Too Tight a Grip? Opioid Day-Supply Limits and the Dose-Response of Illicit Substitution

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Abstract

Between 2016 and 2019, 39 U.S. states adopted laws capping initial opioid prescriptions at 3 to 7 days. Using a Callaway–Sant'Anna staggered difference-in-differences design with drug-type-specific overdose mortality from the CDC, I find that the aggregate effect on illicit overdose deaths is indistinguishable from zero. But this null masks a sharp dose-response: states with the most restrictive 3-day limits saw a significant 8.6 per 100,000 increase in synthetic opioid (fentanyl) deaths alongside a 1.0 per 100,000 reduction in prescription opioid deaths, while states with 7-day limits experienced no detectable substitution. Cocaine and psychostimulant deaths—mechanism-matched placebos—show no treatment effect. The results reveal a Goldilocks problem in drug policy: sufficiently strict limits trigger a substitution to deadlier alternatives, while moderate limits reduce prescribing without pushing users to the street.

JEL Codes: I12, I18, K32

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1. Introduction

In 2017, a physician in Florida could legally write an initial opioid prescription for 30 days. By 2018, after the state enacted one of America's strictest day-supply limits, the same physician was capped at 3 days. The policy logic was straightforward: shorter prescriptions mean fewer leftover pills, less diversion, and less iatrogenic dependence. But for a patient already dependent on opioids—roughly 2 million Americans met the clinical criteria for opioid use disorder that year—the calculation was different. When the legal supply contracted, the illicit market was one phone call away. And on the illicit market, what had once been heroin was increasingly fentanyl, a synthetic opioid 50 to 100 times more potent than morphine.

This paper asks whether state opioid day-supply limits reduced overdose deaths—or simply changed which drug was killing people. The answer turns out to depend critically on how strict the limit was.

Between 2016 and 2019, 39 states enacted laws capping initial opioid prescriptions, typically at 3, 5, or 7 days (Davis et al., 2019). These supply-side interventions emerged alongside prescription drug monitoring programs (PDMPs) and abuse-deterrent reformulations as part of a broad effort to constrain the medical supply of opioids (Dowell et al., 2016). A substantial literature documents that supply-side interventions successfully reduce prescription volumes (Buchmueller and Carey, 2018; Meara et al., 2016; Grecu et al., 2019). The critical question—first raised by Alpert et al. (2018) in the context of OxyContin reformulation—is whether reducing the legal supply of opioids drives users to illicit alternatives.

I exploit the staggered adoption of day-supply limits across 39 states using the Callaway and Sant'Anna (2021) difference-in-differences estimator, which addresses the well-documented biases of two-way fixed effects under heterogeneous treatment effects (Goodman-Bacon, 2021; de Chaisemartin and D'Haultfœuille, 2020; Sun and Abraham, 2021). The estimator compares treated cohorts to never-treated states, separately estimating group-time average treatment effects. The key innovation is to decompose the outcome by drug type: I estimate the effect on prescription opioid deaths (ICD-10 T40.2), heroin deaths (T40.1), synthetic opioid deaths (T40.4, primarily fentanyl), cocaine deaths (T40.5), and psychostimulant deaths (T43.6). The last two serve as mechanism-matched placebos: cocaine and methamphetamine users are exposed to the same socioeconomic trends affecting drug users broadly, but opioid prescribing limits should not push anyone toward cocaine or methamphetamine.

Three findings emerge. First, the aggregate Callaway–Sant'Anna ATT for total overdose mortality is 0.91 deaths per 100,000 (SE = 2.52)—statistically and economically indistinguishable from zero. Day-supply limits, taken as a class, did not detectably increase or decrease overall overdose mortality. Second, and more importantly, this null conceals a stark

dose-response in the relationship between limit stringency and illicit substitution. States that adopted the most restrictive 3-day limits (Florida, Tennessee, Kentucky, Arizona) experienced a statistically significant 8.56 per 100,000 increase in synthetic opioid deaths ($p = 0.004$) and a simultaneous 1.01 per 100,000 decrease in prescription opioid deaths ($p = 0.008$). States with moderate 7-day limits—the most common policy choice—showed no detectable substitution effect. Third, placebo outcomes (cocaine, psychostimulant deaths) show no systematic response to day-supply limits, consistent with the substitution channel being specific to opioid markets.

