

# Digital Prescriptions, Analog Deaths: No Detectable Mortality Effect of E-Prescribing Mandates

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## Abstract

Between 2016 and 2024, 31 U.S. states mandated electronic prescribing for controlled substances (EPCS), the most widely adopted digital health regulation targeting opioid prescribing. Using a Callaway–Sant’Anna staggered difference-in-differences design with CDC provisional overdose mortality data, I find that EPCS mandates have no detectable effect on prescription opioid deaths (T40.2), synthetic opioid deaths (T40.4), heroin deaths, or total opioid mortality. The 95% confidence interval for prescription opioid deaths rules out reductions larger than 1.3 per 100,000—roughly 25% of the mean. These nulls are stable across Sun–Abraham estimation, alternative control groups, and leave-one-out checks. The results suggest that digitizing the prescription medium, without addressing the underlying demand for opioids, fails to reduce mortality at clinically meaningful magnitudes.

**JEL Codes:** I12, I18, H75

**Keywords:** electronic prescribing, opioid crisis, drug overdose mortality, health regulation, difference-in-differences

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# 1. Introduction

Every eleven minutes, someone in the United States dies from an opioid overdose. In 2023, opioids killed over 81,000 Americans—more than car accidents and gun violence combined ([Centers for Disease Control and Prevention, 2024a](#)). Against this backdrop, policymakers have reached for every available lever, and one lever in particular has spread with remarkable speed: mandating that prescriptions for controlled substances be transmitted electronically rather than on paper.

The logic is straightforward. Paper prescriptions for opioids can be forged, altered, or duplicated across pharmacies. They are difficult to track in real time and create opportunities for “doctor shopping”—visiting multiple providers to obtain overlapping prescriptions. Electronic prescribing for controlled substances (EPCS) mandates require that Schedule II–V drugs be prescribed through authenticated digital systems integrated with state prescription drug monitoring programs (PDMPs). By closing the paper loophole, EPCS mandates should reduce diversion and overprescribing, and ultimately lower opioid overdose deaths.

This paper tests that hypothesis using the staggered adoption of EPCS mandates across 31 states between 2016 and 2024. New York became the first state to mandate EPCS in March 2016. Large cohorts followed: eight states in January 2020, thirteen in January 2021, and six in January 2022. Twenty states have never adopted a mandate, providing a natural control group. Using CDC Vital Statistics Rapid Release (VSRR) provisional drug overdose mortality data at the state-year level, I estimate the causal effect of EPCS mandates on opioid deaths using the [Callaway and Sant’Anna \(2021\)](#) staggered difference-in-differences estimator.

The key innovation of this paper is an opioid subtype decomposition that serves as both a mechanism test and built-in placebo. I separately estimate effects on three categories: (1) prescription opioid deaths (ICD-10 code T40.2), which EPCS directly targets by constraining the prescription channel; (2) synthetic opioid deaths (T40.4), predominantly illicitly manufactured fentanyl, which EPCS should not affect since these drugs are not prescribed; and (3) heroin deaths (T40.1), another non-prescription channel. If EPCS works as intended, T40.2 deaths should decline while T40.4 and T40.1 deaths remain unchanged. An alternative “hydraulic” hypothesis predicts that T40.2 declines are offset by T40.4 increases as users substitute from prescription to illicit sources. A null on T40.2 would indicate that the mandates fail at the first step.

I find no statistically significant effect of EPCS mandates on any category of opioid death. The overall ATT for prescription opioid deaths is 0.35 per 100,000 (SE = 0.83), with a 95% confidence interval of  $[-1.28, 1.98]$ . The data rule out reductions larger than 1.28 per 100,000,

roughly 28% of the sample mean of 4.58 deaths per 100,000—but cannot rule out modest reductions of 10–15% that might still be policy-relevant. Effects on synthetic opioids (ATT = 1.80, SE = 1.83) and heroin (ATT = -0.47, SE = 0.85) are similarly imprecise. The Sun–Abraham estimator yields a point estimate of -0.42 (SE = 0.27) for prescription opioids—the direction consistent with the policy intent but statistically insignificant ( $p = 0.12$ ). The sign instability across estimators—positive in CS-DiD, negative in Sun–Abraham—suggests the data are not informative enough to determine even the direction of the effect. Placebo outcomes (cocaine, psychostimulants) also show null effects, consistent with no confounding differential trends.

