Carpenter et al., 2018; Eldridge and Meyerson, 2020; Evoy et al., 2018).

By explicitly allowing pharmacists to act as naloxone prescribers, prescriptive authority laws may further reduce pharmacists' actual or perceived costs associated with dispensing naloxone. By more directly involving pharmacists in naloxone access efforts, pharmacist prescriptive authority laws may mitigate pharmacists' concerns about dispensing naloxone relative to a NPS prescription model, enhance pharmacists' confidence around naloxone and thus increase their willingness to dispense the medication, and improve accuracy of processes for billing insurance for dispensation under a standing or protocol order (Evoy et al., 2018; Santa et al., 2021; Thakur et al., 2020). To the extent that engaging pharmacists more directly in harm reduction efforts reduces stigmatizing beliefs about individuals seeking naloxone (Santa et al., 2021), these policies may also address discriminatory behavior by pharmacists that results in inequitable naloxone distribution across age, race/ethnicity, or community characteristics.

These factors motivate our approach to study different types of NALs, starting with traditional-prescription NALs which may reduce some liability risks to prescriptions, dispensers, or lay administrators of naloxone, but that do not affect the costs to individuals of obtaining a naloxone prescription through the traditional prescriber-patient relationship model. We then proceed to consider the differential effects of both NPS prescription models and prescriptive authority policies, considering them separately because of conceptual differences in how they affect pharmacists' practices. Because pharmacy-access NALs specifically target the indirect costs associated with obtaining a prescription, we test for differential effects of these policies based on proxies for access to prescribers. Pharmacy-access NALs should have greater impact where the indirect costs to obtaining a prescription are higher. However, NPS distribution models still require collaboration with a prescriber, suggesting that they may not be as effective when there is a shortage of such prescribers. In addition, we consider the role of interactive barriers, testing whether reducing access barriers to naloxone matter more for those with low or high cost-sharing.

2.3. Existing literature

While a small literature has evaluated the effects of NALs on naloxone distribution, most studies have either focused on laws mandating naloxone co-prescription with high-dose opioids (Tormohlen et al., 2024; Green et al., 2020; Sohn et al., 2019) or have evaluated early iterations of NALs prior to the expanded adoption of pharmacist prescriptive authority laws (Gertner et al., 2018; Xu et al., 2018). Abouk et al. (2019) evaluated the effects of "direct authority" NALs, which they defined as state policies providing pharmacists explicit authority to dispense naloxone without a prescription or granting pharmacists prescriptive authority. They found statistically insignificant effects of these laws on naloxone prescribing. However, their analysis was restricted to Medicaid naloxone prescribing and likely underpowered given the noisiness of those data, and the implementation features that accurately distinguish "direct authority" and "indirect authority" are somewhat unclear (Hill et al., 2019).

Most closely related to our current work is a study by Xu and Mukherjee (2021) that evaluated the effects of pharmacist prescriptive authority laws on naloxone dispensing. Using all-payer pharmacy data from 2010 to 2018, they find a significant 53 percent increase in naloxone prescriptions dispensed following prescriptive authority adoption. However, their approach may produce biased estimates of policy effects in the context of policy effect heterogeneity (Sun and Abraham, 2021).

3. Data

To estimate the effects of naloxone access laws on pharmacy distribution of naloxone, we combine data from several sources over the period of 2010 to 2018. Our outcome and policy data are defined at the quarterly level, while our covariate data are quarterly or annual.

Data on state naloxone access laws come from the Prescription Drug Abuse Policy System (PDAPS), supplemented by original legal research. In cases where our legal research disagreed with information in PDAPS, we contacted PDAPS to resolve the discrepancies. In these cases, PDAPS subsequently changed their dates to align with our interpretation; these changes are documented in PDAPS's protocols and reflected in the updated release of its data in January 2022. Specifically, we identified effective dates for: (1) laws that grant pharmacists prescriptive authority for naloxone; (2) laws authorizing dispensing of naloxone by pharmacists without a patient-specific prescription; or (3) traditional-prescription NALs that do not allow pharmacists to dispense naloxone without a patient-specific prescription from another provider.[2] While NALs vary in many ways, we focus on the pharmacy/pharmacist dimension because it directly addresses important non-monetary costs[3] of obtaining naloxone for individuals who may not regularly engage with a healthcare provider or who may not be able or willing to obtain a naloxone prescription from a provider prior to visiting a pharmacy. We test the importance of the traditional-prescription NAL dimension specifically and control for it when studying the two types of pharmacy-access NALs. Table 1 lists the effective dates of the relevant legislation for all states.

We use naloxone pharmacy distribution data from Symphony Health. The Symphony Health data describe a 77 percent sample of naloxone prescriptions dispensed at retail pharmacies. These data were aggregated and provided to us in cells defined by 3-digit zip code and year-quarter. We crosswalked the zip codes to counties for our analysis.[4] We observe fills by insurance coverage status.

We convert the number of naloxone fills by county to per capita rates using population data from the Surveillance, Epidemiology, and End Results (SEER) Program, which modifies published Census data (National Center for Health Statistics, 2021). For the analyses by

[2]Oklahoma is difficult to categorize within this typology as the statute effective in November 2014 (Ok. Stat. Ann. tit. 63 § 2–312.2) directly authorized pharmacists to dispense naloxone without a prescription (and without a standing order), which is not permitted by federal law. Subsequent changes to the law in 2017 clearly grant pharmacists prescriptive authority. We test the sensitivity of treating the 2014 law as NPS prescription distribution and 2017 law as pharmacist prescriptive authority (done in the main analysis) by (1) redefining Oklahoma as adopting pharmacist prescriptive authority in November 2014, and (2) dropping Oklahoma from the analysis.

[3]The policies also potentially address the total costs of obtaining naloxone by removing the need to see a physician, which often carries monetary costs in addition to time costs.

[4]Using Census Bureau geographic crosswalks, 3 digit zip codes are matched to county/state to geolocate fills. When the 3 digit zip codes match to multiple counties/states, population size is used to proportionally allocate the fills.

payer type, we conduct the analysis at the state level since health insurance enrollment figures are available by coverage type through the Kaiser Family Foundation and because we do not conduct any sub-state analyses by health insurance type.

We characterize primary care shortage areas using the Health Professional Shortage Area (HPSA) designations from the end of 2010 (prior to adoption of any of the pharmacy-access NALs). HPSA designations are determined by the Health Resources and Services Administration based on several criteria, with the largest weight given to the population-to-provider ratio (HRSA, 2024). These designations are further discussed in Streeter et al. (2020). The data were accessed as part of the Area Health Resources File which classifies counties into the following three categories: none of the county designated as a shortage area, the whole county designated as a shortage area, and one or more parts of the county designated as a shortage area. We stratify analyses based on these designations. We also stratify some analyses based on whether the county is urban or rural, using county metropolitan designation based on the 2013 Rural-Urban Continuum Codes (RUCCs) from the U.S. Department of Agriculture (metropolitan: codes 1–3, nonmetropolitan: codes 4–9).

To consider the role of pharmacy access, we used the National Plan & Provider Enumeration System (NPPES) to identify the number of pharmacies in each county.[5] We scaled the number of pharmacies by the population size and then categorized counties as below- and above-median per-capita pharmacy access based on this metric. As with the HPSAs, we fixed counties into these categories based on 2010 values (prior to any pharmacy-access NALs).

Finally, covariate data are drawn from several sources. Demographic information is collected from SEER. We include share non-Hispanic White as well as five variables measuring age composition (share aged 0–17, 18–34, 35–44, 45–54, and 55–64). We also condition on several state policy variables that were implemented throughout the same period. Information on adoption of state ACA Medicaid expansion (Abouk et al., 2021), pain management clinic laws (Cerdá et al, 2021; Mizushima at al., 2024), active and legal medical cannabis dispensaries, mandatory-access PDMPs, and Good Samaritan Laws were all available through the RAND-USC Schaeffer OPTIC Policy Database (OPTIC, 2022). When studying both dimensions of pharmacy-access NALs, we also include a control for whether a state has a traditional-prescription NAL.

4. Empirical strategy

We implement a difference-in-differences strategy, comparing quarterly naloxone fills per 100,000 population in treated counties to those in non-adopting counties both before and after policy implementation, using methods that can appropriately accommodate heterogeneous treatment effects. While NALs are state policies, we conduct our analyses at the county-level because of our interest in understanding heterogeneous treatment effects based on more local factors, such as HPSA designation. For the sake of consistency, we perform most analyses at the county-level even when not exploring county-specific

[5]The NPPES only includes pharmacies that accept Medicare and Medicaid reimbursements.

heterogeneity, although results are similar if performed at the state level (see Appendix Fig. 3, discussed below).