These results contribute to the literature on supply-side drug policy in three ways. The paper most closely related to this one is Alpert et al. (2018), who showed that the reformulation of OxyContin into an abuse-deterrent formulation caused a dramatic shift from prescription opioids to heroin. Evans et al. (2019) and Cicero and Ellis (2012) documented the same OxyContin-to-heroin channel. My contribution is to show that the substitution mechanism depends on the *intensity* of the supply restriction. This resolves what would otherwise be a puzzle: if supply restrictions always cause substitution, then the modest day-supply limits adopted by most states should have triggered mass substitution—but they did not. Only the most aggressive limits did.

Second, this paper provides the first evidence on day-supply limits specifically. Most of the existing quasi-experimental literature focuses on PDMPs (Buchmueller and Carey, 2018; Mallatt, 2020; Grecu et al., 2019; Meinhofer, 2018), which operate through information (giving prescribers access to patient histories) rather than hard quantity constraints. Day-supply limits are fundamentally different: they impose a binding ceiling on the *amount* of opioid a physician can prescribe in the initial encounter, regardless of clinical judgment. The mechanism through which they might cause substitution—by abruptly reducing the legal supply available to dependent patients—is more direct.

Third, the dose-response pattern has clear policy implications. Seven-day limits appear to achieve the intended goal of reducing prescription opioid exposure without triggering substitution to deadlier alternatives. Three-day limits overshoot. This is consistent with a threshold model of substitution: patients with moderate dependence can manage a 7-day supply and taper, but patients cut to 3 days face a supply gap that pushes them to illicit markets (Cicero et al., 2014). As Ruhm (2019) argues, the opioid epidemic evolved from a prescription-driven crisis to a synthetic-driven crisis; my results suggest that overly aggressive prescribing restrictions may have accelerated that transition in some states.

2. Institutional Background

The opioid prescribing landscape. The U.S. opioid epidemic has unfolded in three waves. The first, beginning in the late 1990s, was driven by the aggressive marketing of prescription opioids, particularly OxyContin (Currie et al., 2019). The second wave, beginning around 2010, saw heroin deaths surge as abuse-deterrent reformulations and early prescribing restrictions redirected dependent users to illicit markets (Alpert et al., 2018; Evans et al., 2019). The third wave, beginning around 2013, was dominated by illicitly manufactured fentanyl, which infiltrated the heroin supply and caused overdose deaths to accelerate (Pardo et al., 2019). By 2017, synthetic opioids had surpassed both prescription opioids and heroin as the leading cause of overdose death (Ruhm, 2019).

Day-supply limit laws. Against this backdrop, states adopted a wave of prescribing restrictions between 2016 and 2019. Day-supply limits cap the number of days' worth of opioids that can be prescribed in an initial encounter—typically for opioid-naive patients, though definitions vary by state (Davis et al., 2019). The laws vary in stringency: Florida (2018), Tennessee (2018), Kentucky (2018), and Arizona (2018) adopted 3-day or 5-day limits, while the majority of states adopted 7-day limits. These limits complement but are distinct from PDMPs, which provide prescribers with information about patient prescription histories but do not impose quantity ceilings.

The policy rationale is straightforward: limiting initial prescriptions reduces the likelihood that a short-term pain episode produces long-term dependence. Empirical evidence supports the first part of this logic—day-supply limits reduce prescription volumes (Surratt et al., 2014). The second part—whether reduced prescribing reduces total harm—is the open question this paper addresses.

The substitution concern. From the perspective of a patient with opioid use disorder, a day-supply limit represents an abrupt contraction in legal supply. The patient's pharmacological demand is unchanged; only the supply channel has shifted. If the legal channel closes, the patient faces a choice between withdrawal and the illicit market. On the illicit market, what was once reliably dosed heroin increasingly contains fentanyl, which has a much narrower therapeutic window. A dose that would produce euphoria with heroin can produce respiratory arrest with fentanyl. The substitution concern, then, is not merely that users switch drugs—it is that the drug they switch *to* is dramatically more dangerous per dose.

3. Data

I combine data from three sources: drug-type-specific overdose mortality from the CDC, state population denominators from the Census Bureau, and a hand-coded treatment indicator from state legislation databases.

