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ABSTRACT

Prescription Drug Monitoring Programs and Neonatal Outcomes*

Over the last two decades, the number of delivering mothers using or dependent on opiates has increased dramatically, giving rise to a five-fold increase in the proportion of babies born with neonatal abstinence syndrome (NAS). First, the current study documents NAS trends in the United States and their substantial variation across states. Second, it explores the relationship, if any, between the adoption of prescription drug monitoring programs (PDMPs) and reductions in NAS incidence across the United States. We find that the introduction of operational PDMPs reduced NAS incidence in the United States by 10%. We also examined the effects on birth outcomes, infant mortality, and other pregnancy complications and find little evidence of any effect of PDMPs on birth weight, premature births, and infant mortality.

JEL Classification: I10

Keywords: opioid crisis, infant outcomes, health policy, United States

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1 Introduction

Prescription opioids are often used prenatally as painkillers or because of opiate dependency (Yazdy et al., 2015). Opioid medications can be prescribed to manage lower back and pelvic pain, or other pain conditions such as myalgia, joint pain, and migraine. While opioids may help manage acute pain, there is increasing evidence of their adverse effects on fetal development.

Over the last decade, the number of opioid-addicted children has soared dramatically (Patrick et al., 2015a; O'Donnell et al., 2009; Patrick et al., 2013). Additionally, there is growing evidence that opioids may be associated with birth defects (Yazdy et al., 2015). Furthermore, the number of newborns presenting with neonatal abstinence syndrome (NAS) continues to increase. NAS is a postnatal drug withdrawal syndrome caused by in-utero exposure to opioids. Infants with NAS are more likely to experience serious medical complications and have longer hospital stays (Creanga et al., 2012; Broussard et al., 2011). In particular, NAS has been associated with central nervous system irritability, gastrointestinal dysfunction, and temperature instability (Hudak et al., 2012). Around 40–80% of neonatals exposed in utero to opioid consumption develop NAS and require prolonged hospitalization and pharmacotherapy (Yazdy et al., 2015).

Despite evidence of its adverse effects on pregnancy outcomes (Yazdy et al., 2015), studies consistently document high rates of prescription opioid use during pregnancy (Patrick et al., 2015b). Previous studies suggest that in-utero opioid exposure can stem from maternal prescription opioid use (Desai et al., 2015). Indeed, recent studies show that 14–20% of women during pregnancy had filled a prescription for an opioid, with codeine and hydrocodone being the most commonly prescribed opioids (Desai et al., 2014; Bateman et al., 2014). In a recent report, the Center for Disease Control and Prevention (CDC) suggests that the effective use of prescription drug monitoring programs (PDMPs) may help reduce NAS incidence (Ko, 2016).

The incidence of NAS increased by more than 5 times between 2000 and 2012 (see Figure

1). To illustrate this magnitude of change, if the overall incidence rate of NAS were 1.2 cases per 1,000 hospital births in 1999, this number would have increased to 7.9 in 2013. While over the last two decades NAS incidence increased in most states, the rate of change differed substantially among them. In West Virginia, NAS incidence in 2013 was 33.4 per 1,000 births (Rogerson et al., 2018), while in Hawaii it was 0.7. Such differences reflect both variations across states in opioid-prescription rates and the prevalence of illicit opioid use, but they could also in part reflect differences in how NAS is classified within the data.

The public costs of NAS are high: 80% of the $1.5 billion in NAS-related annual charges, for example, is funded by Medicaid programs (Patrick et al., 2012, 2015a). Thus, shedding light on both the factors behind recent NAS trends and their geographical variations can provide insights and inform governments as they craft public health responses to the opioid epidemic and the recent growth in postnatal opioid withdrawal syndrome. This paper documents geographical variation in NAS incidence across the United States and evaluates the impact on neonatal outcomes of programs that monitor prescribing and dispensing behavior.

PDMPs have been implemented by many states to track electronically both prescribers and patients. Currently, most states have an operational PDMP, and a few have introduced mandatory access provisions that legally require health care practitioners to access records before prescribing and dispensing a controlled substance.

Although a few reports evaluate the local impact of state programs on NAS occurrence (Roussos-Ross and Triplett, 2017), no study has analyzed at the national level the impact of PDMPs on the NAS epidemic; furthermore, no study has analyzed the impact of PDMPs on other at-birth health metrics. As such, through the current study, we make two main contributions. First, we document variations in NAS incidence across US states. Second, we analyze the effects of PDMPs on NAS incidence rates and other pregnancy outcomes. To the best of our knowledge, the current study is the first to analyze the effects of PDMPs on NAS incidence and birth outcomes.

While previous studies found operational PDMPs to have little or no effect on drug

abuse (Meara et al., 2016; Dave et al., 2017; Buchmueller and Carey, 2018), some evidence suggests that PDMPs may be effective in reducing drug abuse in at-risk and disadvantaged populations (Mallatt, 2017). In particular, PDMPs may serve as an additional tool by which to screen pregnant women for drug abuse. Pregnancy provides an opportunity to identify patients at risk of drug abuse, and previous studies suggest that pregnancy can motivate women with substance use disorders to seek treatment (Davis and Yonkers, 2012). Indeed, the American College of Obstetricians and Gynecologists suggests that "the Prescription Drug Monitoring Program is a valuable resource to determine whether patients have received prior opioid prescriptions," as it invites providers to capture a comprehensive patient history of substance use by consulting the PDMP database (American College of Obstetricians and Gynecologists, 2017; Patrick et al., 2017).

Using data drawn from State Inpatient Databases (2000-2013), we find evidence that the adoption of PDMPs reduced NAS incidence by 10%. Furthermore, although not precisely estimated, our results suggest that –if anything–the introduction of mandatory programs may have further contributed to NAS reduction. Finally, we analyze the effects of PDMPs on birth outcomes, and find them to be small or null.

The current study relates to a handful of studies that analyze the effects of PDMPs on drug abuse, crime, and child well-being (Kilby, 2015; Mallatt, 2017; Patrick et al., 2016; Simoni-Wastila and Qian, 2012; Meara et al., 2016; Gihleb et al., 2018). The main contribution of this study with respect to the previous literature is that it evaluates the effects of PDMPs on NAS and other birth outcomes.

This paper is organized as follows. Section 2 discusses the background of this study as well as the data used herein. We present the empirical specification in Section 3, and our main results (including those of robustness checks) are discussed in Sections 4 and 5. Concluding remarks are provided in Section 6.

2 Background and Data

2.1 Background

According to CDC estimates (Rudd, 2016), the rise in the United States of prescription drug use and abuse largely accounts for trends in drug-related deaths. Previous scholars linked the opioid crisis to long-run socioeconomic decline (Case and Deaton, 2015) and documented its contribution over the last two decades to the reversal in the decline of mid-life all-causes mortality. In addition, a growing set of studies relate the opioid epidemic to physician behavior and supply-side regulation (Alpert et al., 2017; Pacula et al., 2015; Ruhm, 2018). Among other factors, the 1996 market entry of OxyContin and the diffusion of aggressive pain management strategies contributed substantially to the surge in opioid use over the last two decades (Laxmaiah Manchikanti et al., 2012; Evans et al., 2019). Reports also suggest that most of the individuals at high risk of fatal overdose obtained prescription drugs from physicians, and doctor shopping is considered the main source of supply.[1]

To respond to the dramatic increase in fatal overdoses and drug abuse, states have introduced several programs to improve opioid-prescribing practices, inform clinical practice, and protect at-risk patients. PDMPs leverage electronic databases that track controlled substance prescriptions in a state; these give health authorities and pharmacies access to timely information about prescribing and patient behaviors. Access to these records can help identify patients who are receiving multiple prescriptions that may be contributing to the epidemic. Nonmandated PDMPs do not legally require health professionals to undertake queries; however, since 2007, a few states have extended their PDMPs with mandatory access provisions that require doctors and pharmacies to query PDMPs before prescribing a controlled substance. Table 1 lists the dates that operational and mandatory PDMPs became effective in each state.[2]

[1] `https://edition.cnn.com/2017/07/31/health/opioid-doctors-responsible-overdose/index.html`

[2] The dates reported in Table 1 in the Appendix were obtained from Mallatt (2017), who in turn collected them from the National Alliance for Model State Drug Laws, Brandeis University's Prescription Drug

Previous studies evaluating the effects of PDMPs on opioid consumption have reached various conclusions. While there is consensus among them that PDMPs reduce oxycodone shipments (Kilby, 2015; Mallatt, 2017), their findings are mixed with regard to hydrocodone shipments or other abuse outcomes. While some researchers found evidence that nonmandated PDMPs reduce fatal nonoxycodone-related overdoses and poisonings (Mallatt, 2017; Patrick et al., 2016; Simoni-Wastila and Qian, 2012), most of them found evidence of small or null effects on drug abuse (Simoni-Wastila and Qian, 2012; Meara et al., 2016). However, recent studies focusing on the effects of mandated PDMPs found significant effects on opioid quantity and shopping behavior, abuse outcomes, substance abuse facility admissions, crime rates, and fatal drug overdoses (Buchmueller and Carey, 2018; Patrick et al., 2016; Dave et al., 2017; Borgschulte et al., forth.; Mallatt, 2017). The lack of consistent evidence on the effectiveness of PDMPs can be partially explained by the fact that physicians do not generally endorse PDMP access as a solution to the opioid crisis (Buchmueller and Carey, 2018). In some of the adopting states, the proportion of physicians using PDMPs has been very low (Poston, 2012). More generally, physicians complained about the difficulty of interpreting and using prescribing history, and about the complexity of accessing this information (Islam and McRae, 2014).

2.2 Data

2.2.1 Neonatal Abstinence Syndrome Data

We drew data on NAS incidence from the State Inpatient Databases, which include deidentified administrative data from all hospital inpatient discharges in a given state. These data are compiled by state partners and then harmonized as part of the Healthcare Cost and Utilization Project (HCUP). Our analysis includes data from 28 states whose data are

Monitoring Program Training and Technical Assistance Center, state legislative laws and bills, government newsletters, news articles, articles from peer-reviewed journals, and pharmacy-board websites. As an alternative definition, we adopt the operational dates reported in Table 2 of Horwitz et al. (2018). Results obtained using these alternative classifications are reported in the Appendix.

publicly available from HCUP's online central distributors for the years 1999–2013.[3]

In the hospital discharge records from the 1999-2013 period, we identified in-hospital births by referencing International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes V30.X-V39.X ending in 00 or 01 (indicating single or multiple live-born infants). Following Ko (2016), we excluded discharge records that did not have a principal or secondary diagnosis code indicating a hospital birth, or which indicated a transfer from another acute care hospital or health care facility. We identified NAS cases as those with ICD-9-CM code 779.5 (i.e., drug withdrawal syndrome in a newborn). We also excluded from the numerator possible iatrogenic withdrawal cases, a condition that results from complications related to prolonged neonatal intensive care stay and not exposure during the antenatal period (ICD-9-CM codes: 765.01-765.05, 770.7, 772.1X, 779.7, 777.5X, 777.6).