The standard two-way fixed-effect (TWFE) estimators used by previous difference-in-differences studies of NAL effects may produce biased treatment effect estimates in the presence of staggered adoption and treatment heterogeneity due to the implicit use of early-adopters as controls for late-adopters (Sun and Abraham, 2021). If the policy effect grows (or attenuates) over time but this dynamic effect is not properly modeled for the early-adopters specifically, those dynamic treatment effects become part of the control for the later-adopters and thus create a "contaminated" control group.

Given concerns about bias due to the interaction of staggered implementation and treatment heterogeneity, we implement an extension of two-stage difference-in-differences (2sDID; Gardner, 2022), an imputation approach that circumvents these concerns.[6] Notably, this approach also accounts for biases induced by additively including covariates in the presence of treatment heterogeneity (Powell, 2023; Caetano et al., 2022). This method models untreated outcomes as a function of county fixed effects, time fixed effects, and covariates, generating parameter estimates using only untreated observations (first stage). Counterfactual outcomes of the treated observations are then imputed based on the parameters estimated in the first stage, with treatment effects then defined as the difference between the observed and counterfactual outcomes for the treated observations. Unlike standard TWFE regressions, this imputation-based approach avoids the problem of "contaminated controls" by imputing counterfactuals based only on untreated observations.

We follow Gardner (2022) by conducting estimation in a GMM framework (Butts, 2023). This approach involves jointly estimating the parameters from both stages such that the standard error estimates account for the variance of the prediction (i.e., the variance associated with the first-stage) (Hansen, 1982). The standard errors are also adjusted for state-level dependence, following the guidance of Rambachan and Roth (2024) to cluster at the level of treatment assignment in quasi-experimental settings. However, many of our analyses rely on few treated units, which potentially creates problems with inference as discussed with "traditional" difference-in-differences methods (Brewer et al., 2018). To provide context for the extent to which our inferential statistics are estimated based on a small number of treated clusters, our main figures and tables list the number of treated states (i.e., clusters) for both NPS and prescriptive authority that are used within each set of analyses.[7] However, we are not aware of any work characterizing or addressing these potential problems specifically for the "new" difference-in-differences estimators.

The introduction of 2sDID, as well as many of the new difference-in-differences methods robust to treatment heterogeneity, considers the case of identifying the average effect of a single policy variable.[8] In our context, we are interested in studying separate dimensions

[6]Borusyak et al. (2024) introduce a related imputation estimator. When the interest is estimation of the average treatment effect (overall or for a specific time period), the estimators produce identical point estimates.

[7]All states help inform the counterfactual since every county must have an untreated pre-period to be included in the analysis to identify the county fixed effect. The not-yet-treated counties help identify the time fixed effects.

[8]de Chaisemartin and D'Haultfœuille (2023) consider multiple treatments.

of NALs, but the policies can be considered non-overlapping. We first study traditional-prescription and pharmacy-access NALs. After that, we jointly study NPS and prescriptive authority policies. We denote prescriptive authority policies as dominating NPS laws, such that analytically we treat data from states that implemented pharmacist prescriptive authority on top of NPS distribution laws as if the NPS policy is no longer in effect. This property provides a straightforward way to extend the imputation approach for our analysis.

We discuss the empirical strategy in the context of studying NPS and prescriptive authority laws. We consider county outcomes untreated if the state has not adopted a pharmacy-based NAL. We designate untreated outcomes for county c and state s at time t as $Y_{cst}(0,\ 0)$, where the first index refers to NPS prescription laws and the second index refers to pharmacist prescriptive authority (equal to 1 if the policy is in place; 0 otherwise). We model

$$Y_{cst}(0,\ 0) = \alpha_{cs} + \gamma_t + \boldsymbol{X}_{cst}^{'}\boldsymbol{\beta} + \varepsilon_{cst}, \tag{1}$$

where α_{cs} represents the county fixed effect, γ_t represents the time (year-quarter) fixed effect, and $\boldsymbol{X}_{st}$ is a vector of time-varying predictors discussed above. Eq. (1) is estimated using only untreated (by pharmacy-access NALs) observations.

The treatment effect for NPS prescription laws is the population-weighted average of outcomes observed with an NPS prescription law in place minus the imputed values for those observations. Let $\mathcal{S}$ represent the set of county-quarters with NPS prescription laws in effect, $P_{\mathcal{S}}$ designate the total population of these observations, and w_{cst} represent the population of county c in state s at time t. The treatment effect then for NPS prescription laws is defined as:

$$\hat{\delta}_1 = \frac{1}{P_{\mathcal{S}}} \sum_{(cs,t) \in \mathcal{S}} w_{cst}(Y_{cst}(1,\ 0) - \hat{Y}_{cst}(0,\ 0)) \tag{2}$$

The pharmacist prescriptive authority treatment effect is defined comparably for the set of state-quarters with pharmacist prescriptive authority NALs, represented by $\mathcal{D}$:

$$\hat{\delta}_2 = \frac{1}{P_{\mathcal{D}}} \sum_{(cs,t) \in \mathcal{D}} w_{cst}(Y_{cst}(0,\ 1) - \hat{Y}_{cst}(0,\ 0)) \tag{3}$$

We also present the equivalent event study estimates defined by year-relative-to-adoption.[9] These estimates help us assess whether the "parallel trends" assumption held prior to adoption and to evaluate dynamic treatment effects. Let t_s represent the quarter of adoption for the state's NPS prescription law and t_D represent the time of adoption for direct authority.

[9]We provide annual event study estimates to improve precision.

The event study estimates are indexed by k, year relative to adoption. As an example, define $\mathscr{D}_{k=1} \equiv \{(c,s,t) \mid 0 \leq t - t_D < 4\}$, which groups the first four quarters post-adoption into a "first year after adoption" estimate. The event study estimates, then, are defined by

$$\hat{\delta}_{2,k} = \frac{1}{P_{\mathscr{P}_k}} \sum_{(cs,t) \in \mathscr{P}_k} w_{cst}(Y_{cst}(0,1) - \hat{Y}_{cst}(0,0)) . \tag{4}$$

For NPS prescription laws, Eq. (3) above implicitly selects on states that have not yet adopted pharmacist prescriptive authority laws as we consider states as not having NPS prescription laws upon adoption of pharmacist prescriptive authority. We apply the same convention to the event study estimates such that, for example, $\mathscr{S}_{k=1} \equiv \{(c,s,t) \mid 0 \leq t - t_s < 4 \ \& \ t - t_D < 0\}$. Thus, the event study estimates for NPS prescription laws do not use any observations from state-quarters with pharmacist prescriptive authority.

The difference-in-differences estimates, defined in Eqs. (2) and (3), are unaffected by jointly studying two dimensions (since they are non-overlapping). However, the pre-treatment event study estimates for the pharmacist prescriptive authority dimension refer only to a subset of the states adopting pharmacist prescriptive authority NALs. By selecting on states without NPS prescription laws, we exclude county-quarters that have NPS prescription laws in place prior to adopting pharmacist prescriptive authority: $\mathscr{D}_{k=-1} \equiv \{(c,st) \mid -4 \leq t - t_D < 0 \ \& \ \text{NPS} = 0\}$. This affects North Dakota and Oregon in our sample. Since these states are "treated" (by NPS prescription policy) prior to adoption of pharmacist prescriptive authority, we should not expect the pre-(pharmacist prescriptive authority)-adoption estimates to be zero, and thus they are not informative about pre-existing trends.

For NPS prescription laws, we present pre-adoption event study estimates relative to 4+, 3, 2, and 1 year prior to adoption. We also present estimates for the year of adoption (year 0)[10] and years 1, 2, and 3+ after adoption. For prescriptive authority, we present estimates referring to the same time-relative-to-adoption time periods, except that the last estimate is for 2+ since we would only observe one state (New Mexico) in the 3+ bin. The "first stage" implicitly normalizes all estimates to the average of the pre-period. All steps in the analyses are population-weighted. Standard errors, as discussed above, are adjusted for the two-stage process and for clustering at the state-level.

While we have data through 2018, our imputation-based approach requires untreated observations to identify the county fixed effects and the time fixed effects. All states adopted one of these policies by 2018q3, implying that the subsequent time fixed effects are not identified. However, even prior to 2018q3, the time fixed effects are identified from only one untreated state, Nebraska,[11] for some of this period. To reduce the potential leverage of a

[10] This is a partially-treated year for many states.

[11] Nebraska is particularly worrisome as the only control state because there is some ambiguity about whether the state should be considered as having an NPS prescription law or not. While Nebraska does not have a statute authorizing NPS prescription distribution

single state driving estimates of the counterfactual, we truncate the sample for our analysis at 2017q2 such that there are always at least three states identifying the time fixed effect. Similarly, Illinois is dropped from the analysis (but not when displaying national trends in naloxone fills) since they adopted a pharmacy-access NAL in January 2010 such that we cannot estimate a state fixed effect for them. Our analysis uses 3031 counties (from 50 states) for 30 time periods ($N = 90{,}930$).