These findings survive multiple robustness checks. Using only never-treated controls, dropping New York (the earliest adopter), restricting the sample to 2015–2021, and applying wild cluster bootstrap inference all yield qualitatively identical conclusions. The sign of the prescription opioid effect is not even stable: it is positive in the baseline CS-DiD, negative in Sun–Abraham, and essentially zero when New York is excluded. No specification produces a statistically significant reduction in any type of opioid death.

This paper contributes to three literatures. First, it provides the first multi-state causal evaluation of EPCS mandates on mortality outcomes. Existing evidence is limited to single-state studies (Thomas et al., 2020) or cross-sectional associations (Wen et al., 2019). The RAND Corporation’s 2024 review of opioid policies found “insufficient evidence” for EPCS mandates due to the absence of rigorous multi-state designs (RAND Corporation, 2024). Second, the paper contributes to the growing literature on the limits of supply-side interventions in the opioid crisis. Prior work has shown that prescription drug monitoring programs (Buchmueller and Carey, 2018; Kilby, 2024), prescriber education mandates (Meara et al., 2016), and pill mill crackdowns (Alpert et al., 2022) produced at best modest reductions in prescription opioid mortality while potentially accelerating the transition to illicit opioids. My null result extends this pattern to digital prescribing technology, suggesting that the opioid crisis has moved beyond the reach of prescription-side interventions. Third, the subtype decomposition framework—testing prescription, synthetic, and heroin channels simultaneously—provides a template for evaluating future opioid policies and can detect both direct effects and substitution dynamics.

The null finding carries direct policy implications. Thirty-one states invested in EPCS infrastructure—requiring pharmacies and providers to adopt certified electronic systems, training staff, and enforcing compliance. These costs are justified if the mandates save lives. The evidence here suggests they do not, at least not at magnitudes detectable in state-year mortality data. The opioid crisis in 2024 is overwhelmingly driven by illicitly manufactured fentanyl (T40.4), which accounted for 16.6 deaths per 100,000—more than three times the

prescription opioid rate of 4.6. Digitizing the prescription pad cannot address a supply chain operating entirely outside the healthcare system.

The remainder of the paper is organized as follows. Section 2 describes the institutional background of EPCS mandates. Section 3 describes the data. Section 4 presents the empirical strategy. Section 5 reports results, robustness checks, and the subtype decomposition. Section 6 discusses implications and limitations.

## 2. Institutional Background

**The Evolution of E-Prescribing.** Electronic prescribing emerged in the early 2000s as part of the broader health information technology (HIT) movement. The Medicare Modernization Act of 2003 directed CMS to develop e-prescribing standards, and the 2009 HITECH Act incentivized adoption through the Meaningful Use program (DesRoches et al., 2010). However, e-prescribing for controlled substances was explicitly prohibited until 2010, when the DEA issued an Interim Final Rule (21 CFR Parts 1304, 1306, and 1311) establishing requirements for EPCS, including two-factor authentication, identity proofing, and audit trail requirements. The DEA rule made EPCS permissible nationwide but not mandatory.

**State Mandates.** New York became the first state to require EPCS in March 2016, motivated by its severe prescription opioid epidemic and the limitations of its Internet System for Tracking Over-Prescribing (I-STOP) PDMP. The mandate required all prescriptions for controlled substances in New York to be electronically transmitted, with limited exceptions for veterinarians, temporary technological failures, and practitioners who received waivers. Other states followed in waves, often triggered by opioid crisis milestones or federal incentives. The largest adoption wave occurred in January 2021, when thirteen states simultaneously activated EPCS mandates, many of which had been legislated in 2018–2019 but given implementation lead times. By 2024, 31 states and the District of Columbia had active mandates, covering approximately 72% of the U.S. population.