We calculated cases per 1,000 births using data available from a subset of states between 1999 and 2013 and determined NAS incidence rates for each state and year for which data were available. Although data are not available for all the US states, when examining birth outcomes we found no evidence of sample selection between states covered in our NAS data and states for which NAS data are not available.

2.2.2 Natality Data

Data on birth outcomes are drawn from CDC Natality Detail Data. This dataset contains state-level counts of births occurring in the United States. We obtained counts by state, birth weight, and gestation period for the years 2000–2017. Using these data, we constructed state-level shares of the children born with low birth weight (i.e., a birth weight below 2,500 grams) or very low birth weight (i.e., a birth weight below 1,500 grams), and the share of children born prematurely (fewer than 37 weeks of gestation). These metrics are all markers of poor health at birth.

[3]See `https://www.hcup-us.ahrq.gov/tech_assist/centdist.jsp`. These states include Arizona, Arkansas, California, Colorado, Florida, Hawaii, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, Mississippi, Nebraska, Nevada, New Jersey, New Mexico, New York, North Carolina, Oregon, Rhode Island, South Carolina, South Dakota, Utah, Vermont, Washington, West Virginia, and Wisconsin.

2.2.3 Infant Mortality Data

We drew infant mortality data from linked birth and infant death records from the CDC (2000-2017). This data collection provides death counts and rates for children under one year of age, occurring within the United States to US residents. Information from death certificates were linked to corresponding birth certificates.

2.2.4 Other Data

We then collected a set of control characteristics at the state level from the Population and Housing Unit Estimates (PHUE; 2000–2016), the US Census (2000), and the American Community Survey (2001–2013). Using PHUE data, we calculated the child population. Furthermore, using 2000 US Census and 2001–2013 American Community Survey data, we constructed a set of demographic controls. Furthermore, following Meara et al. (2016), we controlled for the timing of the adoption of other laws that may have affected prescription drug abuse (e.g., "good Samaritan" laws, doctor shopping, pain clinic regulations, physician exams laws, "ID required" laws, and tamper-resistant prescription form requirement laws). Finally, we control for the OxyContin reformulation following Alpert et al. (2017) and Evans et al. (2019).

3 Empirical Specification

To identify the dynamic response of NAS cases to drug monitoring programs, we adopt an event study methodology and estimate the following equation:

$$Child_{st} = \sum_{t=-10, t\neq 0}^{10} (\gamma_t PDMP_{s,t-\tau}) + \beta X_{st} + \delta_s + \phi_t + \delta_s * t + \epsilon_{st}, \tag{1}$$

where $Child_{st}$ is the number of NAS cases per 1,000 births in year t in state s. $PDMP_{st}$ is an indicator for whether state s has introduced a PDMP in year t. X_{st} are a set of

time-variant state-level controls (i.e., age composition, share of Black population, share of Hispanic population, median income, gender composition, and unemployment rate). δ_s are state fixed effects that capture time-invariant state-level characteristics; ϕ_t are year fixed effects that capture the average national trend in child abuse; $\delta_s * t$ are state-specific time trends. Standard errors are clustered at the state level. In addition, we include in all the tables p-values obtained using the wild cluster bootstrap method. All estimates are weighted by the total number of births. This model isolates the short-run impact of the policy. It is worth noting the restricted number of states for which NAS data are available and the fact that most states adopted a mandate after 2012. On account of these circumstances, we are unable to conduct an event study on the effects of mandatory PDMPs on NAS.

We also report the results obtained using a difference-in-difference (DD) specification. Our identification strategy relies on the assumptions that prior to the adoption of drug monitoring programs, treated and untreated states followed parallel trends and that in the absence of program implementation, their paths would have remained unchanged. To identify the effects of the program, we exploit within-state changes in trends at the time PDMPs were implemented. As shown in our event study, the effect of PDMPs on NAS cases materializes two years after PDMP enactment. Thus, consistent with this evidence and that from previous work on the effects of PDMPs on drug abuse (Buchmueller and Carey, 2018; Dave et al., 2017; Gihleb et al., 2018), we use a two-year lag to estimate our DD model.

As previous studies point out, the lagged effect can be explained in terms of the time it takes for provider practices to diffuse across the state, and that there is a natural lag between increased prescription drug monitoring and a reduction in the overall supply of drugs. Furthermore, in our case, the effects are mechanically delayed by the nine-month duration of a pregnancy.

Like Kolstad and Kowalski (2012), we also present results in terms of pre-, during (τ=0 or τ=1), and post- ($\tau \geq 2$) implementation periods.[4]

[4]As mentioned, for the states adopting a PDMP in the middle of the year, by redefining treatment as starting the year after the adoption, the effect of the program was found to occur slightly earlier.

In practice, we estimated the following ordinary least squares model:

$$NAS_{st} = \beta PDMP_{s,t-2} + \psi X_{st} + \delta_s + \phi_t + \delta_s * t + \epsilon_{st}, \quad (2)$$

where NAS_{st} is the number of NAS cases per 1,000 births or foster-care admissions in year t in state s. $PDMP_{s,t-2}$ is an indicator for whether state s has introduced a PDMP by year t. As mentioned, X_{st} comprises a set of time-variant state-level controls (i.e., age composition, share of Black population, share of Hispanic population, median income, gender composition, and unemployment rate). Following Meara et al. (2016), we control for the adoption of other laws that may have affected prescription drug abuse (e.g., "good Samaritan" laws, doctor shopping, pain clinic regulations, physician exams laws, "ID required" laws, and tamper-resistant prescription form requirement laws). Additionally, following Alpert et al. (2017) and Evans et al. (2019), we control for the OxyContin reformulation. Finally, we include year fixed effects (thus capturing the average national trend in NAS incidence), state fixed effects (thus capturing time-invariant county-level characteristics), and state-specific time trends. All estimates are weighted by child population.

4 Results

Figure 2 shows trends in NAS incidence, treatment admissions for opiates and synthetic drugs abuse, and drug-related deaths between 2000 and 2013. The three series describe growth relative to 2000. There is a remarkably close relationship between the spread of the opioid epidemic and the dramatic increase in cases of NAS. In particular, NAS trends closely mirror those regarding admissions for opiate and synthetic drug abuse treatment. By contrast, the relationship to drug-related deaths becomes less evident after 2006. While NAS incidence increased in most states, there has been large geographical variation in the rate of change across US states. Figure 3 shows NAS incidence across US states between 2011 and 2013. Recall that NAS data are available for only 28 states (see also Table 2) and

there is marked variation across the United States: the incidence is highest in Vermont, West Virginia, and Maine (more than 20 cases per 1,000 births) and lowest in Hawaii and South Dakota (less than one case per 1,000 births). The change in NAS incidence between 2000 and 2013 was highest in West Virginia, where it increased 21.5-fold (see column 3, Table 2).

Table 3 reports the summary statistics of our study outcomes. While natural concerns may arise regarding sample selection and the external validity of the results, we show that the 28 states for which we had data are no different from the rest of the United States with respect to the incidence of low birth weight and infant mortality. (These results are available upon request).

Figure 4 presents the results of our event study on the effects of an operational PDMP on NAS incidence. The figure visualizes the dynamic response of NAS cases to the adoption of operational PDMPs. In our baseline specification, we include year and state fixed effects as well as state-specific time trends.[5] This analysis highlights a marked decline in the number of NAS cases following PDMP implementation. That decline becomes statistically significant two years after PDMP enactment (see also Table 4 and Figure A.2). Consistent with previous evidence on the effects of PDMPs, the effects of the policy were not immediate; as mentioned, the effect may have been delayed for various reasons. First, some time may need to pass before health practitioners can gather representative information on patients in the PDMP database (Buchmueller and Carey, 2018). Second, practices do not diffuse immediately within a state. Third, it may take some time to observe effects, as in the short run, drug abusers may have access to alternative supply sources (Dave et al., 2017). Fourth, given the nine-month duration of a pregnancy, the effects on NAS and birth outcomes may be mechanically delayed. Fifth, many states adopted a PDMP late in the year, and thus the effects of the program may become apparent only the year after adoption.[6] The results

[5]The inclusion of state-specific time trends reduces the noise significantly, yet Figure A.4 documents a similar trend when we do not include state-specific time trends in the event-study.

[6]Unfortunately, we do not have access to monthly NAS data. However, in redefining treatment such that a state is treated in the first full year after implementing the policy, we show that, as expected, the effect of operational PDMPs materializes earlier than in our baseline figure. (These results are available upon request.)

remain substantially unchanged when we include time-varying controls at the state level (e.g., other state policies that may have affected opioid consumption, or socio-demographic characteristics; see Figure A.1).

As only a few of the states for which we have NAS data adopted a mandatory PDMP before 2013, we do not have enough variation to conduct an event study to estimate the effects of mandatory PDMPs on NAS.

Given this evidence, we adopt a DD strategy that focuses on the effect of mandatory PDMPs two years after program implementation. However, we report alternative definitions of the model while separately considering in the robustness checks the pre- (before t), during (t to $t+1$), and post- ($t+2$ and onwards) implementation periods.

Table 5 presents the estimated effect of PDMPs on NAS incidence. We find evidence that PDMP adoption reduced NAS incidence, and the magnitude of the effects is economically significant. In column 1, we include only controls for state and year fixed effects. The point estimate suggests an approximate 20% reduction in NAS incidence. In column 2, we include controls for the introduction of other state-level laws that may correlate with reduction in opioid use, and account for the reformulation of OxyContin (Alpert et al., 2017; Evans et al., 2019). If anything, the effects become larger and is more precisely estimated. When controlling for demographic characteristics, the effects reduce NAS incidence by approximately 50% but remain economically and statistically significant, pointing to a 13% reduction in the incidence of NAS cases with respect to the mean. The results are robust to the introduction of state-specific time trends (column 4) and the inclusion of a control that accounts for the reformulation of OxyContin (Alpert et al., 2017; Evans et al., 2019) (column 5). The coefficient becomes slightly smaller, but still negative and statistically significant. The point estimate of column 5 suggests that the introduction of an operational PDMP implies a 9% reduction in NAS incidence with respect to the mean: in the average state, this is equivalent to approximately 28 fewer cases per year. Previous studies suggest a $17,000 (in 2018 dollars) higher hospital cost for children born with NAS (Winkelman et al., 2018), and so our results

imply an annual nationwide reduction in hospital costs of $24.2 million. It is worth noting that we estimate intention-to-treat effects and thus the treatment-on-the-treated effects are likely to be substantially larger.