We also report the counterfactual mean, which we define as the average of the outcome variable for observations with pharmacy-access NALs after adjusting for the causal impact of the policies. We subtract off the NPS and prescriptive authority estimates and then calculate the weighted average of this counterfactual for the treated observations. In principle, this is the value of the outcome observed if the state had not implemented a pharmacy-access NAL.

5. Results

We first provide national trends in pharmacy-based naloxone distribution for 2010 to the first half of 2018, presented in Fig. 2. There is a notable increase in naloxone pharmacy distribution starting in 2015, which corresponds with expansion in state laws allowing naloxone distribution without a patient-specific prescription, FDA approval of the first intranasal formulation of naloxone (Narcan), and rising opioid-related overdose deaths nationwide due to the spread of fentanyl.

In the remainder of this section, we present estimates for how adoption of different types of NALs affected pharmacy distribution of naloxone, first presenting aggregate effects (Sections 5.1–5.3), then assessing potential heterogeneous policy effects by community characteristics (Section 5.4) and by patient characteristics (Section 5.5).

5.1. Traditional-prescription and pharmacy-access NALs

We first evaluate the impact of traditional-prescription NALs on naloxone pharmacy distribution. We exclude county*time observations with pharmacy-access NALs from this analysis. We estimate only small (and statistically insignificant) changes in naloxone claims. The event study estimates are shown in Fig. 3 along with the average effect. We estimate that traditional-prescription NALs increased naloxone fills at pharmacies by 0.4 per 100,000. Our pharmacy-access NAL estimates are over 10 times as large, showing statistically significant increases in the first year after adoption with an increasing impact in subsequent years. There is little evidence of pre-existing trends driving this effect. Pre-treatment naloxone dispensing is extremely low—partially because of pre-NAL barriers to obtain a naloxone prescription but also potentially due to limited naloxone access more generally. As a result, for many of our event studies, the pre-treatment estimates are close to zero with tight confidence intervals. None of the pre-treatment estimates are statistically significant (in Fig. 3 or any of the subsequent event studies).

by standing order or otherwise, the state has had a statewide standing order drafted and posted since at least August 2018 (see current version of the order at https://dhhs.ne.gov/DOP%20document%20library/Naloxone%20standing%20order.pdf). The statute referenced within the standing order document as allowing dispensation without a prescription does not in fact do so.

The literature has often assumed that traditional-prescription NALs have little impact on naloxone access, but this assumption is rarely tested or only tested for specific sub-populations (e.g., Abouk et al., 2019; Gertner et al., 2018). This paper provides evidence that these policies do not meaningful impact naloxone distribution through pharmacies. The small magnitudes for the effects of traditional-prescription NALs support our choice to include traditional-prescription NALs as part of the comparison group when analyzing pharmacy-access NALs. However, we will also show results excluding these observations from the analysis entirely. We focus on pharmacy-access NALs for the remainder of this paper.

5.2. NPS and prescriptive authority policies

Next, we study the overall effects of NPS and prescriptive authority policies on naloxone distribution, distinguishing between the two types of pharmacy-access NALs. Table 2 presents the average policy effects, while Fig. 4 presents event study results from several different models. We first show results in which we do not condition on any time-varying covariates (Fig. 4, Panel A). We observe little evidence of pre-existing trends–the pre-period estimates are small and never statistically different from zero. Once adopted, we see uniquely large (relative to pre-period movements) increases in the number of naloxone prescriptions dispensed for both types of pharmacy-access NAL; however, the growth is more immediate and persistent for prescriptive authority laws. Prescriptive authority policies increase naloxone claims by 7.1 per 100,000 on average versus 2.8 per 100,000 for NPS policies (Table 2, column 1). This difference is statistically significant at the 10 % level.

Conditioning on our set of time-varying covariates produces generally similar results (see Panel B of Fig. 4). In the first year after adoption, NPS prescription laws increase quarterly pharmacy naloxone purchases by 2.8 claims per 100,000 (11.2 per year); prescriptive authority laws increase purchases by 7.4 claims per 100,000 (29.6 per year), as presented in Table 2, column 2. The difference between the two policies is statistically significant at the 5 % level.

Panel C includes additional predictors to address concerns that illicitly-manufactured fentanyl, which became increasingly incorporated into the U.S. drug supply around the same time our policies of interest were increasingly adopted, may independently drive purchasing of naloxone. To model the fentanyl crisis, we add a control for non-medical OxyContin misuse rates (measured in 2004–2009 prior to reformulation) interacted with year indicators; these interactions have been shown to predict a large share of heroin (Alpert et al., 2018) and synthetic opioid deaths (Powell and Pacula, 2021).[12] Across both sets of analyses, our estimates are relatively unaffected by the exclusion or inclusion of these controls.

In Panel D of Fig. 4, we limit the analysis to observations with NALs, such that the comparison group is observations with traditional-prescription NALs.[13] We provide the average effect estimates in Table 2, Column 4. We also provide the equivalent results for

[12]While these variables may not fully predict the geography of the fentanyl crisis, Powell and Pacula (2021) show that setting the 2017 interaction to zero would eliminate all excess (relative to 2010) synthetic opioid deaths in 2017.

[13]This approach eliminates counties in states that did not have a traditional-prescription NAL prior to pharmacy-access NAL adoption. Since there is no “pre-period” for these counties, they must be dropped from the analysis.

when the comparison is observations without any type of NAL in Column 5 (see Appendix Fig. 1 for the event study results). The results are generally comparable to the main results regardless of these changes to the comparison group.

5.3. Additional sensitivity analyses

We estimate large effects of pharmacy-access NALs on the distribution of naloxone through retail pharmacies. There is little evidence that these increases are driven by pre-existing trends, and the results are stable regardless of whether we account for demographic and policy changes as well as differential exposure to the fentanyl crisis, suggesting coefficient stability. In addition, we find that the results are stable to how we categorize Oklahoma's 2014 policy (see footnote 2) (Appendix Fig. 2). In addition, the results are similar when we re-estimate the event studies using state-level data and condition on state fixed effects (Appendix Fig. 3).

As shown above in Fig. 2, naloxone distribution increased substantially over time nationally. One concern with the difference-in-differences approach is that pre-period naloxone fill rates were low for the early-adopters and may not adequately predict post-adoption counterfactuals. Notably, however, the pre-treatment event study estimates (from Fig. 4) are never statistically significant. To the extent that the treated states were differentially increasing naloxone dispensing for secular reasons, we would expect to see some differential growth prior to policy adoption, even if the magnitude of that growth is not comparable to the post-treatment magnitudes. We do not observe any evidence of growing differences in the pre-period. The small magnitudes of the estimates appear to reflect the importance of pharmacy-access NALs such that there was little retail distribution of naloxone prior to their adoption.

As a sensitivity test to including time periods in which naloxone prescription fills were low, we replicate our results while using only NAL adopters that adopted in 2014 or later. We present the results in Appendix Fig. 4 (Panel A) and Table 2, Column 6. We observe similar (although larger) results and little evidence of pre-existing trends despite amplified scope to observe such trends for this sample. We replicate this analysis while only using adopters that adopted in 2015 or later (see Column 7 and Appendix Fig. 4, Panel B). This group is even more likely to exhibit pre-existing trends if the policies were adopted endogenously. As before, the results are not sensitive to time of adoption and there is still little evidence of pre-existing trends. If the main estimates were an artifact of exponential growth, then we would expect to see some evidence of differential growth in the pre-period when we select on late adopters. Instead, the small placebo effect sizes seem to reflect the small year-to-year changes in dispensing prior to pharmacy-access NAL adoption.

Results from the sensitivity tests support the validity of our approach's identifying assumptions, but they do not address the fact that NALs have not been adopted in isolation. It is possible that some state NALs have been spurred or accompanied by campaigns to increase awareness of the benefits of naloxone, or by general changing attitudes towards naloxone. To the extent that such campaigns are transitory, they are unlikely to explain the dynamic, growing effects shown in Fig. 4, suggesting that the policies themselves are critical. Pre-existing campaigns or attitudinal shifts would be revealed in the pre-treatment

estimates. However, it is difficult to directly observe and model these other factors. In the next sections, we consider heterogeneity of the policy effects to test whether pharmacy-access NALs disproportionately increase naloxone access in the areas that we would expect. A secondary motivation of this analysis is to test the causal nature of the estimates since we would expect statewide campaigns to target areas with high risk of overdose deaths, not necessarily areas with primary care shortages. Notably, shortage and non-shortage areas have nearly-identical opioid-related overdose death rates prior to pharmacy-access NAL adoption,[14] suggesting that differences across these areas are due to policy effect heterogeneity and not due to concurrent awareness campaigns or other factors disproportionately targeting HPSAs.