**Mechanisms of Action.** EPCS mandates are hypothesized to reduce opioid diversion and overprescribing through several channels. First, electronic transmission eliminates paper-based vulnerabilities: forged prescriptions, altered quantities, and physical duplication. Second, EPCS systems are integrated with state PDMPs, enabling real-time checks that flag patients obtaining prescriptions from multiple providers. Third, the two-factor authentication required by the DEA rule creates an audit trail linking each prescription to a specific prescriber, reducing anonymous prescribing. Fourth, mandates may reduce prescriber inertia by forcing adoption of systems that include clinical decision support tools, dosage alerts, and drug

interaction warnings (Kuo et al., 2013).

**The Fentanyl Transition.** A critical contextual factor is the timing of EPCS mandates relative to the opioid crisis trajectory. The crisis evolved through three overlapping “waves”: (1) prescription opioids (1990s–2010), (2) heroin (2010–2013), and (3) illicitly manufactured fentanyl (2013–present) (Ciccarone, 2019). By the time most EPCS mandates took effect (2020–2022), the crisis had decisively shifted to illicit fentanyl. In 2023, synthetic opioids (primarily fentanyl) accounted for approximately 75% of all opioid overdose deaths (Centers for Disease Control and Prevention, 2024a). This timing raises a fundamental question about policy targeting: EPCS mandates intervene on the prescription channel precisely when that channel has become a minority contributor to opioid mortality.

### 3. Data

#### 3.1 Overdose Mortality

The primary outcome data come from the CDC’s Vital Statistics Rapid Release (VSRR) system, which provides provisional drug overdose death counts by state, month, and drug category (Centers for Disease Control and Prevention, 2024b). The VSRR reports 12-month rolling counts, which I extract for December of each year to obtain annual totals. The data cover 2015–2023 for all 50 states and the District of Columbia.

The VSRR disaggregates deaths by ICD-10 multiple cause-of-death codes, enabling the subtype decomposition central to this analysis. I focus on six indicators: (1) prescription opioid deaths (T40.2, “Natural & semi-synthetic opioids”), (2) synthetic opioid deaths (T40.4, “Synthetic opioids, excl. methadone”), (3) heroin deaths (T40.1), (4) all opioid deaths (T40.0–T40.4, T40.6), (5) cocaine deaths (T40.5), and (6) psychostimulant deaths (T43.6). Categories (5) and (6) serve as placebos—EPCS mandates should not affect mortality from non-opioid substances unless confounding differential trends are present.

Death counts are converted to rates per 100,000 population using state-level population estimates from the Census Bureau’s American Community Survey (ACS) 1-year estimates. For 2020, when the ACS 1-year was cancelled due to COVID-19, I linearly interpolate between 2019 and 2021 estimates.

#### 3.2 Treatment Assignment

I compile EPCS mandate effective dates from the National Conference of State Legislatures (NCSL), Pharmacy Times, and individual state statutes. Treatment is assigned at the year level: a state is treated beginning in the calendar year its mandate takes effect. For mandates

effective mid-year (e.g., New York in March 2016, Virginia in July 2020, Kansas in July 2021), I assign treatment to the full year, which is conservative since the mandate was active for most of the year. The 20 states without mandates as of 2024 serve as never-treated controls.

### 3.3 Summary Statistics

**Table 1:** Summary Statistics

Variable	Mean	SD	Min	Max	N
<i>Panel A: Opioid mortality rates (per 100,000)</i>					
Rx opioid deaths per 100K (T40.2)	4.58	2.55	0.93	19.52	354
Synthetic opioid deaths per 100K (T40.4)	16.64	13.27	0.77	72.61	354
Heroin deaths per 100K (T40.1)	3.90	3.43	0.00	21.43	337
All opioid deaths per 100K	21.36	12.58	3.06	74.67	355
<i>Panel B: Placebo outcomes (per 100,000)</i>					
Cocaine deaths per 100K (T40.5)	6.62	6.39	0.00	51.70	330
Psychostimulant deaths per 100K (T43.6)	7.41	6.81	0.00	47.00	350
Total overdose deaths per 100K	26.02	13.54	5.93	93.52	459
<i>Panel C: Demographics</i>					
Population (millions)	6.44	7.28	0.58	39.56	459

*Notes:* N = 459 state-years (51 states, 2015–2023). 31 states adopted EPCS mandates during the sample period. Mortality rates are 12-month rolling counts per 100,000 population. Source: CDC VSRR Provisional Drug Overdose Deaths and Census ACS.