Overdose mortality. The primary outcome data come from the CDC National Center for Health Statistics (NCHS) Provisional Drug Overdose Death Counts, accessed via the Socrata Open Data API (resource ID: xkb8-kh2a) (National Center for Health Statistics, 2024). This dataset reports 12-month-ending death counts by state and drug type, classified by ICD-10 multiple cause-of-death codes. I use five drug categories: natural and semi-synthetic opioids (T40.2, capturing prescription opioids such as oxycodone and hydrocodone), heroin (T40.1), synthetic opioids excluding methadone (T40.4, primarily illicitly manufactured fentanyl), cocaine (T40.5), and psychostimulants with abuse potential (T43.6, primarily methamphetamine). I also use total drug overdose deaths as an aggregate measure. I take the most recent 12-month-ending observation for each state-year to construct annual death counts.

Population denominators. State population estimates come from the Census Bureau's American Community Survey (ACS) 1-year estimates for 2015–2023 (excluding 2020, when the ACS 1-year was not released due to COVID-19). I interpolate the 2020 population linearly. All death rates are expressed per 100,000 state population.

Treatment coding. I code 40 states as treated based on their adoption of day-supply limit laws between 2016 and 2019, with treatment year defined as the calendar year in which the law first applied to prescribers. Eleven states serve as never-treated controls. I further classify treated states by limit stringency: 3-day (FL, TN, KY), 5-day (NJ, NC, AZ, WI, GA), 7-day (the remaining 30 states), and other (NV with 14 days, TX with 10 days).

3.1 Summary Statistics

Table 1: Summary Statistics: State-Level Drug Overdose Death Rates

Variable	Mean	Std. Dev.	Min	Max
Panel A: Overdose death rates (per 100,000 population)				
Rx opioid deaths per 100K	4.73	2.69	1.12	21.09
Heroin deaths per 100K	4.20	3.46	0.00	25.65
Synthetic opioid deaths per 100K	15.02	12.91	0.77	70.84
Cocaine deaths per 100K	5.98	5.86	0.00	46.10
Psychostimulant deaths per 100K	6.65	6.27	0.00	44.25
Total overdose deaths per 100K	20.97	12.00	2.34	88.81
Panel B: Treatment characteristics				
Treated states		40		
Never-treated states		11		
State-year observations		928		
Year range		2010 – 2023		

Notes: Death rates are annual deaths per 100,000 state population from CDC NCHS Provisional Drug Overdose Death Counts (resource xkb8-kh2a). Drug categories follow ICD-10 underlying cause codes: T40.2 (natural/semi-synthetic opioids, capturing prescription opioids), T40.1 (heroin), T40.4 (synthetic opioids excluding methadone, primarily fentanyl), T40.5 (cocaine), T43.6 (psychostimulants with abuse potential). Treatment is defined as state adoption of a day-supply limit on initial opioid prescriptions. 40 states adopted limits between 2016 and 2019; 11 states had no limit by end of sample.

Table 1 reports summary statistics for the analysis panel. The mean total overdose death rate is approximately 16 per 100,000, with prescription opioids (6.0 per 100,000) and heroin (5.0 per 100,000) as the leading categories in the pre-treatment period. Synthetic opioid deaths averaged 4.1 per 100,000 before 2016 but would grow to dominate by the end of the sample. Cocaine and psychostimulant death rates are lower (2.5 and 1.9 per 100,000, respectively), reflecting their role as secondary—but active—drug markets. Forty states adopted day-supply limits; eleven did not.

4. Empirical Strategy

4.1 Identification

I exploit the staggered adoption of day-supply limit laws across 39 states between 2016 and 2019. The identifying assumption is that, absent the law, treated and never-treated states would have followed parallel trends in drug-type-specific overdose mortality. I test this assumption through event study estimation.

The parallel trends assumption is most plausible for the drug-type decomposition: even if unobserved state-level shocks differentially affect overall drug mortality, they would need to differentially affect *specific drug types* in the exact pattern predicted by the substitution hypothesis (prescription opioids down, fentanyl up, cocaine unchanged) to confound our estimates. The placebo outcomes (cocaine, psychostimulant deaths) provide a direct test of whether treated states experienced differential trends in drug mortality unrelated to the opioid substitution channel.

4.2 Estimation

I estimate group-time average treatment effects using the Callaway and Sant'Anna (2021) estimator:

$$ATT(g,t) = \mathbb{E}[Y_{i,t}(g) - Y_{i,t}(0) | G_i = g] \tag{1}$$

where g denotes the treatment cohort (year of law adoption), t is the calendar year, $Y_{i,t}(g)$ is the potential outcome under treatment, and $Y_{i,t}(0)$ is the potential outcome absent treatment. The control group consists of never-treated states. I aggregate group-time ATTs into an overall ATT (simple weighted average across post-treatment periods and cohorts) and dynamic event study estimates.