5.4. Effects by health professional shortage status and pharmacy access

We find that pharmacy-access NALs, which reduce the costs of obtaining a prescription before visiting a pharmacy, have large impacts on naloxone access. In this section, we explore the extent to which we observe disproportionate effects in areas where we might expect that a patient-specific prescription would represent a major cost. Specifically, we stratify counties by whether they were designated as a Health Professional Shortage Area for primary care physicians. Fig. 5 repeats our main analysis for each set of counties. In Panel A, we observe small effects in counties which were not designated shortage areas. The average effects, as shown in Table 3, for the two types of policies are both statistically significantly different from zero at the 5 % level and are similar to each other. In contrast, counties with a primary care shortage experience large effects resulting from prescriptive authority policies in particular (see Panel B of Fig. 5 and Column 2 of Table 3). We also study counties which are considered “partial shortage areas.” The prescriptive authority effects are in-between the non-shortage and shortage county estimates, as shown in Panel C of Fig. 5 and Column 3 of Table 3.

The results for NPS prescription laws show relatively consistent effects on naloxone dispensing regardless of shortage status–the effect of NPS laws is estimated to be slightly smaller in counties with a primary care shortage. This could reflect the fact that many NPS prescription models still require pharmacists and pharmacies to work with a collaborating provider to implement the NPS prescription model; thus, while patients/consumers in primary care shortage areas experience larger cost reductions with the passage of an NPS prescription law, the costs to pharmacies of finding a collaborating provider may still pose an important barrier.

Shortage areas are not predominantly rural, so these results are unlikely to reflect differences due to rurality.[15] For reference, we provide event study estimates stratified by rurality in Appendix Fig. 5. We estimate much larger prescriptive authority effects in urban areas. In Appendix Fig. 6, we stratify the analysis by the interaction of shortage areas (we show

[14]Using restricted National Vital Statistics System (NVSS) mortality data with county identifiers, we calculated the mean opioid-related overdose death rate for shortage and non-shortage counties in the four quarters prior to adoption (since policy adoption is at the state level, this approach compares these counties within the same calendar time periods). Shortage counties experienced 9.98 opioid-related overdose deaths per 100,000 in the 4 quarters prior to pharmacy-access NAL adoption, compared to 9.97 / 100,00 for non-shortage counties in the same time periods.

[15]In our data, 44 % of rural counties are designated as primary care shortage areas, compared to 38 % of urban counties.

results only for shortage and non-shortage areas) and rurality. We find that prescriptive authority policies primarily increase naloxone dispensing in urban counties designated as shortage areas (see Table 3, Column 7). We estimate much smaller effects in all other sets of counties (see Table 3, Columns 4–6). These results would be consistent with superior pharmacy access in urban areas such that prescriptive authority policies primarily help areas in which it is both relatively costly to get a prescription and relatively easy to find a pharmacy dispensing naloxone.

To consider this hypothesis specifically, we quantify pharmacy access at the county-level and then stratify based on this dimension. Using data from the National Plan & Provider Enumeration System (NPPES), we collect information on pharmacies and geolocate them to their county. We designate "low pharmacy access" as counties with below-median pharmacies per capita.[16] "High pharmacy access" counties are those with above-median pharmacy access. Appendix Fig. 7 presents estimates based on the interaction of primary care shortage areas and pharmacy access. We find that prescriptive authority policies have the largest effects in primary care shortage areas which also have above-median pharmacy access.

These findings suggest that prescriptive authority policies are disproportionately effective in exactly the areas that we would expect. When the cost to obtaining a timely naloxone prescription is relatively high, prescriptive authority policies increase naloxone dispensing through pharmacies at greater rates. These increases are even larger when there is greater pharmacy access. NPS policies have less of a relationship with primary care shortage areas and pharmacy access.

5.5. Effects by insurance status

The monetary cost of naloxone is another barrier to access (Jacobson and Powell, 2024). Pharmacy-access NALs do not directly address the price of naloxone to the recipient; thus, the reduction in non-monetary costs due to pharmacy-access NALs may not be effective if other meaningful barriers such as price are jointly preventing naloxone purchases. In this section, we consider the differentials effects of these policies on naloxone purchases by insurance status given the large differences in out-of-pocket prices by payer type (Peet et al., 2022). We conduct the analysis at the state-level given the availability of health insurance enrollment figures by payer type back to 2010.

We provide event study estimates in Fig. 6 and average effects in Table 4. For both NPS and pharmacist prescriptive authority NALs, we estimate large and statistically significant increases in naloxone distribution regardless of payer type. However, the largest effects are for the Medicare and Medicaid populations, the groups that face the lowest out-of-pocket costs for naloxone (Peet et al., 2022). This result is consistent with interactive returns to reducing both legal barriers and monetary costs, although other explanations are also possible and we only consider this evidence suggestive.[17] However, we also

[16] As with the shortage areas, we fix this metric in time for a period prior to any pharmacy-access NAL adoption.
[17] In particular, these populations might be disproportionately in need of naloxone due to high overdose death rates (Kuo et al., 2019; Lindner et al., 2023).

estimate relatively small effects for the privately-insured population. The privately-insured typically face out-of-pocket prices much higher than those of the Medicaid and Medicare populations, although they are still subsidized. We also estimate small effects for the uninsured population. This population has high need for naloxone given their high rate of overdose deaths (Altekruse et al., 2020), and they likely faced the highest pre-policy costs to obtaining naloxone through the traditional prescription model; however, they also face high out-of-pocket costs to acquiring naloxone (Peet et al., 2022).[18] The findings by insurance status are generally consistent with the idea that price operates as an additional barrier to naloxone purchases, though this evidence is only suggestive.

6. Conclusion

In 2022, more than 109,000 Americans died from a drug overdose, continuing the two decades long upward trend despite substantial government efforts to change the trajectory (Tanz et al., 2024). The toll of opioid-related mortality is high enough to bear responsibility for declining U.S. life expectancy after 2013 (Currie and Schwandt, 2020). While there have been dramatic increases in the volume of naloxone dispensed from pharmacies, there remains substantial need to further expand access through both community-based programs and pharmacy channels (Irvine et al., 2022).

Our findings provide some insights into the inconsistent conclusions of the public health impacts of NALs that characterize the prior literature. We find that traditional-prescription NALs have small and statistically insignificant effects on dispensing of naloxone through pharmacies, which could mute the impact of these policies on downstream outcomes. However, laws removing the need for an individual to obtain a patient-specific prescription prior to entering a pharmacy are highly effective at expanding naloxone dispensing through pharmacies. Both NPS prescription and pharmacist prescriptive authority laws significantly increase naloxone dispensing, suggesting that these laws may be more effective at expanding distribution and increasing the likelihood that naloxone will be used to save a life. By studying differential effects based on primary care shortage areas—a proxy for the cost of obtaining a prescription for naloxone—we found that prescriptive authority policies in particular are effective at improving naloxone dispensing in exactly the areas that we would expect, where access to prescribers is limited and where pharmacies may find it difficult to collaborate with a prescriber if required by law to do so (Green et al., 2015). These results add to the broader literature suggesting that expansions in scope of practice of pharmacists may be important in achieving timely responses to emerging public health crises (Hilts et al., 2022; Rodriguez et al 2020; Sachdev et al., 2020).

Our results also suggest that NPS prescription laws reduce important barriers to naloxone access through pharmacies, but there may be additional administrative and informational costs that NPS laws alone fail to alleviate. We cannot speak specifically to which barriers were the most important in the case of naloxone, although our finding of smaller effects of these laws in primary care shortage areas suggests that placing the onus on pharmacists to

[18]The uninsured would likely face the highest costs to obtaining a patient-specific prescription for naloxone, suggesting they should be disproportionately responsive to pharmacy-access NALs. Their relative lack of response is consistent with the independent importance of the out-of-pocket costs they face for the product itself.

find a collaborating prescriber may be a contributing factor. Additionally, it is possible that pharmacists are more aware of changes in their scope of practice than the implementation of NPS prescription laws. Informational barriers may mitigate the potential effects of these laws on naloxone distribution through several mechanisms, including confusion around insurance billing or a failure to adequately stock naloxone, which has been noted as common issue (Abbas et al., 2021; Eldridge et al., 2020; Evoy et al., 2018; Graves et al., 2019; Meyerson et al., 2018; Spivey et al., 2020). Because we only observe filled prescriptions, we cannot directly assess the extent to which individuals might be unable to fill naloxone prescriptions due to inadequate pharmacy supply.