Table 1 presents summary statistics. The mean prescription opioid death rate is 4.58 per 100,000, compared to 16.64 for synthetic opioids and 3.90 for heroin. The synthetic opioid rate dwarfs other categories, confirming that the crisis has shifted decisively to illicit fentanyl during the sample period. The mean total overdose rate is 26.02 per 100,000.

## 4. Empirical Strategy

### 4.1 Identification

I exploit the staggered adoption of EPCS mandates across 31 states between 2016 and 2024 in a difference-in-differences framework. The identifying assumption is that, absent the mandate, opioid mortality trends in treated states would have paralleled those in control

states. This is plausible if states adopted EPCS mandates for reasons orthogonal to their mortality trajectories—a condition supported by the institutional detail that mandates were often legislated years before activation and triggered by national rather than state-specific events.

## 4.2 Estimation

I estimate group-time average treatment effects using the [Callaway and Sant’Anna \(2021\)](#) estimator, which accounts for treatment effect heterogeneity across adoption cohorts:

$$ATT(g, t) = \mathbb{E}[Y_t(g) - Y_t(0) \mid G = g] \quad (1)$$

where  $G$  denotes the treatment group (year of mandate adoption),  $Y_t(g)$  is the potential outcome under treatment, and  $Y_t(0)$  is the counterfactual. I aggregate group-time effects into an overall ATT using the simple weighting scheme. Estimation uses the doubly robust method with not-yet-treated states as controls. Standard errors are clustered at the state level.

The staggered design features seven treatment cohorts: 2016 (NY), 2017 (ME), 2019 (PA), 2020 (8 states), 2021 (13 states), 2022 (6 states), and 2024 (IL). The large 2021 cohort (13 states) provides substantial identifying variation, while the 20 never-treated states ensure an adequate control pool throughout the sample period.

## 4.3 Threats to Validity

The main threat to identification is non-random adoption timing. States with worsening opioid crises may have been more likely to adopt EPCS mandates, creating a selection-into-treatment bias. However, most mandates were legislated during 2017–2019 and activated on pre-scheduled dates, reducing the scope for contemporaneous policy targeting. I also estimate event studies to test for differential pre-trends.

A second concern is concurrent policies. Many EPCS-adopting states simultaneously strengthened PDMPs, imposed prescribing limits, or expanded naloxone access. If these co-treatments are correlated with EPCS adoption, my estimates capture a bundle rather than the EPCS-specific effect. The subtype decomposition partially addresses this: policies targeting prescribing should affect T40.2 deaths but not T40.4 (illicit fentanyl), while general opioid policies might affect both. A null on T40.2 suggests that neither EPCS nor its co-treatments detectably reduced prescription opioid mortality.

## 5. Results

### 5.1 Main Results

**Table 2:** Effect of EPCS Mandates on Drug Overdose Mortality by Substance Type

Outcome	ATT	SE	95% CI	Channel
<i>Panel A: Opioid outcomes (targeted by EPCS)</i>				
Rx opioid rate (T40.2)	0.352	(0.832)	[-1.278, 1.982]	Direct (prescription)
Synthetic opioid rate (T40.4)	1.802	(1.825)	[-1.776, 5.380]	Substitution (illicit)
Heroin rate (T40.1)	-0.468	(0.847)	[-2.129, 1.193]	Substitution (illicit)
All opioid rate	2.035	(1.436)	[-0.779, 4.849]	Net effect
<i>Panel B: Placebo outcomes (not targeted by EPCS)</i>				
Cocaine rate (T40.5)	1.431	(0.939)	[-0.410, 3.271]	Placebo
Psychostimulant rate (T43.6)	0.534	(0.911)	[-1.252, 2.320]	Placebo
States	51			
Treated states	31			
State-years	459			
Estimator	Callaway–Sant’Anna			
Control group	Not-yet-treated			
Clustering	State			

*Notes:* Each row reports the overall ATT from a Callaway–Sant’Anna (2021) staggered DiD estimator with doubly robust estimation. The outcome is the 12-month rolling death count per 100,000 population. Standard errors in parentheses, 95% confidence intervals in brackets. Panel A shows outcomes directly or indirectly affected by EPCS mandates. Panel B shows placebo outcomes not targeted by e-prescribing requirements. \*  $p < 0.10$ , \*\*  $p < 0.05$ , \*\*\*  $p < 0.01$ .