Our results suggest that the introduction of a mandatory PDMP may have resulted in further reduced NAS incidence (see Table 6); however, given the limited availability of NAS data across states and the more recent implementation of mandatory PDMPs nationally, the effects of mandatory PDMPs are less precisely estimated.

A few studies found little evidence of the effects of nonmandated PDMPs in the general population (Simoni-Wastila and Qian, 2012; Meara et al., 2016; Buchmueller and Carey, 2018; Dave et al., 2017; Gihleb et al., 2018). However, previous research has also shown that doctors are more likely to query nonmandated PDMPs when dealing with patients from high-abuse populations, or for whom the adverse effects of drug abuse may be particularly harmful (Goodin et al., 2012; Irvine et al., 2014; Ross-Degnan et al., 2004; Mallatt, 2017). In particular, doctors may be more careful in prescribing drugs to pregnant women following the guidelines of the American College of Obstetricians and Gynecologists (American College of Obstetricians and Gynecologists, 2017). We view these results as consistent with those of previous studies.

4.1 Effects on Birth Outcomes

Using the Natality Detail Data—which contain information on the universe of live births between 2000 and 2017—we examine the effects of PDMP adoption on birth weight, gestational age, and infant mortality. Overall, we find little evidence of significant effects on these metrics of infant health.

Additionally, we find no significant effect of PDMP adoption on the share of children born with a low birth weight (LBW; see Figure 5 and Table 7). We find some evidence of small and only marginally significant effects of mandatory PDMPs on the share of children born with low birth weight (see Figure 6).

We also find no significant effects on prematurity or on the share of very low birth weight children. Finally, there is no evidence of significant effects on infant mortality (see Figure A.6 and Table 8). Yet, consistent with the results shown in Figure 6, there is some mild evidence of a decline in the share of very low birth weight and premature children after the adoption of mandatory PDMPs (Figure A.7). Nonetheless, these estimates are largely imprecise and should be interpreted as suggestive at best.

Previous studies show a significant association between NAS and the risk of low birth weight (Patrick et al., 2015a). As we estimate an average reduction of 28 NAS cases per state per year as a result of PDMP adoption, it is not surprising to find nonsignificant effects on low birth weight when one aggregates results at the state level, especially given the much higher incidence of low birth weight. Over the study period, the average number of low birth weight children was 80 per 1,000, while there were on average only 3.75 children per 1,000 born with NAS. Similarly, given the relatively small effects of PDMPs on NAS and the overall low incidence of NAS compared to other outcomes, it is not surprising that one finds no evidence of any significant effects of the adoption of operational PDMPs on prematurity and infant mortality. Furthermore, there is evidence suggesting that different opioids may have heterogeneous effects on weight gain (Kandall et al., 1976; Hulse et al., 1997), and recent evidence finds no evidence of significant differences in the weight trends of NAS children compared to appropriately matched counterparts (Corr et al., 2018). At the same time, there is increasing evidence regarding the long-run effects of NAS on child development (Reddy et al., 2017; Fill et al., 2018). Thus, even if NAS may have little effects on birth weight and other coarse measures of infant health, it may still have a substantial impact on human capital.

5 Robustness Checks

First, we check the sensitivity of our results to the use of PDMP effective start dates, as suggested by Horwitz et al. (2018). As Figure A.2 shows, the results are substantially confirmed. The DD point estimates are slightly smaller but generally comparable in magnitude and significance, and not statistically different from our baseline estimates (see Table A.1). We also confirm the lack of significant effects of operational PDMPs on birth outcomes (see Figure A.3).

In a recent study, Goodman-Bacon (2018) shows that the average treatment effect in a DD study is biased when effects change over time. As a robustness check, we reweight the results using the balanced test suggested by (Goodman-Bacon, 2018). We show that the unconditional coefficient estimated through this procedure is only marginally smaller (-.58) than that obtained in our original specification (-.82). We also perform a placebo test with multiple random permutations of treatment assignment. Figure A.5 shows the distribution of the placebo coefficient. Reassuringly, we reject the null hypothesis as our baseline estimate is far outside the distribution under the null (p-value: 0.004).

While the timing of PDMP adoption is likely to be endogenous, we show that to explain away our main result on NAS incidence, the extent of selection on unobservables should be at least 12 times larger than the extent of selection on observables that determine PDMP adoption (Oster, 2017).

We also present estimates using alternative models in Table 9. In particular, in column 1, we consider the date of PDMP adoption as the beginning of treatment period. In column 2, we exclude from the treatment period the year of adoption. In column 3, we exclude from the treatment the first two years following the adoption of the PDMP. Finally in column 4, we define examine separately the period of the initial implementation (first two years (t_0, t_1) and the subsequent period (t_2+). Consistent with the evidence from the event-study, the effect of PDMP is not immediate, and materializes only after the firs year.

Finally, we test the robustness of our findings to omitting one state at a time from our

sample. Figure 7 shows that the point estimate of the effects of PDMPs on NAS incidence is not significantly affected when any one state is excluded from the analysis. Similarly, we show that the point estimate of the effect of mandatory PDMPs on the share of low birth weight children is not affected by the exclusion of a particular state (Figure 8).

6 Conclusion

In the United States, the incidence of neonatal abstinence syndrome (NAS) has increased dramatically over the last two decades. However, there is substantial variation across states.

States have implemented various strategies in response to NAS. The adoption of prescription drug monitoring programs (PDMPs) has been shown to reduce inappropriate prescribing practices and the number of overdose deaths. In the current study, we show that the adoption of PDMPs reduced the incidence of NAS in the United States. In fact, using data drawn from the State Inpatient Databases, we find evidence that the adoption of PDMPs reduced NAS incidence by 10%. Mandatory programs reduced NAS by a further 4%, although estimates are not precisely estimated. Examining vital statistics from the Natality Detail Data, we find no evidence that operational PDMPs reduced the share of low birth weight children; however, states that adopted a mandatory PDMP reduced the share of low birth weight children by 1.5%. It is worth remarking that we estimate intention-to-treat effects. On one hand, our results align with previous evidence that mandatory PDMPs have been more effective than operational PDMPs; however, at the same time, our findings align with those of previous studies showing that operational PDMPs reduce drug abuse among high-abuse populations and individuals at higher risk of adverse effects.

The current study contributes to our understanding of the connection between parental opioid use and neonatal outcomes. Furthermore, it estimates the effectiveness of policies that aim to monitor prescription behavior. Taken together, our results suggest that PDMPs may help reduce the incidence of NAS and additionally have small but nonetheless relevant

effects on the share of children born with low birth weight. Policy-makers should not neglect these indirect effects when evaluating the costs and benefits of PDMPs. In any case, it is worth stressing that PDMPs are not an effective tool in monitoring illicit drug use, and so these programs might be less effective in the current context—namely, where heroin and illicit fentanyl are driving the opioid crisis—than they were during the period analyzed in this study.