This study shows that pharmacy-access laws are effective at increasing the distribution of naloxone to a broad group of recipients, particularly those in primary care shortage areas. Significant and substantive increases in naloxone distribution through retail pharmacies are observed even among the uninsured, although effects for those with higher out-of-pocket costs are meaningfully smaller than for those with public insurance. Overall, our findings suggest that the recent FDA policies making Narcan and RiVive available over-the-counter (OTC) may do even more to provide greater access to naloxone. It also suggests, however, that the impacts of Opvee, a new opioid antagonist with similar properties to naloxone that is believed to be more effective at reducing an overdose from fentanyl, may not be as widespread as anticipated since it requires a prescription.

Our results are subject to several limitations. First, we use the date in which the state law went into effect, not when these policies became widely known by pharmacists and other prescribers. Our event study analyses help address the problem of implementation lags by considering delayed effects of these policies, but the use of methods robust to heterogenous policy effects across states and over time comes with the tradeoff of truncating our data series such that we cannot reliably estimate longer term effects past 2018.[19] Second, we only examine the impact of these policies through one access channel for naloxone: pharmacies. While our limited focus on pharmacies is helpful for identifying the direct impact of the policy on the targeted mechanism, it is possible that these policies —particularly NPS prescription laws—have additional impacts through other channels. Future work should consider the possible impact these policies have on distribution of naloxone through overdose education and naloxone distribution programs, law enforcement agencies, and in criminal justice settings, which are not directly captured through pharmacy data. Finally, the timing of NAL adoption coincides with other broad efforts to encourage wider dissemination and use of naloxone, but we do not have systematic data on these non-statutory interventions. To the extent that states implemented public awareness campaigns for pharmacy-based naloxone or subsidized naloxone purchases coincident with their NALs, our estimates will reflect the joint effect of these efforts. We view the results of our heterogeneity analysis as supporting a causal attribution of our estimated effects to NALs. Our heterogeneity analysis suggests that such confounding awareness campaigns are less likely to be driving the results since we observe larger effects in exactly the areas that we

[19]With homogenous treatment effects and estimating a TWFE model, the specification implicitly assumes that any effect estimated among early adopters holds in later periods, permitting estimation of relative differences for a second policy. With heterogeneous treatment effects, this type of extrapolation is not imposed.

would expect the policies to be most effective. Those are not necessarily the same places that would be targeted by awareness campaigns given that, on average, they do not have higher overdose death rates (see footnote 13).

This study provides the first empirical evidence that the differential costs faced by individuals and pharmacists are important considerations for achieving the goal of broader distribution of naloxone, which is a necessary first step for strategies seeking to reduce the mortality burden of the opioid crisis. It further provides important insights into the complex and interactive role that prescribing, dispensing and consumer costs play in shaping the prescribing and distribution of vital medications. As states consider potential expansions of pharmacists' scope of practice, it provides yet another example of how pharmacist prescriptive authority can be a broadly effective strategy for achieving greater dispensing or distribution of medications that seek to improve public health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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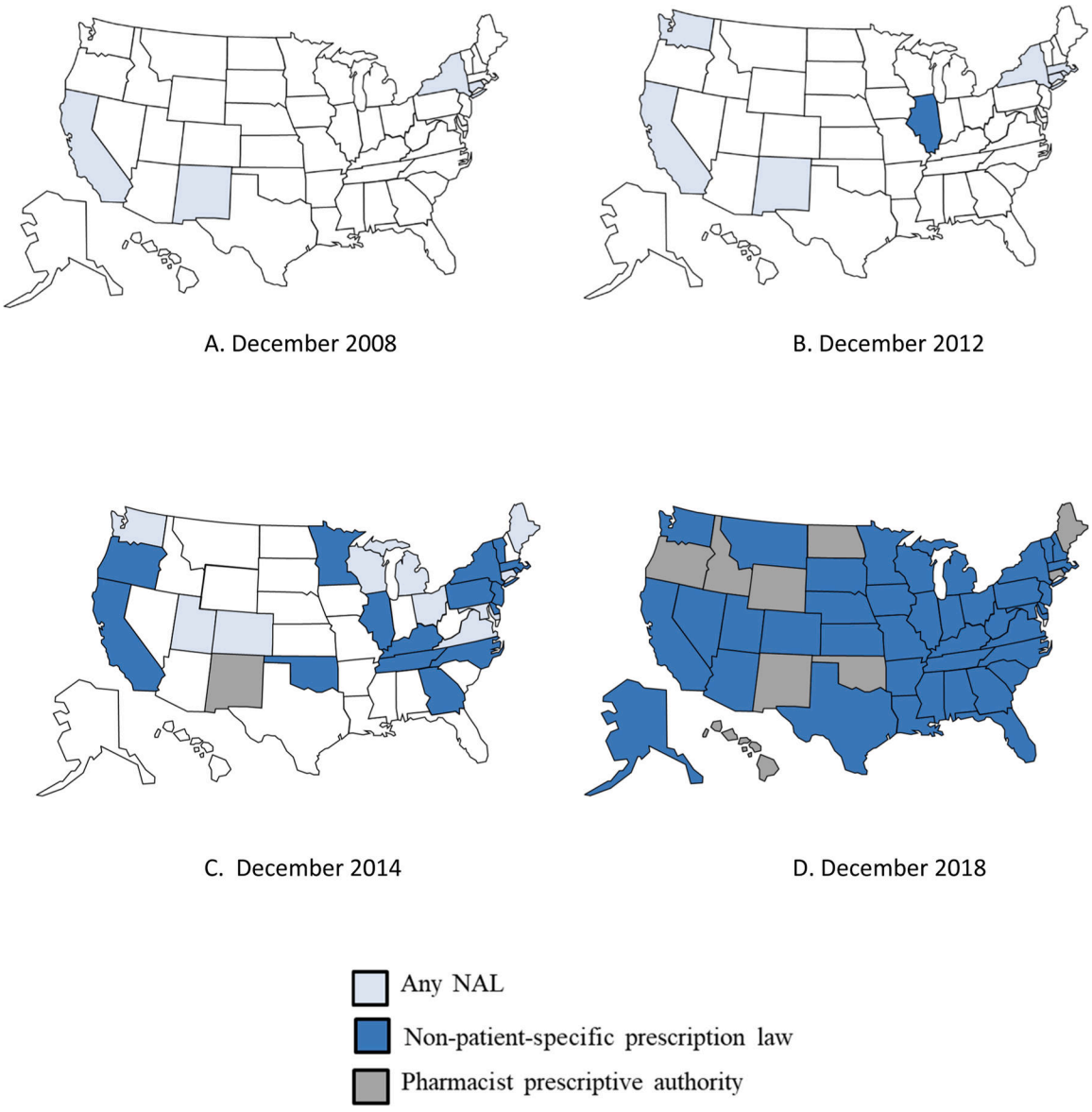


Fig. 1.

Map of state naloxone access laws over time.

Notes and sources: PDAPS and authors' own legal analysis. As of December 2018, the following states had both non-patient-specific prescription and pharmacist prescriptive authority laws: Connecticut, District of Columbia, Hawaii, Maine, New Mexico, Oklahoma, Oregon, and Wyoming.

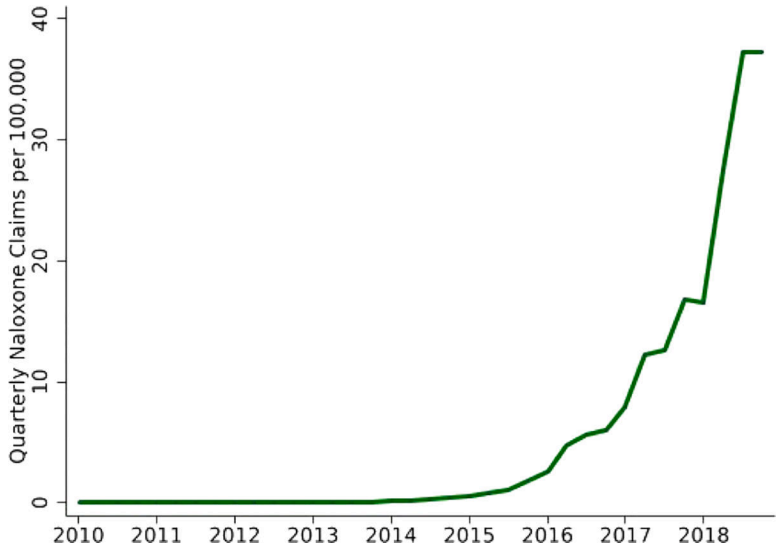
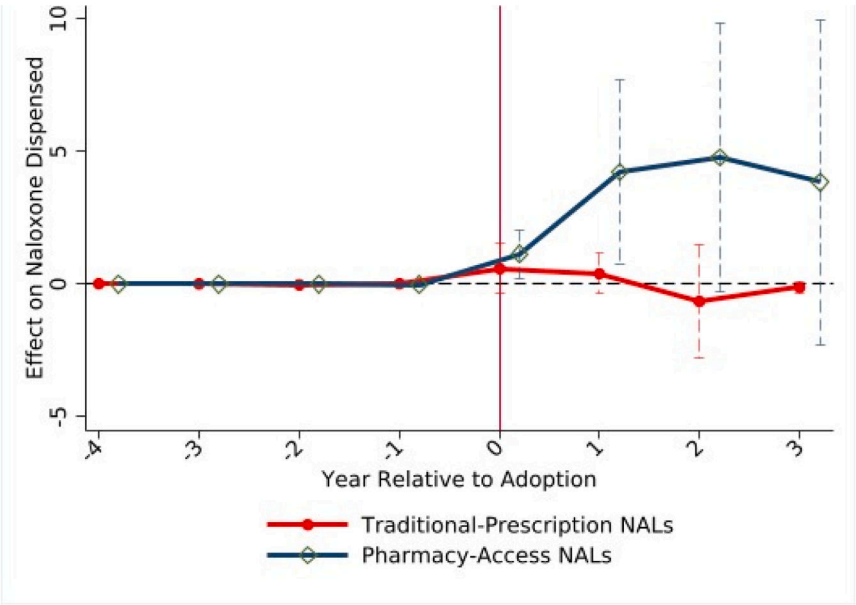


Fig. 2.