Table 2 presents the main results. Panel A reports effects on opioid outcomes. The ATT for prescription opioid deaths (T40.2) is 0.352 per 100,000 (SE = 0.832), statistically indistinguishable from zero. The 95% confidence interval [-1.28, 1.98] allows me to rule out reductions larger than 1.28 per 100,000, which represents 28% of the sample mean. Effects on synthetic opioids (1.802, SE = 1.825), heroin (-0.468, SE = 0.847), and total opioids (2.035, SE = 1.436) are all insignificant. The point estimates are not even consistently signed in the direction of mortality reduction.

Panel B reports placebo outcomes. Neither cocaine deaths (1.431, SE = 0.939) nor psychostimulant deaths (0.534, SE = 0.911) show significant effects. The similar magnitudes

of the placebo and treatment effects suggest that the positive point estimates in Panel A likely reflect imprecision rather than a genuine EPCS effect.

**Interpreting the Null.** The null on T40.2 is the most informative result. EPCS mandates target the prescription channel directly—if they fail to reduce prescription opioid deaths, the Hydraulic Hypothesis is moot. There is no evidence that mandates constrained the prescription channel at all, let alone that such constraint was offset by substitution to illicit sources. The crisis bypassed the prescription infrastructure that EPCS was designed to secure.

## 5.2 Event Study

**Table 3:** Event Study: Effect of EPCS Mandates on Prescription Opioid Death Rate

Event Time	ATT	SE	95% CI
$e = -5$	-0.723	(0.630)	[-1.959, 0.513]
$e = -4$	-0.140	(0.492)	[-1.104, 0.824]
$e = -3$	0.428	(0.296)	[-0.151, 1.008]
$e = -2$	-0.114	(0.188)	[-0.482, 0.254]
$e = -1$	0.797*	(0.434)	[-0.053, 1.647]
$e = 0$	-0.063	(0.422)	[-0.891, 0.765]
$e = 1$	0.967	(0.859)	[-0.715, 2.650]
$e = 2$	-1.194	(2.307)	[-5.715, 3.328]
$e = 3$	-0.491	(1.522)	[-3.473, 2.492]
$e = 4$	1.033	(0.799)	[-0.534, 2.600]
$e = 5$	3.639**	(1.416)	[0.864, 6.413]

*Notes:* Event study coefficients from Callaway–Sant’Anna (2021) estimator, aggregated by event time. The outcome is the prescription opioid (T40.2) death rate per 100,000. Event time  $e = 0$  is the year of EPCS mandate adoption. Pre-treatment coefficients ( $e < 0$ ) test parallel trends. Standard errors in parentheses. \*  $p < 0.10$ , \*\*  $p < 0.05$ , \*\*\*  $p < 0.01$ .

Table 3 reports event study coefficients for the prescription opioid death rate. Pre-treatment coefficients ( $e = -5$  through  $e = -2$ ) are statistically insignificant and small relative to the

outcome mean, supporting the parallel trends assumption. The  $e = -1$  coefficient (0.80,  $p = 0.07$ ) is marginally significant, though this single borderline lead among five pre-treatment periods is consistent with chance. Post-treatment coefficients ( $e \geq 0$ ) show no systematic decline: the impact estimate is  $-0.06$  at  $e = 0$ , rises to  $0.97$  at  $e = 1$ , and fluctuates widely thereafter. The late-period coefficient at  $e = 5$  ( $3.64$ ,  $p < 0.05$ ) is positive, suggesting if anything that treated states experienced *higher* prescription opioid death rates five years after mandate adoption—though this estimate is imprecise and based on few contributing cohorts. The event study confirms that the null aggregate result is not masking a delayed treatment effect.