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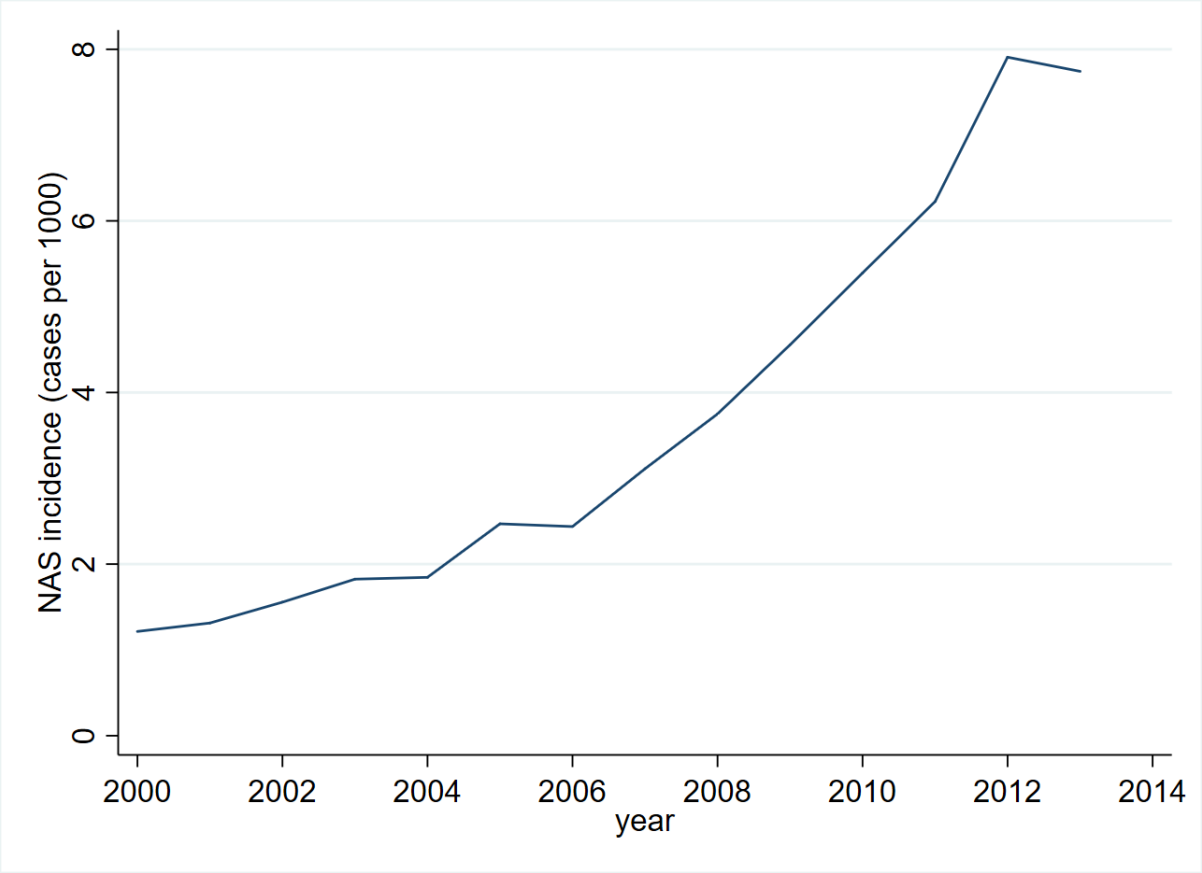
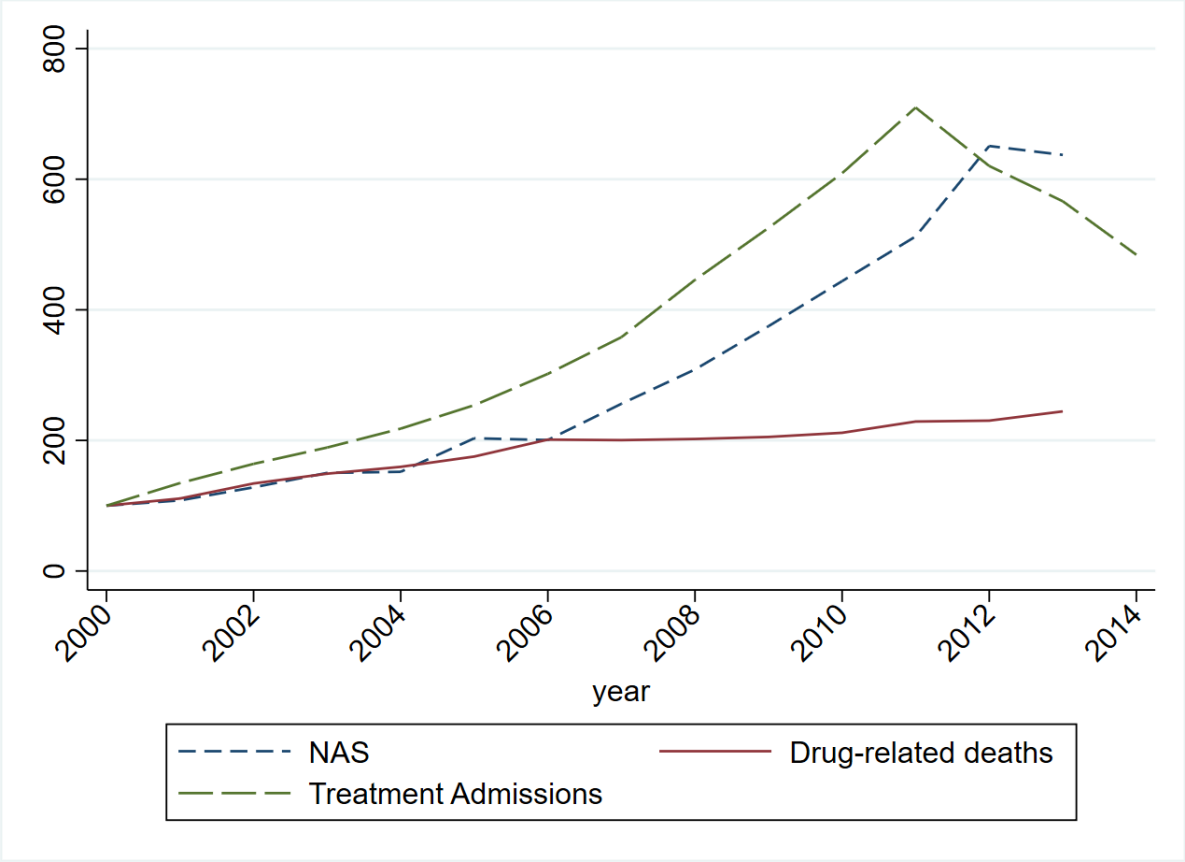
Figure 1: NAS Incidence, 2000–2013



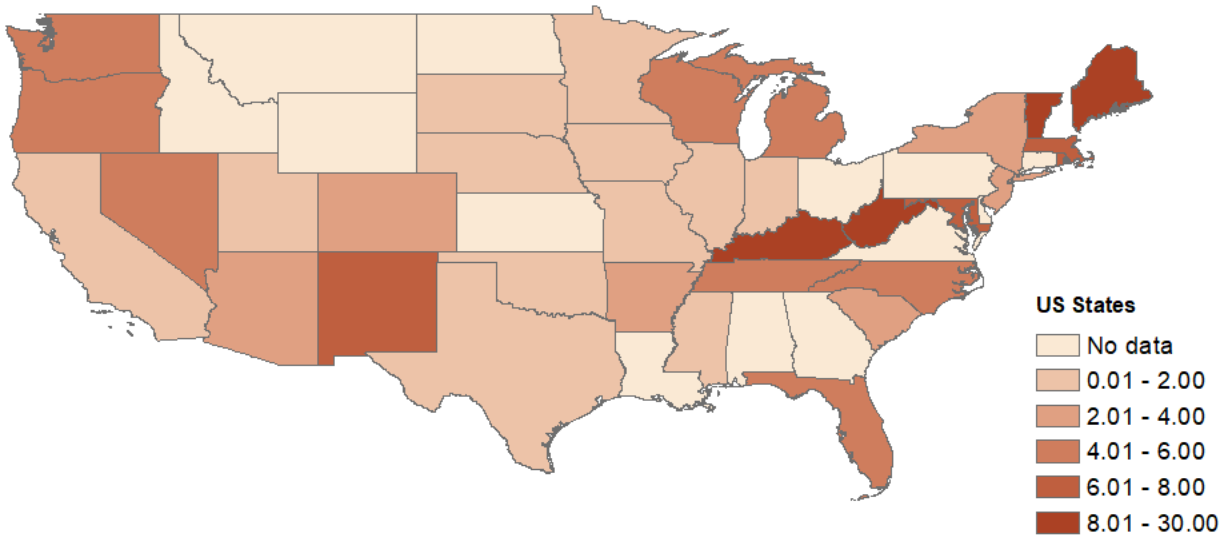
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility.

Figure 2: Share of NAS Births, Treatment admissions, and Drug-related Deaths, 2000–2013



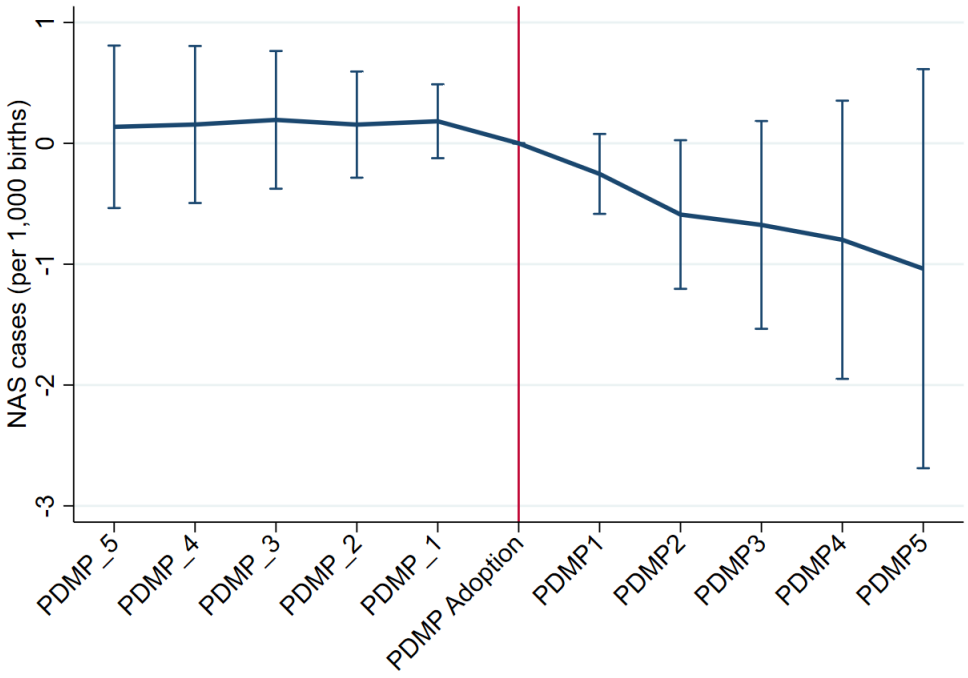
Notes - Data are drawn from State Inpatient Databases. Drug-related deaths are drawn from the Underlying Cause of Death Data (Source: CDC). We exclude cases of iatrogenic withdrawal; the NAS rate is calculated as the share of NAS cases over state in-hospital births excluding transfers from another acute care hospital or health care facility. Data are drawn from the Treatment Episode Dataset. This dataset contains information on the substance abuse characteristics of all admissions to treatment facilities that receive federal funding. We normalized trends using the year 2000 as a base year.

Figure 3: NAS Incidence across US States, 2011–2013



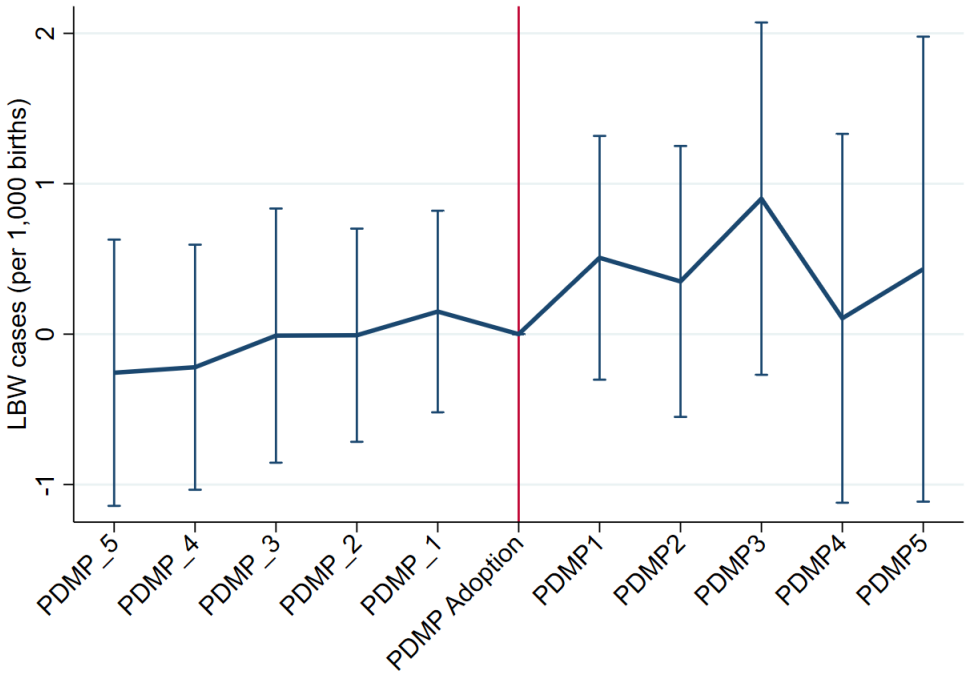
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility.