Quarterly national naloxone claims per 100,000.

Sources: Symphony Health Data: 2010q1–2018q2.



Mean Effect Estimate for traditional-prescription NALs = 0.401 (0.329)
Mean Effect Estimate for pharmacy-access NALs = 4.021*** (1.250)
p-value for difference in effects = 0.006

Fig. 3.

Effects of NALs on rates of naloxone distribution through retail pharmacies.

Notes and sources: Symphony Health data (2010q1–2017q2). *N* = 90,930 (3031 counties). Number of treated states = 17. Outcome is quarterly naloxone prescription fills per 100,000 population. 95 % confidence intervals are adjusted for state-level clustering. 2sDID used for estimation. The traditional-prescription NAL and pharmacy-access NAL estimates are estimated in separate analyses. The traditional-prescription NAL sample excludes any observations with a pharmacy-access NAL. The pharmacy-access NAL sample excludes any observations with a traditional-prescription NAL. We condition on county fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no NALs) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. The −4 estimate refers to 4 years or before; the 3 estimate refers to 3 years or after. All models and estimates are population-weighted.

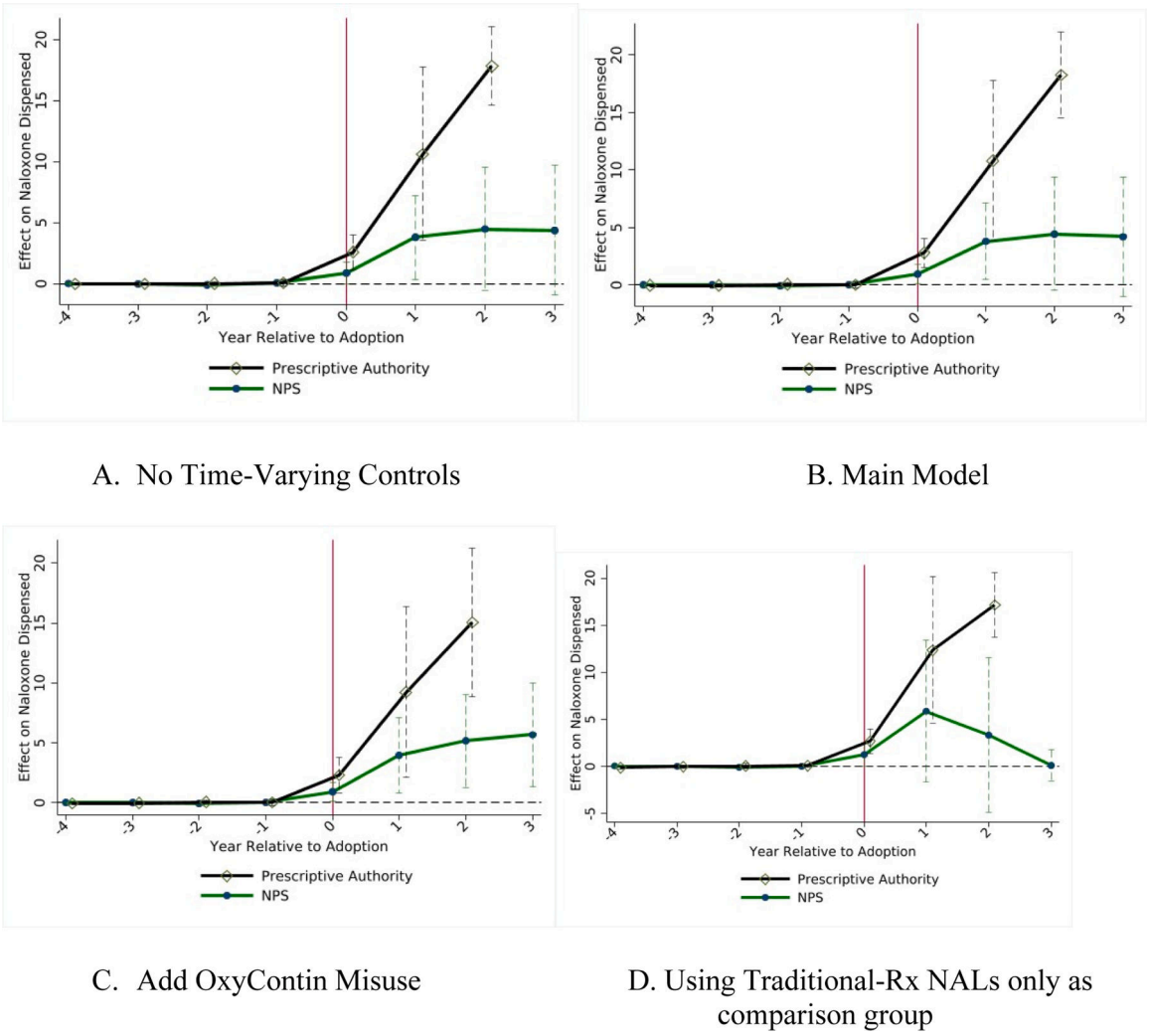


Fig. 4.

Effects of pharmacy-access NALs on naloxone distribution rates.

Notes and sources: Symphony Health data (2010q1–2017q2). $N = 90{,}930$ (3031 counties). In Panels A–C, Number of NPS states = 42; Number of Prescriptive Authority states = 6. In Panel D, Number of NPS states = 17; Number of Prescriptive Authority states = 3. Outcome is quarterly naloxone fills per 100,000. 95 % confidence intervals are adjusted for state-level clustering. 2sDID used for estimation. We condition on county fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no non-patient-specific prescription or pharmacist prescriptive authority laws) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, non-pharmacy NALs, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. The −4 estimate refers to 4 years or before; the 3 estimate refers to 3 years or after. For prescriptive authority, the 2 estimate refers to 2+. See text for definition of the estimates. All models and estimates are population-weighted.