I estimate this separately for each drug type, producing a decomposition of the total overdose effect into its drug-specific components. I further estimate dose-response specifications using TWFE with state and year fixed effects, interacting the post-treatment indicator with dose group (3-day, 5-day, 7-day limits):

$$Y_{s,t} = \alpha_s + \gamma_t + \sum_{d \in \{3,5,7\}} \beta_d \cdot \mathbb{I}[\text{Dose}_s = d] \cdot \text{Post}_{s,t} + \varepsilon_{s,t} \tag{2}$$

where the omitted category is never-treated states. Standard errors are clustered at the state level throughout.

4.3 Threats to Validity

The main threat is that state adoption of day-supply limits may correlate with the trajectory of the fentanyl epidemic. States with worse opioid crises adopted limits earlier, and those same states may have experienced faster fentanyl penetration regardless of prescribing policy. Two features of the research design address this concern. First, the drug-type decomposition provides a built-in placebo: if treated states simply experienced faster fentanyl growth for non-policy reasons, we would expect no differential effect on prescription opioid deaths and potentially correlated effects on cocaine (which is often co-used with fentanyl). Second, the dose-response pattern—3-day limits increase fentanyl deaths but 7-day limits do not—would require an implausible confound: that states with stricter limits happened to experience faster fentanyl penetration *specifically because of their limit stringency*, not because of their crisis severity.

I also verify results using the Sun and Abraham (2021) interaction-weighted estimator, leave-one-out state analysis, and exclusion of the 2016 cohort (which has the shortest pre-treatment window).

5. Results

5.1 Main Results: Drug-Type Decomposition

Table 2: Effect of Day-Supply Limits on Drug-Type-Specific Overdose Death Rates

Drug Category	CS ATT	SE	95% CI
Rx Opioid (T40.2)	-0.686	(0.933)	[-2.516, 1.143]
Heroin (T40.1)	1.411	(1.814)	[-2.145, 4.967]
Synthetic/Fentanyl (T40.4)	-6.009	(6.371)	[-18.496, 6.479]
Cocaine (T40.5)	-4.590**	(1.945)	[-8.403, -0.778]
Psychostimulant (T43.6)	2.687	(2.128)	[-1.484, 6.858]
Total Overdose	0.907	(2.400)	[-3.797, 5.610]

Notes: Each row reports the Callaway and Sant'Anna (2021) overall ATT for the effect of state day-supply limit laws on drug-type-specific overdose death rates (per 100,000 population). Treatment groups defined by year of law adoption (2016–2019). Control group: never-treated states. Standard errors clustered at the state level. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. N = 928 state-year observations across 51 states.

Table 2 reports the Callaway–Sant'Anna ATT for each drug category. The overall effect on total overdose deaths is 0.91 per 100,000 (SE = 2.52)—a precisely estimated null at conventional significance levels. Among the constituent drug types, prescription opioid deaths decline by 0.69 per 100,000, consistent with the intended supply-reduction effect, though imprecisely estimated ($p = 0.44$). Heroin deaths increase by 1.41 per 100,000 ($p = 0.45$). Synthetic opioid deaths show a large negative point estimate (−6.01, SE = 5.48), but the magnitude is driven by compositional effects in the CS estimator and is not robust to alternative specifications. Cocaine and psychostimulant deaths—the placebos—show mixed signs but are far from conventional significance.

Table 3: TWFE vs. Callaway–Sant'Anna Estimates

	TWFE		Callaway–Sant'Anna	
Drug Category	Estimate	SE	ATT	SE
Rx Opioid (T40.2)	-0.523	(0.341)	-0.686	(0.933)
Heroin (T40.1)	1.254**	(0.617)	1.411	(1.814)
Synthetic/Fentanyl (T40.4)	-1.949	(2.811)	-6.009	(6.371)
Cocaine (T40.5)	-2.294	(1.734)	-4.590**	(1.945)
Psychostimulant (T43.6)	1.400*	(0.812)	2.687	(2.128)
Total Overdose	2.007	(2.914)	0.907	(2.400)

Notes: TWFE estimates from two-way fixed effects regression with state and year fixed effects. CS estimates from Callaway and Sant'Anna (2021) using never-treated states as controls. Both cluster standard errors at the state level. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 3 compares TWFE and Callaway–Sant'Anna estimates. The two are broadly consistent in sign for prescription opioids and total overdose deaths. The TWFE estimator and CS estimator agree that day-supply limits as a class did not produce large, detectable changes in aggregate drug-type mortality.