Figure 4: Event Study: Effect of Operational PDMPs on NAS Cases



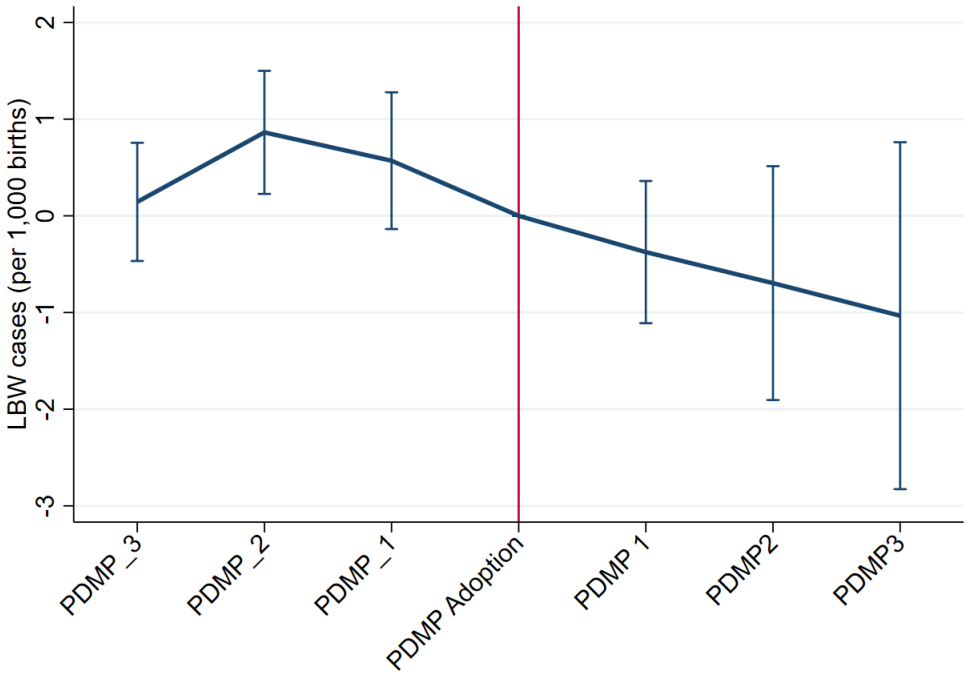
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include state and year fixed effects as well as state-specific time trends.

Figure 5: Event Study: Effect of Operational PDMPs on Low Birth Weight



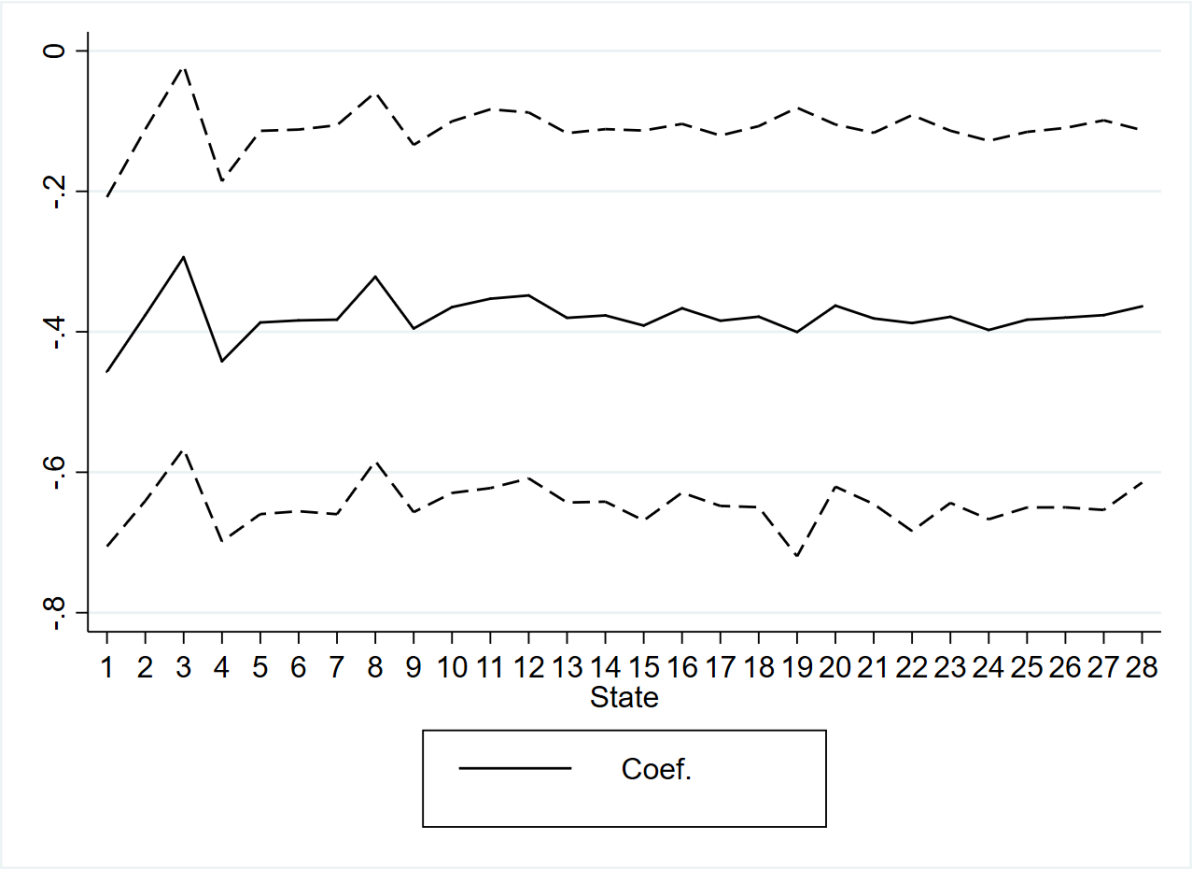
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility.

Figure 6: Event Study: Effect of Mandatory PDMPs on Low Birth Weight



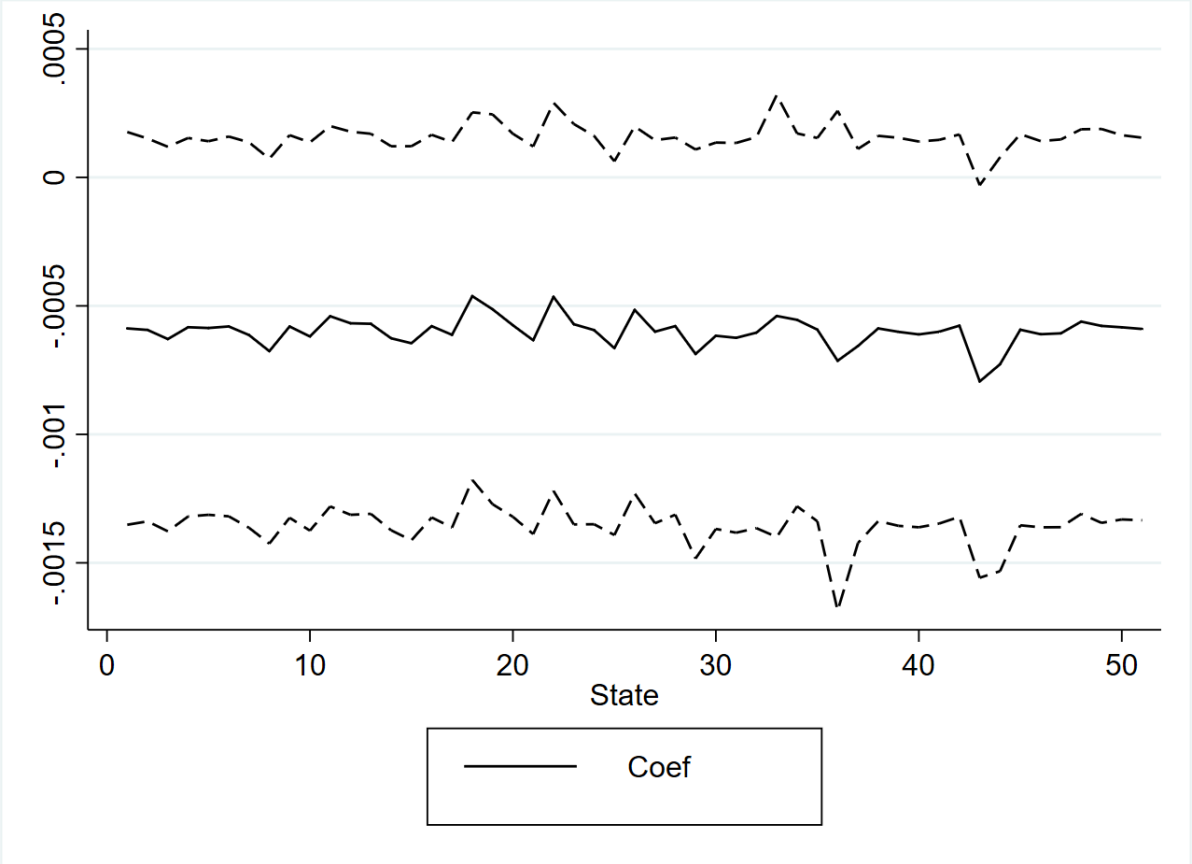
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility.

Figure 7: Sensitivity Test: Effect of PDMPs on NAS Cases, Omitting One State at a Time



Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility.

Figure 8: Sensitivity Test: Effect of Mandatory PDMPs on Share of Low Birth Wight Children, Omitting One State at a Time



Notes - Data are drawn from the Natality Detail Data (2000–2017).