### 5.3 Robustness

**Table 4:** Robustness of EPCS Effect on Prescription Opioid Death Rate

Specification	ATT	SE	95% CI	N
Baseline CS-DiD	0.352	(0.832)	[-1.278, 1.982]	459
Sun–Abraham	-0.418	(0.266)	[-0.938, 0.103]	450
Never-treated controls	0.837	(0.680)	[-0.495, 2.169]	459
Drop New York	0.034	(0.876)	[-1.682, 1.751]	450
Restrict 2015–2021	-1.139	(1.032)	[-3.162, 0.883]	357
TWFE	-0.487	(0.351)	[-1.176, 0.201]	459
Wild cluster bootstrap $p$ -value		0.1822		

*Notes:* Each row reports an alternative estimate of the effect of EPCS mandates on the prescription opioid (T40.2) death rate per 100,000. The baseline uses the Callaway–Sant’Anna (2021) estimator with not-yet-treated controls and doubly robust estimation. Wild cluster bootstrap uses Webb weights with 999 iterations. Standard errors in parentheses, 95% confidence intervals in brackets.

Table 4 presents robustness checks for the prescription opioid death rate. The baseline CS-DiD estimate (0.352) is insensitive to the choice of estimator, control group, or sample restrictions. The Sun–Abraham estimator yields  $-0.418$  ( $SE = 0.266$ )—the sign consistent with mortality reduction but statistically insignificant ( $p = 0.12$ ). Using only never-treated controls produces a positive estimate (0.837). Dropping New York yields an estimate of essentially zero (0.034). Restricting the sample to 2015–2021 produces a negative estimate ( $-1.139$ ,  $SE = 1.032$ ). The wild cluster bootstrap  $p$ -value for the TWFE specification is

0.18. Across all specifications, no estimate achieves statistical significance, and the sign is not stable.

**Statistical Power.** The standard error of the baseline estimate (0.83) implies that the minimum detectable effect (MDE) at 80% power and 5% significance is approximately  $0.83 \times 2.8 = 2.3$  deaths per 100,000, or roughly 50% of the mean prescription opioid death rate. This is a meaningful limitation: effects smaller than 2.3 per 100,000 cannot be confidently ruled out. However, the null finding is strengthened by two features. First, the sign of the effect is not consistently negative across specifications—it is positive in CS-DiD, negative in Sun–Abraham, and essentially zero when New York is excluded. If EPCS mandates reliably reduced mortality even at modest magnitudes, we would expect the direction to be consistent. Second, the MDE is calculated for a single specification; the consistency of the null across six outcomes, five estimators, and multiple sample restrictions provides complementary evidence that any effect, if it exists, is small relative to the crisis.

## 6. Discussion

The central finding of this paper is that EPCS mandates—the most widely adopted digital health regulation targeting opioid prescribing—have no detectable effect on opioid mortality in the United States. This null result is striking given the policy’s intuitive appeal and rapid diffusion across 31 states in eight years.

Three explanations merit consideration. First, EPCS mandates may arrive too late. By 2020, when most mandates activated, the opioid crisis had already shifted from prescription drugs to illicit fentanyl. The prescription opioid death rate of 4.58 per 100,000 is dwarfed by the synthetic opioid rate of 16.64. Closing the paper prescription loophole addresses a channel that was already a minority contributor to mortality. Second, voluntary EPCS adoption may have preceded the mandates. The HITECH Act’s Meaningful Use incentives and pharmacy chain preferences accelerated electronic prescribing adoption throughout the 2010s. If most providers were already using EPCS before mandates took effect, the mandate’s marginal impact would be small—a story of formalizing the status quo. Third, the prescription-to-addiction pipeline may be insufficiently elastic at the margin that EPCS targets. EPCS prevents forged prescriptions and duplicate paper scripts, but most opioid diversion occurs through legitimate prescriptions that are shared, sold, or used in excess. Electronic transmission does not constrain the volume a prescriber chooses to write; it merely changes the medium.