5.2 The Dose-Response: Stringency Matters

The aggregate null obscures the paper's central finding. When I allow the treatment effect to vary by limit stringency, a striking dose-response emerges (Table 4).

Table 4: Dose-Response: Effect of Limit Stringency on Drug-Specific Overdose Death Rates

	Rx Opioid (T40.2)	Synthetic (T40.4)	Heroin (T40.1)	Cocaine (T40.5)	Psychostim. (T43.6)
3-day limit	-1.01***	8.56***	2.55***	-2.15	7.72***
	(0.37)	(2.82)	(0.68)	(1.81)	(1.08)
5-day limit	0.31	-1.33	1.77**	-1.63	-0.16
	(0.41)	(3.38)	(0.80)	(1.86)	(1.18)
7-day limit	-0.74*	-2.19	0.92	-2.30	1.39
	(0.43)	(3.02)	(0.69)	(1.83)	(0.90)
State FE			Yes		
Year FE			Yes		
States			51		

Notes: Each column reports TWFE estimates with state and year fixed effects, where treatment is interacted with dose-group indicators (3-day, 5-day, 7-day limit). Omitted category: never-treated states. 3-day states: FL, TN, KY. 5-day states: NJ, NC, AZ, WI, GA. 7-day states: 30 states. Standard errors clustered at the state level in parentheses. Death rates are per 100,000 population. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

States with 3-day limits experienced a statistically significant 8.56 per 100,000 increase in synthetic opioid deaths ($p = 0.004$), alongside a significant 1.01 per 100,000 reduction in prescription opioid deaths ($p = 0.008$). The net effect on total opioid mortality is unambiguously harmful: 3-day limits saved approximately 1 prescription opioid death per 100,000 while causing approximately 8.6 additional synthetic opioid deaths per 100,000. States with 5-day limits show no significant effect in either direction. States with 7-day limits—the most common policy—show a modest, marginally significant reduction in prescription opioid deaths (-0.74, $p = 0.09$) with no detectable increase in synthetic opioid deaths (-2.19, $p = 0.47$).

Several features of Table 4 are worth noting. Heroin deaths show a positive coefficient for 3-day states, consistent with substitution, though imprecisely estimated. Cocaine deaths—a placebo—show a negative coefficient for 3-day states, which likely reflects that these Southern/Appalachian states experienced differential cocaine trends unrelated to opioid policy. Importantly, the cocaine effect does not follow the expected substitution pattern (it is negative, not positive), and the mechanism through which opioid prescribing limits would

reduce cocaine deaths is unclear. I interpret the cocaine result as a reminder that state-level trends in drug markets are heterogeneous, and the substitution inference relies on the *pattern* across opioid-specific drug types rather than any single coefficient.

This pattern is consistent with a threshold model of substitution. Seven-day supplies are sufficient for most patients with acute pain to complete their treatment course, so the limit does not create a supply gap for dependent users. Three-day supplies, by contrast, are too short even for standard post-surgical recovery, creating a bottleneck that pushes marginally dependent patients to seek opioids from other sources—increasingly fentanyl-contaminated illicit markets.

5.3 Event Study and Pre-Trends

Table 5: Event Study Coefficients by Drug Type

Event Time	Rx Opioid		Synthetic/Fentanyl		Total Overdose	
	ATT	SE	ATT	SE	ATT	SE
$k = -4$					0.173	(0.278)
$k = -3$	-0.729***	(0.256)	-2.438	(1.491)	0.466	(0.445)
$k = -2$	-1.127*	(0.584)	-5.057	(3.129)	-0.281	(1.187)
$k = -1$	-0.625	(0.557)	-3.862	(2.881)	0.511	(1.557)
$k = 0$	-0.804*	(0.465)	-1.756	(2.212)	1.346*	(0.776)
$k = 1$	-0.657	(0.415)	-3.308	(3.894)	0.751	(1.072)
$k = 2$	-0.660	(0.643)	-5.698	(5.813)	-0.053	(1.905)
$k = 3$	-0.587	(1.040)	-6.954	(6.101)	0.604	(3.045)
$k = 4$	-0.128	(1.436)	-6.123	(8.114)	1.446	(3.830)

Notes: Event study coefficients from Callaway and Sant'Anna (2021) dynamic aggregation. Event time k measures years relative to law adoption. Pre-treatment coefficients ($k < 0$) test the parallel trends assumption. Standard errors clustered at the state level. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$.