Table 1: Effective Dates of Electronic PDMPs and Mandates

State	PDMP		Mandate	
Alaska	January	2012		
Alabama	August	2007		
Arkansas	March	2013		
Arizona	December	2008		
California	July	2009		
Colorado	February	2008		
Connecticut	July	2008		
Delaware	August	2012	March	2012
Florida	October	2011		
Georgia	July	2013		
Hawaii	January	1982		
Iowa	March	2009		
Idaho	July	2008		
Illinois	Janurary	2008		
Indiana	July	2008		
Kansas	April	2011		
Kentucky	March	2005	July	2012
Louisiana	January	2009	August	2014
Massachusetts	December	2010	June	2013
Maryland	January	2014		
Maine	January	2005		
Michigan	March	2011		
Minnesota	April	2010		
Missouri	July	2017		
Mississippi	March	2011	September	2011
Montana	October	2012		
North Carolina	October	2008		
North Dakota	January	2007		
Nebraska	April	2011		
New Hampshire	October	2014		
New Jersey	January	2012		
New Mexico	August	2005	September	2012
Nevada	October	2004	October	2007
New York	August	2013	August	2013
Ohio	October	2006	November	2011
Oklahoma	July	2006		
Oregon	September	2011		
Pennsylvania	August	2016		
Rhode Island	September	2012		
South Carolina	June	2008		
South Dakota	March	2012		
Tennessee	December	2006	January	2013
Texas	August	2012		
Utah	January	2006		
Virginia	June	2006		
Vermont	April	2009	November	2013
Washington	January	2012		
Wisconsin	May	2013		
West Virginia	January	2004	June	2012
Wyoming	July	2004		

Notes - Dates obtained from the National Alliance for Model State Drug Laws, Brandeis University's Prescription Drug Monitoring Program Training and Technical Assistance Center, state legislative laws and bills, government newsletters, news articles, articles from peer reviewed journals, and pharmacy board websites.

Table 2: Neonatal abstinence syndrome (NAS) incidence rates per 1,000 hospital births (2000 and 2013, by State)

State	Nas Incidence (2011-2013)	Nas Incidence (2000-2003)	Change
VT	30.00	1.70	16.65
ME	25.85	1.97	12.14
WV	24.00	1.07	21.50
KY	12.60	0.87	13.54
MA	11.65	2.60	3.48
MD	11.00	6.77	0.63
RI	7.70	2.80	1.75
NM	7.37	.	.
WA	7.17	1.53	3.67
WI	6.37	0.40	14.92
FL	6.03	0.50	11.07
MI	5.70	0.50	10.40
NC	5.30	0.47	10.36
NJ	4.93	3.23	0.53
OR	4.63	1.23	2.76
NV	4.37	1.10	2.97
UT	4.10	.	.
AZ	3.70	.	.
SC	3.30	0.63	4.21
NY	3.00	1.33	1.25
CO	2.73	0.63	3.32
AR	2.50	1.00	1.50
IA	1.80	0.40	3.50
CA	1.30	1.20	0.08
MS	1.30	.	.
NE	1.27	0.15	7.44
SD	0.97	.	.
HI	0.77	0.20	2.83

Notes - Data are drawn from the State Inpatient Databases. Incidence rate numerator consisted of NAS cases excluding cases of iatrogenic withdrawal; incidence rate denominator consisted of state in-hospital births excluding transfers from another acute care hospital or healthcare facility.

Table 3: Summary statistics- Outcome Variables

Cases per 1,000 births	Mean	St. Dev
NAS	3.75	5.10
LBW	80.22	13.08
VLBW	14.19	3.30
Premature	119.90	17.79
Infant mortality	6.70	1.58

Notes - Data on NAS cases are drawn from the State Inpatient Databases (2000-2013). Data on LBW, VLBW, and premature cases are are drawn from the Natality Detail Data (2000-2017). Data on infant mortality are drawn from the linked birth and infant death records from the CDC (2000-2017).

Table 4: Effect of Operational PDMP on NAS cases, Event Study

	Coef.	Std.Err.
Before PDMP adoption		
PDMP_5	0.136	0.328
PDMP_4	0.155	0.317
PDMP_3	0.194	0.277
PDMP_2	0.155	0.214
PDMP_1	0.182	0.148
After PDMP adoption		
PDMP1	-0.225	0.161
PDMP2	-0.589*	0.299
PDMP3	-0.675	0.418
PDMP4	-0.798	0.560
PDMP5	-1.037	0.804

Notes - Data are drawn from the State Inpatient Databases (2000-2013). All estimates controls for the following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement; an indicator accounting for the OxyContin reformulation; time-varying control at the state level for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18), state and year fixed effects, and state-specific time trends. Significance levels: $***p < 0.01$, $**p < 0.05$, $*p < 0.1$.

Table 5: Effects of Operational PDMPs on NAS Incidence

	(1)	(2)	(3)	(4)	(5)
$PDMP_{t-2}$	-0.803	-0.931**	-0.487**	-0.386***	-0.319**
	(0.482)	(0.425)	(0.220)	(0.131)	(0.155)
State fixed effects	YES	YES	YES	YES	YES
Year fixed effects	YES	YES	YES	YES	YES
Other state laws		YES	YES	YES	YES
Socio-demographic controls			YES	YES	YES
State specific time trends				YES	YES
Reformulation of Oxycontin					YES
Observations	341	341	341	341	341
R-squared	0.753	0.811	0.855	0.980	0.980
Mean of Dep. Var.	3.752	3.752	3.752	3.752	3.752
Std.Dev. of Dep. Var.	5.101	5.101	5.101	5.101	5.101
Wild-cluster bootstrap p-value	0.141	0.036	0.019	0.007	0.050

Notes - All estimates include state and year fixed effects. Columns 2-4 include controls for he following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement. Columns 3-4 include time-varying control at the state level for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18). Column 4 includes state-specific time trends. Column 5 includes accounts for the OxyContin reformulation. Data are drawn from the State Inpatient Databases (2000-2013). Standard errors adjusted for clustering at the state level are reported in parenthesis. Significance levels: $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.

Table 6: Effects of PDMPs on NAS Incidence

	(1)	(2)	(3)	(4)	(5)
$PDMP_{t-2}$	-0.806	-0.939**	-0.491**	-0.387***	-0.319*
	(0.482)	(0.423)	(0.218)	(0.131)	(0.156)
$Mandate_{t-2}$	-0.333	-0.956***	-0.375	-0.131	-0.072
	(0.286)	(0.319)	(0.471)	(0.241)	(0.264)
State fixed effects	YES	YES	YES	YES	YES
Year fixed effects	YES	YES	YES	YES	YES
Other state laws		YES	YES	YES	YES
Socio-demographic controls			YES	YES	YES
State specific time trends				YES	YES
Reformulation of Oxycontin					YES
Observations	341	341	341	341	341
R-squared	0.753	0.811	0.855	0.980	0.980
Mean of Dep. Var.	3.752	3.752	3.752	3.752	3.752
Std.Dev. of Dep. Var.	5.101	5.101	5.101	5.101	5.101
Wild-cluster bootstrap p-value (PDMP)	0.112	0.0460	0.0140	0.00601	0.0480
Wild-cluster bootstrap p-value (Mandate)	0.465	0.422	0.549	0.621	0.807

Notes - All estimates include state and year fixed effects. Columns 2-4 include controls for he following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement. Columns 3-4 include time-varying control at the state level for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18). Column 4 includes state-specific time trends. Data are drawn from the State Inpatient Databases (2000-2013). Standard errors adjusted for clustering at the state level are reported in parenthesis. Significance levels: $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.

Table 7: Effects of Operational PDMPs on LBW cases (per 1,000 births)

	(1)	(2)	(3)	(4)	(5)
$PDMP_{t-2}$	0.405	0.201	-0.020	-0.067	0.448
	(0.398)	(0.623)	(0.444)	(0.410)	(0.499)
State fixed effects	YES	YES	YES	YES	YES
Year fixed effects	YES	YES	YES	YES	YES
Other state laws		YES	YES	YES	YES
Socio-demographic controls			YES	YES	YES
State specific time trends				YES	YES
Reformulation of Oxycontin					YES
Observations	867	867	867	867	816
R-squared	0.977	0.979	0.983	0.988	0.988
Mean of Dep. Var.	80.23	80.08	80.08	80.08	80
Std.Dev. of Dep. Var.	13.09	13.13	13.13	13.13	13.20
Wild-cluster bootstrap p-value	0.375	0.812	0.970	0.879	0.375

Notes - All estimates include state and year fixed effects. Columns 2-4 include controls for he following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement. Columns 3-4 include time-varying control at the state level for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18). Column 4 includes state-specific time trends. Column 5 includes accounts for the OxyContin reformulation. Data are drawn from the State Inpatient Databases (2000-2013). Standard errors adjusted for clustering at the state level are reported in parenthesis. Significance levels: $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.

Table 8: Effects of Operational PDMPs on other outcomes

Dependent variable	(1) LBW	(2) VLBW	(3) Premature	(4) Infant Death
$PDMP_{t-2}$	0.448	0.191	-0.998	-0.097
	(0.499)	(0.140)	(1.007)	(0.108)
Observations	867	867	867	867
R-squared	0.988	0.969	0.978	0.942
Mean of Dep. Var.	80	14.24	119.9	6.804
Std.Dev. of Dep. Var.	13.20	3.355	17.79	1.593
Wild-cluster bootstrap p-value	0.396	0.144	0.394	0.451

Notes - Data for columns 1-3 are drawn from the Natality Detail Data. Data for column 4 are drawn from the linked birth and infant death records from the CDC. All estimates include state and year fixed effects, controls for the following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement, time-varying controls for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18), and state-specific time trends. Data are drawn from the Natality Detail Data (2000-2016). Standard errors adjusted for clustering at the state level are reported in parenthesis. Significance levels: $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.