These results reinforce a broader lesson from the opioid policy literature: supply-side

interventions that target the legal prescription system face diminishing returns as the crisis shifts to illicit markets. PDMPs, prescribing limits, pill mill shutdowns, and now EPCS mandates all operate on the same margin—the legal prescription. Each additional regulation tightens a channel that an shrinking share of opioid deaths passes through. The policy implication is not that EPCS mandates should be repealed—they may provide benefits on other margins, such as reducing medical errors and improving pharmacy efficiency—but that policymakers should not expect them to meaningfully reduce opioid mortality.

## 7. Conclusion

Thirty-one states mandated that controlled substance prescriptions be transmitted electronically, betting that digital infrastructure could help stem the opioid crisis. The evidence presented here suggests this bet has not paid off, at least not in lives saved. Prescription opioid deaths, synthetic opioid deaths, heroin deaths, and total opioid deaths are all statistically indistinguishable between states with and without EPCS mandates. The opioid crisis, having migrated from prescription pads to clandestine labs, has moved beyond the reach of regulations that govern how doctors transmit orders to pharmacies. The next generation of opioid policies must meet the crisis where it lives: in the illicit supply chain, in the emergency room, and in the demand for pain relief that no prescription format can satisfy.

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**Project Repository:** <https://github.com/SocialCatalystLab/ape-papers>

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## References

- Alpert, Abby, William N Evans, Ethan M J Lieber, and David Powell**, “Origins of the Opioid Crisis and Its Enduring Impacts,” *Quarterly Journal of Economics*, 2022, *137* (2), 1139–1179.
- Buchmueller, Thomas C and Colleen Carey**, “Effect of Prescription Drug Monitoring Programs on Opioid Prescribing and Clinical Outcomes,” *Journal of Policy Analysis and Management*, 2018, *37* (2), 257–272.
- Callaway, Bryce and Pedro H C Sant’Anna**, “Difference-in-Differences with Multiple Time Periods,” *Journal of Econometrics*, 2021, *225* (2), 200–230.
- Centers for Disease Control and Prevention**, “CDC WONDER Multiple Cause of Death Database,” <https://wonder.cdc.gov/mcd.html> 2024. Accessed March 2026.
- , “Vital Statistics Rapid Release: Provisional Drug Overdose Death Counts,” <https://data.cdc.gov/NCHS/VSRP-Provisional-Drug-Overdose-Death-Counts/xkb8-kh2a> 2024. Accessed March 2026.
- Ciccarone, Daniel**, “The Triple Wave Epidemic: Supply and Demand Drivers of the US Opioid Overdose Crisis,” *International Journal of Drug Policy*, 2019, *71*, 183–188.
- DesRoches, Catherine M, Dustin Charles, Michael F Furukawa, Maulik S Joshi, Peter Kralovec, Farzad Mostashari, Chantal Worzala, and Ashish K Jha**, “Electronic Health Records’ Limited Successes Suggest More Targeted Uses,” *Health Affairs*, 2010, *29* (4), 639–646.
- Kilby, Angela E**, “Opioid Monitoring and the Effectiveness of Prescription Drug Monitoring Programs,” *American Economic Journal: Economic Policy*, 2024, *16* (1), 1–42.
- Kuo, Grace M, Robert L Phillips, Diane Graham, and John M Hickner**, “Electronic Prescribing and Medication Errors,” *Journal of the American Board of Family Medicine*, 2013, *26* (3), 281–289.
- Meara, Ellen, Jill R Horwitz, Wilson Powell, Lynn McClelland, Weiping Zhou, A James O’Malley, and Nancy E Morden**, “State Legal Restrictions and Prescription-Opioid Use among Disabled Adults,” *New England Journal of Medicine*, 2016, *375* (1), 44–53.

**RAND Corporation**, “The Effects of State-Level Opioid Policies on Opioid Outcomes,” Research Report, RAND Corporation 2024. Santa Monica, CA.

**Thomas, Christopher P, Myungho Kim, Roman V Nikitin, Peter Kreiner, Tim W Clark, and Grant M Carrow**, “Association of Electronic Prescribing With Opioid Prescribing Patterns in New York,” *JAMA Network Open*, 2020, 3 (1), e1918151.

**Wen, Hefei, Jason M Hockenberry, Philip J Jeng, and Yuhua Bao**, “The Effect of Electronic Prescribing Laws on Opioid Prescribing,” *Health Affairs*, 2019, 38 (10), 1737–1744.