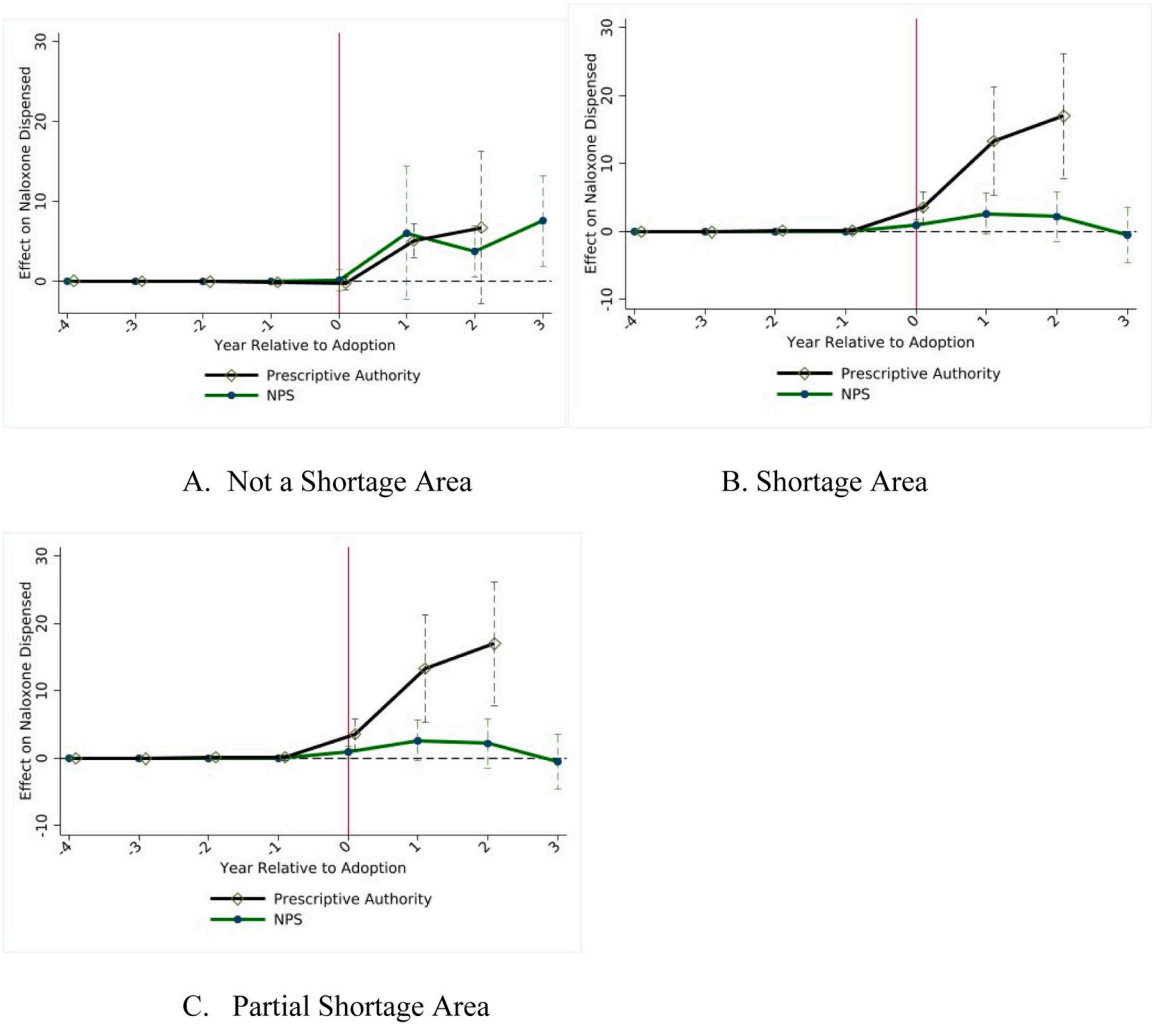


Fig. 5.

Effects of pharmacy-access NALs on naloxone distribution, stratified by primary care shortage areas.

Notes and sources: Symphony Health data (2010q1–2017q2). Outcome is quarterly naloxone fills per 100,000. 95 % confidence intervals are adjusted for state-level clustering. Samples are stratified based on whether county was designated as a primary care shortage area in 2010. 2sDID used for estimation. We condition on county fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no non-patient-specific prescription or pharmacist prescriptive authority laws) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, non-pharmacy NALs, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. The −4 estimate refers to 4 years or before; the 3 estimate refers to 3 years or after. For prescriptive authority, the 2 estimate refers to 2+. See text for definition of the estimates. All models and estimates are population-weighted. Panel A uses $N = 16{,}020$ (534 counties); Panel B uses $N = 38{,}190$ (1273 counties); Panel C uses

N = 36,660 (1222 counties). Panel A: Number of NPS states = 35; Number of Prescriptive Authority states = 3. Panel B: Number of NPS states = 41; Number of Prescriptive Authority states = 6. Panel C: Number of NPS states = 42; Number of Prescriptive Authority states = 5.

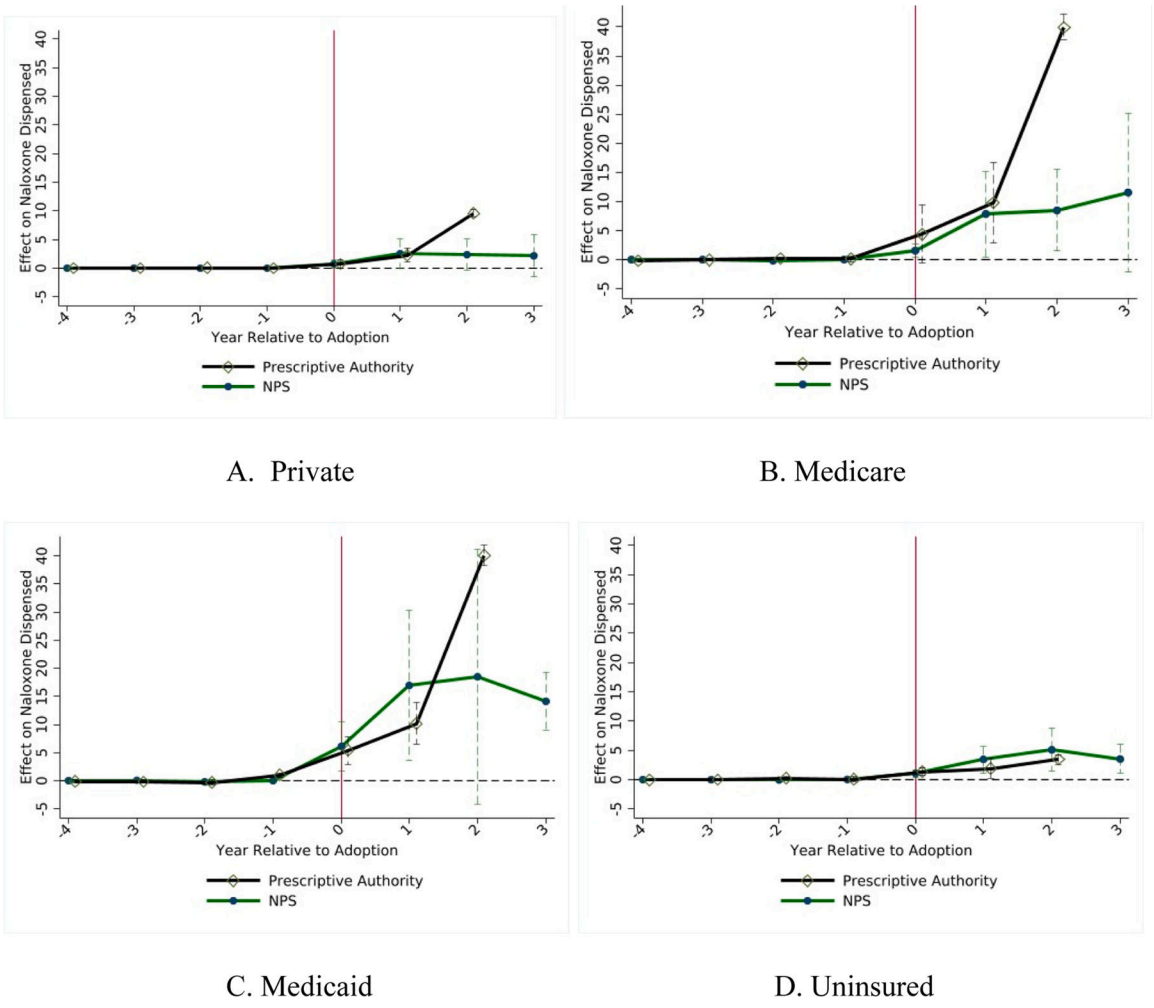


Fig. 6.

Effects of pharmacy-access NALs on naloxone distribution, stratified by naloxone recipient insurance status.

Notes and sources: Symphony Health data (2010q1–2017q2). $N = 1500$ (50 states). Number of NPS states = 42; Number of Prescriptive Authority states = 6. Outcome is quarterly naloxone fills by insurance coverage type per 100,000 (people in that county with listed insurance coverage). 95 % confidence intervals are adjusted for state-level clustering. 2sDID used for estimation. We condition on state fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no non-patient-specific prescription or pharmacist prescriptive authority laws) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, non-pharmacy NALs, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. The −4 estimate refers to 4 years or before; the 3 estimate refers to 3 years or after. For prescriptive authority, the 2 estimate refers to 2+. See text for definition

of the estimates. All models and estimates are population-weighted (by type of insurance coverage).

Table 1

State naloxone access laws (NALs) as of December 2018.