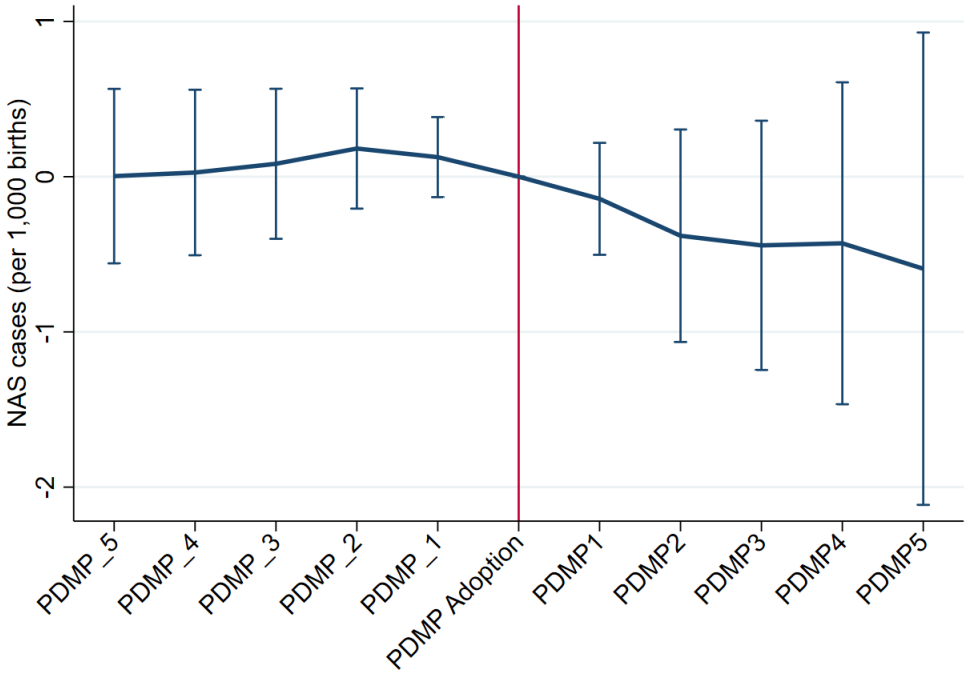
Table 9: Effects of Operational PDMPs on NAS Incidence: Robustness Checks Using Alternative Models

	(1)	(2)	(3)	(4)
PDMP t_0	-0.089			
	(0.070)			
PDMP $t-1$		-0.289**		
		(0.115)		
PDMP $t_0, t-1$				-0.089
				(0.105)
PDMP $t-2$			-0.386***	-0.345**
			(0.131)	(0.125)
Observations	341	341	341	341
R-squared	0.979	0.980	0.980	0.980
Mean of Dep. Var.	3.752	3.752	3.752	3.752
Std.Dev. of Dep. Var.	5.101	5.101	5.101	5.101

Notes - All estimates include state and year fixed effects. Columns 2-4 include controls for he following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement. Columns 3-4 include time-varying control at the state level for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18). Column 4 includes state-specific time trends. Data are drawn from the State Inpatient Databases (2000-2013). Standard errors adjusted for clustering at the state level are reported in parenthesis. Significance levels: $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.

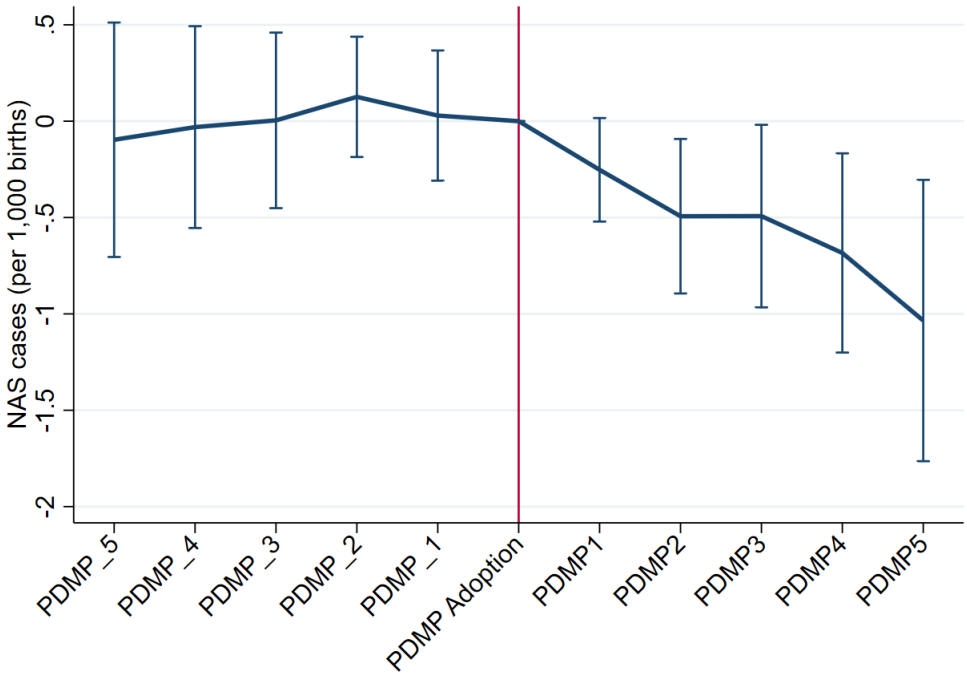
Appendix

Figure A.1: Event Study: Effect of Operational PDMPs on NAS Cases (Including Controls)



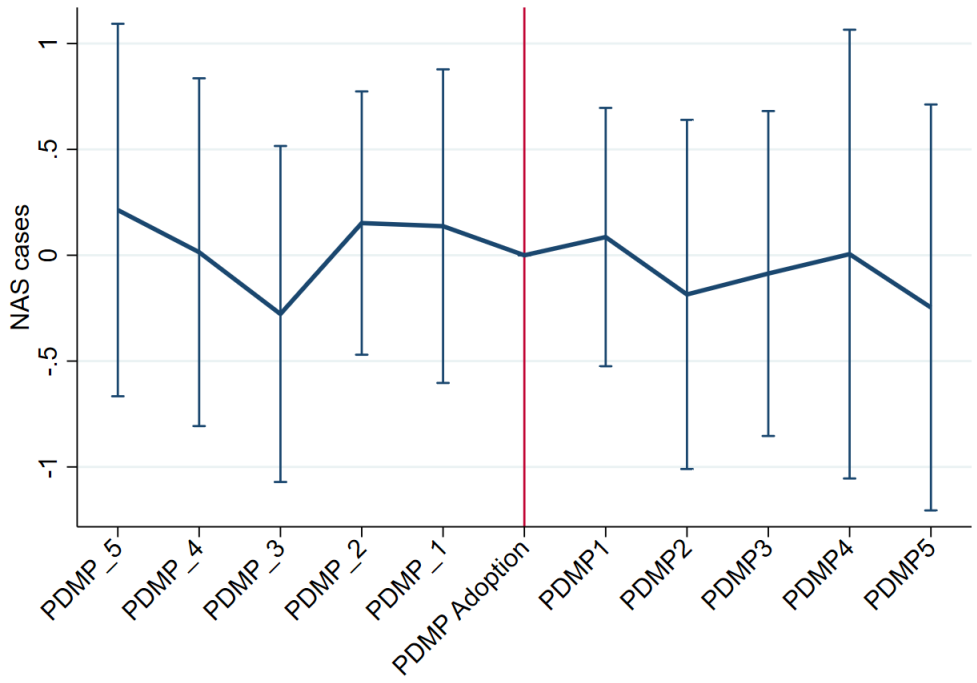
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include a set of time-variant state-level controls (age composition, share of Black population, share of Hispanic population, median income, gender composition, and unemployment rate), dummies for the adoption of other laws that may have affected prescription drug abuse (e.g., "good Samaritan" laws, doctor shopping, pain clinic regulations, physician exams laws, "ID required" laws, and tamper-resistant prescription form requirement laws), an indicator accounting for the OxyContin reformulation, state and year fixed effects, and state-specific time trends.

Figure A.2: Event Study: Effect of Operational PDMPs on NAS Cases, Using the PDMP Dates of Horwitz et al. (2018)



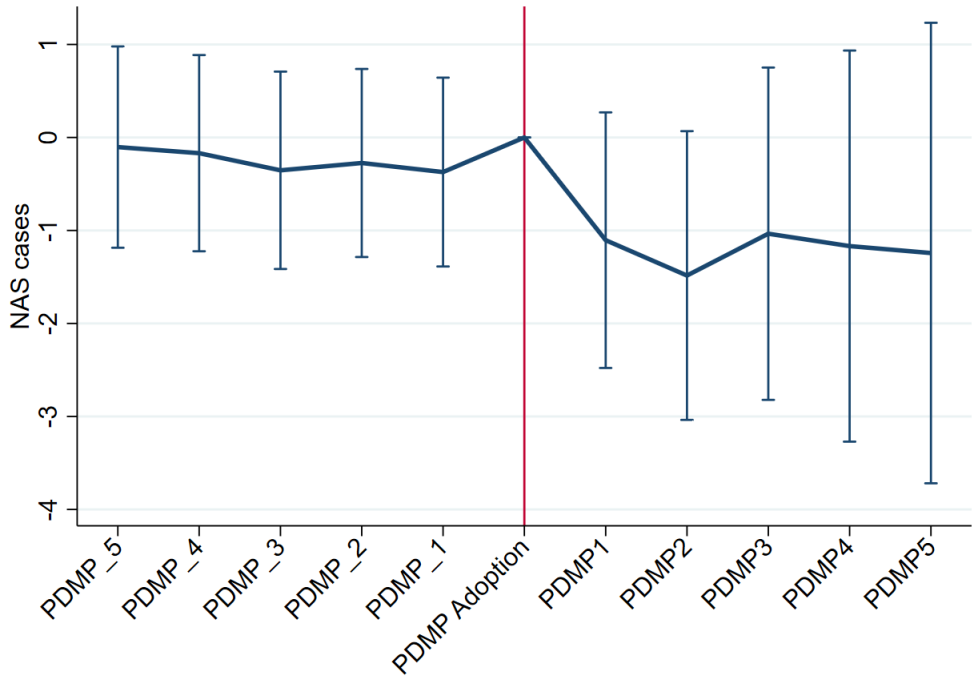
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include state and year fixed effects as well as state-specific time trends.