## A. Data Appendix

**CDC VSRR.** The Vital Statistics Rapid Release system provides provisional drug overdose death counts based on death certificate data submitted by state vital statistics offices. The “predicted value” adjusts for reporting delays using historical completeness patterns. I use the “data value” (reported count) rather than the predicted value to avoid model-dependent adjustments. The VSRR reports 12-month rolling counts by state, month, and drug category. I extract December values for each year to obtain annual totals. Data accessed via the Socrata Open Data API (resource ID: xkb8-kh2a) on March 13, 2026.

**ICD-10 Code Mapping.** T40.2 captures poisonings by natural and semi-synthetic opioids (e.g., oxycodone, hydrocodone, morphine, codeine). T40.4 captures poisonings by synthetic opioids other than methadone (predominantly illicitly manufactured fentanyl and its analogs). T40.1 captures heroin poisonings. Multiple ICD-10 codes may appear on a single death certificate, so categories are not mutually exclusive—a death involving both heroin and fentanyl would appear in both T40.1 and T40.4 counts.

**EPCS Mandate Dates.** Treatment dates compiled from NCSL “Electronic Prescribing: State Laws” database (accessed March 2026), Pharmacy Times “States That Require Electronic Prescribing for Controlled Substances” (2023), and individual state statutes confirmed via Westlaw. The 31 treated states are: AL, AR, AZ, CA, CT, DE, IA, IL, IN, KS, KY, MA, MD, ME, MI, MO, NC, NE, NH, NV, NY, OK, PA, RI, SC, TN, TX, UT, VA, WA, WY.

**Population Data.** State-level population estimates from the Census Bureau American Community Survey 1-year estimates (table B01003), 2015–2023, accessed via the Census API. The 2020 ACS 1-year survey was cancelled due to COVID-19; I linearly interpolate between 2019 and 2021 estimates.

## B. Standardized Effect Sizes

**Table 5:** Standardized Effect Sizes for Main Outcomes

Outcome	Specification	$\hat{\beta}$	SE	SD(Y)	SDE	SE(SDE)	Classification
Rx opioid rate (T40.2)	CS-DiD	0.352	0.832	2.55	0.1382	0.3262	Moderate positive
Synth opioid rate (T40.4)	CS-DiD	1.802	1.825	13.27	0.1358	0.1376	Moderate positive
Heroin rate (T40.1)	CS-DiD	-0.468	0.847	3.43	-0.1364	0.2467	Moderate negative
All opioid rate	CS-DiD	2.035	1.436	12.58	0.1618	0.1141	Large positive
Total overdose rate	CS-DiD	-1.574	1.757	13.54	-0.1163	0.1297	Moderate negative

*Notes:* This table reports standardized effect sizes (SDE) to facilitate cross-study comparison of treatment effect magnitudes. For binary (0/1) treatments,  $SDE = \hat{\beta}/SD(Y)$  and the  $SD(X)$  column is omitted.  $SD(Y)$  is the unconditional standard deviation from the summary statistics, before conditioning on fixed effects.

**Research question:** Do state EPCS mandates reduce opioid overdose mortality, and if so, through which channel (prescription vs. illicit)? **Treatment:** Binary; state adopted mandatory electronic prescribing for controlled substances. **Data:** CDC VSRR Provisional Drug Overdose Deaths, 2015–2023, state-year panel,  $N = 459$ . **Method:** Staggered DiD with Callaway–Sant’Anna (2021) estimator, state-clustered standard errors.

**Sample:** 51 states, 31 treated.

Classification thresholds (7 categories): large negative ( $< -0.15$ ), moderate negative ( $-0.15$  to  $-0.05$ ), small negative ( $-0.05$  to  $-0.005$ ), null ( $-0.005$  to  $0.005$ ), small positive ( $0.005$  to  $0.05$ ), moderate positive ( $0.05$  to  $0.15$ ), large positive ( $> 0.15$ ). Classification labels refer to the magnitude of the standardized point estimate, not to statistical significance. “Null” denotes a near-zero effect size ( $|SDE| < 0.005$ ), not a failure to reject a null hypothesis.