	Any NAL	Non-patient-specific prescription law	Pharmacist prescriptive authority law
Alabama	July 2015	July 2015	
Alaska	April 2016	April 2016	
Arizona	September 2016	September 2016	
Arkansas	August 2015	August 2015	
California	January 2008	January 2014	
Colorado	June 2013	May 2015	
Connecticut	October 2003	October 2017	July 2015
Delaware	September 2014	September 2014	
District of Columbia	April 2013	March 2017	March 2017
Florida	July 2015	July 2016	
Georgia	May 2014	May 2014	
Hawaii	July 2016	July 2016	July 2018[a]
Idaho	July 2015		July 2015
Illinois	January 2010[a]	January 2010[b]	
Indiana	May 2015	May 2015	
Iowa	June 2016[b]	June 2016 [c]	
Kansas	July 2017	July 2017	
Kentucky	July 2013	July 2013	
Louisiana	September 2015	September 2015	
Maine	May 2014	November 2015	June 2018[a]
Maryland	October 2013	October 2015	
Massachusetts	September 2012	July 2014	
Michigan	November 2014	April 2017	
Minnesota	June 2014	June 2014	
Mississippi	July 2015	July 2015	
Missouri	September 2016	September 2016	
Montana	May 2017	May 2017	

	Any NAL	Non-patient-specific prescription law	Pharmacist prescriptive authority law
Nebraska	June 2015	September 2018	
Nevada	October 2015	October 2015	
New Hampshire	July 2015	July 2015	
New Jersey	July 2013	July 2013	
New Mexico	May 2001	April 2016	April 2014
New York	Apr 2006	July 2014	
North Carolina	May 2013	May 2013	
North Dakota	August 2015	August 2015	April 2016
Ohio	April 2014	August 2015	
Oklahoma	November 2013	November 2014	November 2017[a]
Oregon	July 2013	July 2013	April 2016
Pennsylvania	December 2014	December 2014	
Rhode Island	July 2012	April 2014	
South Carolina	July 2015	July 2016	
South Dakota	July 2016	July 2016	
Tennessee	July 2014	July 2014	
Texas	September 2015	September 2015	
Utah	June 2014	June 2016	
Vermont	July 2013	July 2013	
Virginia	July 2013	May 2015	
Washington	July 2010	August 2015	
West Virginia	June 2015	July 2016	
Wisconsin	May 2014	January 2016	
Wyoming	July 2017	July 2017	July 2017

Notes: Effective month is assigned based on the first full month the law was effective. I.e., if the law was effective the first of a given month, that month is used; if the law was effective the 2nd or later in a given month, the subsequent month is used.

[a]To ensure sufficient control units, our primary analysis truncates the sample period to end in 2017q2, and thus these states are not used to identify pharmacist prescriptive authority law effects.

[b]Because Illinois had a standing order before the beginning of our sample period, we exclude it from our policy effect analyses. The imputation approach requires estimates of a county fixed effect, which is not possible if we never observe the county as untreated. However, we include Illinois when presenting summary statistics (i.e., Fig. 2).

[c]Note that for Iowa, the legislature adopted two different bills (one house bill and one senate bill) regarding the naloxone access law section, both with an effective date of May 27, 2016. However, one amended the section and made those amendments retroactive to April 6, 2016, implying that the entire statute must be retroactive to April 6, 2016; for the purposes of our analyses, however, we use the May date.

Table 2

Difference-in-differences estimates for effects of non-patient-specific prescription and pharmacist prescriptive authority laws on rates of naloxone distribution through retail pharmacies (quarterly naloxone prescription fills per 100,000).

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Non-patient-specific (NPS) prescription	2.820*** (1.024)	2.841*** (0.956)	3.091*** (0.791)	3.187 (1.945)	2.846** (1.136)	2.951*** (1.122)	3.187 (1.945)
Pharmacist prescriptive authority (PA)	7.140*** (2.089)	7.417*** (2.086)	6.338*** (2.296)	9.769*** (1.412)	7.426*** (2.291)	8.287*** (2.251)	9.769*** (1.412)
p-value for test of equality	0.056	0.046	0.174	0.006	0.057	0.034	0.006
Counterfactual NPS mean	1.776	1.754	1.504	2.539	1.75	1.847	2.539
Counterfactual PA mean	2.146	1.869	2.948	2.529	1.86	1.672	2.529
Time-varying controls?	No	Yes	Yes	Yes	Yes	Yes	Yes
Control for Oxycontin misuse?	No	No	Yes	No	No	No	No
Sample	Full	Full	Full	NALs only	Traditional-Rx NALs excluded	2014+ adopters and non-adopters	2015+ adopters and non-adopters
Number of Observations	90,930	90,930	90,930	16,337	81,740	82,200	66,720
Number of Counties	3031	3031	3031	1065	3031	2740	2224
Number of NPS states	42	42	42	17	42	37	29
Number of PA states	6	6	6	3	6	5	4

Notes:

*** 1 %

** 5 %

* 10 % statistical significance.

The outcome is county quarterly naloxone prescription fills per 100,000 based on Symphony Health data. Standard errors in parentheses adjusted for state-level clustering and the two-step estimation process. 2sDID used for estimation. We condition on county fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no NPS prescription or pharmacist prescriptive authority) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, non-pharmacy NALs, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. “OxyContin misuse” refers to including the 2004–2009 rate of OxyContin misuse interacted with year indicators. All models and estimates are population-weighted. *P*-value is result of a test of equality of the NPS prescription and pharmacist prescriptive authority law estimates. Counterfactual means are the estimated number of claims per 100,000 in NPS or prescriptive authority state-quarters if they had no pharmacy-access NAL.

Table 3

Difference-in-differences estimates for effects of non-patient-specific prescription and pharmacist prescriptive authority laws on rates of naloxone distribution through retail pharmacies, by health professional shortage area status and rurality outcome is quarterly naloxone prescription fills per 100,000.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Non-patient-specific (NPS) prescription	3.410** (1.508)	1.639* (0.976)	3.559*** (1.159)	2.449* (1.449)	−0.279 (1.782)	3.641** (1.662)	2.324** (0.940)
Pharmacist prescriptive authority (PA)	3.246*** (1.172)	9.016*** (2.313)	7.108*** (1.595)	5.203 (4.423)	0.329 (1.990)	2.668*** (0.772)	11.514*** (2.163)
p-value for test of equality	0.928	0.002	0.077	0.553	0.687	0.545	0.000
Counterfactual NPS mean	1.432	2.092	1.622	1.142	3.561	1.538	1.465
Counterfactual PA mean	1.408	2.529	1.422	0.359	3.959	1.738	1.770
Sample	Non-Shortage Counties	Shortage Counties	Partial Shortage Counties	Rural Non-Shortage Counties	Rural Shortage Counties	Urban Non-Shortage Counties	Urban Shortage Counties
Number of Observations	16,020	38,190	36,660	8910	25,500	12,690	7110
Number of Counties	534	1273	1222	297	850	423	237
Number of NPS states	35	41	42	28	39	28	41
Number of PA states	3	6	5	3	5	1	5

Notes:

*** 1 %

** 5 %

* 10 % statistical significance.

The outcome is county quarterly naloxone prescription fills per 100,000 based on Symphony Health data. Standard errors in parentheses adjusted for state-level clustering and the two-step estimation process. 2sDID used for estimation. We condition on county fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no NPS prescription or pharmacist prescriptive authority) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, non-pharmacy NALs, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. All models and estimates are population-weighted. *P*-value is result of a test of equality of the NPS prescription and pharmacist prescriptive authority law estimates. Counterfactual means are the estimated number of prescription fills per 100,000 in NPS or prescriptive authority state-quarters if they had no pharmacy-access NAL.

Table 4

Difference-in-differences estimates for effects of non-patient-specific prescription and pharmacist prescriptive authority laws on rates of naloxone distribution through retail pharmacies, by insurance status. outcome is quarterly naloxone prescription fills per 100,000.

	Private insurance	Medicare	Medicaid	Uninsured
Non-patient-specific (NPS) prescription	1 718 *** (0.647)	5.518 *** (1.698)	12.716 *** (4.424)	2.549 *** (0.737)
Pharmacist prescriptive authority (PA)	2.078 *** (0.606)	10.386 *** (2.876)	15.253 *** (1.965)	1.811 *** (0.464)
p-value for test of equality	0.684	0.139	0.588	0.399
Counterfactual NPS mean	1.153	3.571	2.349	0.755
Counterfactual PA mean	1.434	3.940	2.567	0.645

Notes:

*** 1 %

** 5 %

* 10 % statistical significance.

N = 1500 (50 states). Number of NPS states = 42; Number of Prescriptive Authority states = 6. The outcome is state quarterly naloxone prescription fills per 100,000 based on Symphony Health data. Standard errors in parentheses adjusted for state-level clustering and the two-step estimation process. 2sDID used for estimation. We condition on state fixed effects, quarter fixed effects, and covariates. The parameters associated with these variables are estimated using untreated (no NPS prescription or pharmacist prescriptive authority) observations only. The covariates include the share of the population that is White, ages 0–17, ages 18–34, ages 35–44, ages 45–54, and ages 55–64 plus policy variables. The policy variables are Good Samaritan Laws, Medicaid expansions under the ACA, pain management clinic laws, non-pharmacy NALs, mandatory-access PDMPs, and legal and operational medical marijuana dispensaries. All models and estimates are population-weighted (by type of insurance coverage). *P*-value is result of a test of equality of the NPS prescription and pharmacist prescriptive authority law estimates. Counterfactual means are the estimated number of prescription fills per 100,000 in NPS or prescriptive authority state-quarters if they had no pharmacy-access NAL.