Figure A.3: Event Study: Effect of Operational PDMPs on Low Birth Weight Cases, Using the PDMP dates of Horwitz et al. (2018)



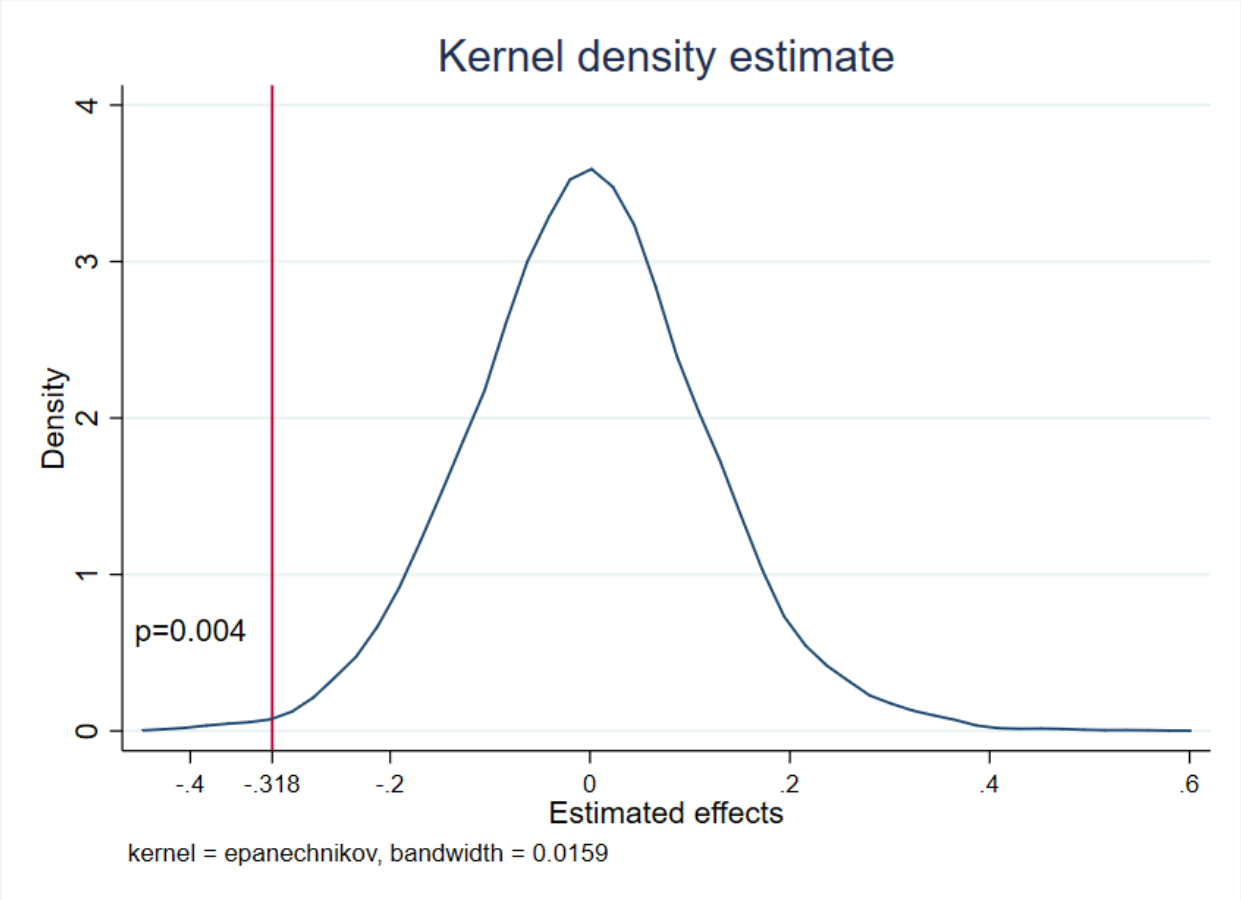
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include state and year fixed effects as well as state-specific time trends.

Figure A.4: Event Study: Effect of Operational PDMPs on NAS, No Time Trends)



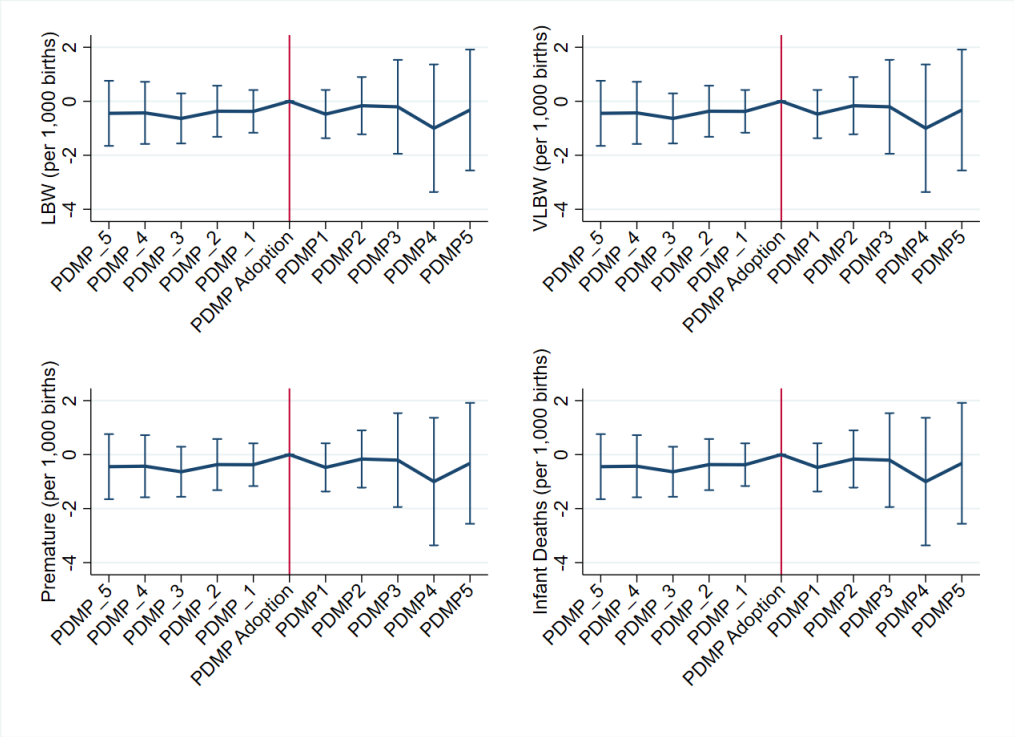
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consisted of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include state and year fixed effects as well as state-level time-varying demographic controls .

Figure A.5: Effect of Operational PDMPs on NAS, Multiple Permutation Test)



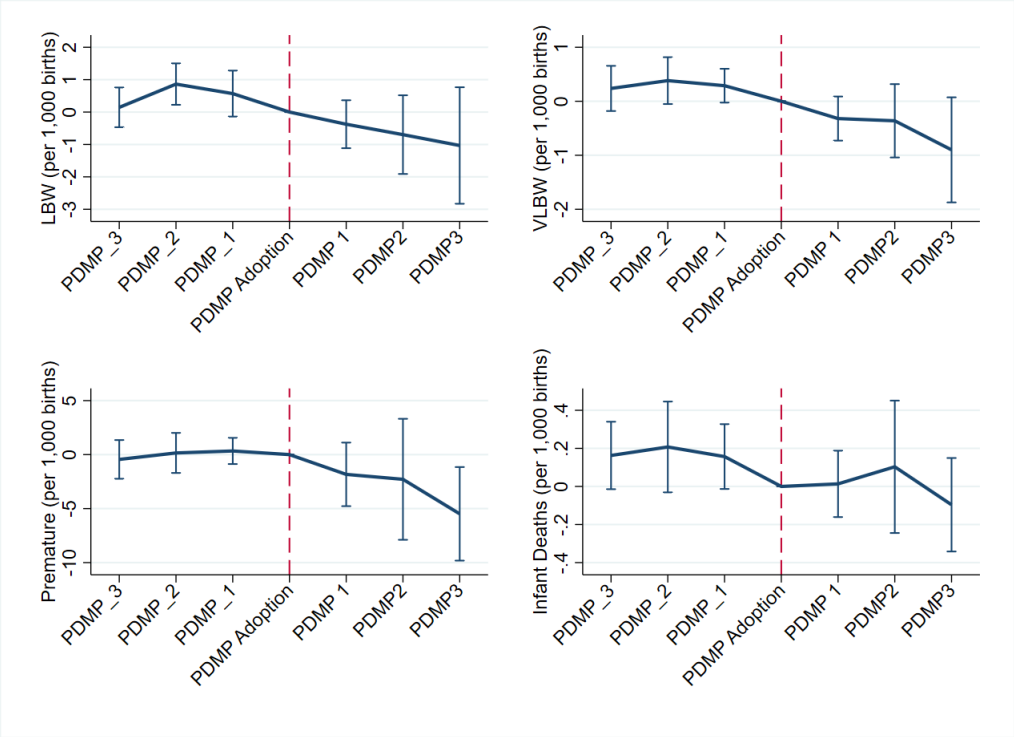
Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include state and year fixed effects as well as state-level time-varying demographic controls.

Figure A.6: Event Study: Effect of Operational PDMPs on Birth Outcomes



Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include a set of time-variant state-level controls (i.e., age composition, share of Black population, share of Hispanic population, median income, gender composition, and unemployment rate), dummies for the adoption of other laws that may have affected prescription drug abuse (e.g., "good Samaritan" laws, doctor shopping, pain clinic regulations, physician exams laws, "ID required" laws, and tamper-resistant prescription form requirement laws), an indicator accounting for the OxyContin reformulation, state and year fixed effects, and state-specific time trends.

Figure A.7: Event Study: Effect of Mandatory PDMPs on Birth Outcomes



Notes - Data are drawn from State Inpatient Databases. The incidence rate numerator consists of NAS cases excluding cases of iatrogenic withdrawal; the incidence rate denominator consists of state in-hospital births excluding transfers from another acute care hospital or health care facility. All estimates include a set of time-variant state level controls (age composition, share of Black population, share of Hispanic population, median income, gender composition, and unemployment rate), dummies for the adoption of other laws that may have affected prescription drug abuse (e.g., "good Samaritan" laws, doctor shopping, pain clinic regulations, physician exams laws, "ID required" laws, and tamper-resistant prescription form requirement laws), an indicator accounting for the OxyContin reformulation, state and year fixed effects, and state-specific time trends.

Table A.1: Effects of Operational PDMPs on NAS, Using the PDMP Dates of Horwitz et al. (2018)

	(1)	(2)	(3)
PDMP $(t-2)$	-0.899**	-0.369*	-0.268*
	(0.418)	(0.200)	(0.135)
Observations	341	341	341
R-squared	0.754	0.971	0.974
Mean of Dep. Var.	3.752	3.752	3.752
Std.Dev. of Dep. Var.	5.101	5.101	5.101
Wild-cluster bootstrap p-value	0.0430	0.163	0.0981

Notes - All estimates include state and year fixed effects. Columns 2-4 include controls for he following laws/regulations: Good Samaritan laws, Doctor Shopping, Pain Clinic regulations, Physician exams, require ID, and tamper-resistant prescription form requirement. Columns 3-4 include time-varying control at the state level for the share of female, Hispanic, African-American, White, foreign-born, non-citizen population, average family income (log), unemployment rate, children population (0-18). Column 4 includes state-specific time trends. Column 5 includes accounts for the OxyContin reformulation. Data are drawn from the State Inpatient Databases (2000-2013). Standard errors adjusted for clustering at the state level are reported in parenthesis. Significance levels: $^{***}p < 0.01$, $^{**}p < 0.05$, $^{*}p < 0.1$.