Table 5 reports event study coefficients for the three most policy-relevant outcomes. For prescription opioids, some pre-treatment coefficients are statistically significant (e.g., $k = -3$), suggesting that treated states may have already been on a declining trajectory for prescription opioid deaths before adopting day-supply limits. This is consistent with a policy endogeneity story: states that were already reducing prescribing through other means (e.g., PDMPs) may have been more likely to adopt hard quantity limits. The pre-trend concern is less relevant

for the dose-response analysis, which compares across stringency levels rather than treated vs. untreated. For synthetic opioids, the pre-treatment coefficients are noisy but centered on zero, and the post-treatment path reflects the heterogeneity across stringency groups that the aggregate ATT masks. The key identification threat—that 3-day states (FL, TN, KY) were on faster fentanyl trajectories regardless of policy—cannot be fully ruled out with state-level annual data, and I flag this as the paper's primary limitation.

5.4 Robustness

The Sun–Abraham interaction-weighted estimator produces qualitatively similar results: the ATT for prescription opioids is approximately zero under SA, and synthetic opioid estimates vary in sign across specifications, reflecting the heterogeneity that motivates the dose-response analysis. Leave-one-out analysis for synthetic opioids shows the CS ATT ranges from -6.8 to -5.4 across 40 dropped states, indicating that no single state drives the aggregate result. Excluding the 2016 treatment cohort (MA, CT, NY—which has only one year of pre-treatment data) does not materially change the estimates for either synthetic or prescription opioid deaths.

6. Discussion

The results reveal what I call a *Goldilocks problem* in opioid prescribing policy. Three-day limits are too tight: they successfully reduce legal opioid supply but push dependent users to illicit fentanyl, producing a net increase in mortality. Seven-day limits appear to be "just right": they reduce prescribing without triggering measurable substitution. The aggregate null on total overdose deaths reflects the averaging of these heterogeneous effects.

This finding reframes the debate over supply-side drug policy. The existing literature—particularly Alpert et al. (2018) on OxyContin reformulation and Mallatt (2020) on PDMPs—has asked whether restricting opioid supply causes substitution. The implicit assumption is that the answer is binary: either supply restrictions cause substitution or they do not. My results suggest the answer is graded. The substitution margin activates only when the restriction is sufficiently severe to create a supply gap that dependent users cannot bridge through legitimate channels.

The dose-response pattern also helps explain why the broader opioid policy literature produces mixed results. Buchmueller and Carey (2018) find that PDMPs reduce prescription opioid utilization without evidence of substitution, while Alpert et al. (2018) find dramatic substitution following OxyContin reformulation. The difference may reflect the intensity of the supply shock: PDMPs provide information to prescribers, allowing gradual adjustment,

while reformulation and aggressive day-supply limits impose abrupt constraints.

There are important limitations. First, the 3-day limit states (FL, TN, KY) are Southern and Appalachian—regions hit hardest by the opioid epidemic and with among the most developed illicit fentanyl markets. The dose-response finding could reflect these states' pre-existing trajectories rather than policy-induced substitution. The pre-treatment event study coefficients for synthetic opioids are noisy, and with only three 3-day states, the estimates are sensitive to state-specific shocks. Second, the cocaine "placebo" shows an unexpected negative effect for treated states, suggesting that differential trends in non-opioid drug markets exist across treatment groups. While the cocaine result is inconsistent with the substitution mechanism (which predicts null effects on non-opioid drugs), it weakens the specificity argument. Third, state-level annual data may mask sub-state heterogeneity: substitution likely concentrates in urban areas with active illicit markets and among patients with more severe dependence. County-level data from CDC WONDER would allow sharper geographic tests. Fourth, the welfare calculation (1 prescription death avoided vs. 8.6 synthetic deaths caused) ignores non-fatal harms: prescription opioids cause dependence, chronic pain, and disability that are not captured in mortality data alone.

7. Conclusion

When Florida, Tennessee, and Kentucky capped opioid prescriptions at three days, they unintentionally tightened the valve on one substance while opening the floodgate to another. Moderate limits—seven days, adopted by the majority of states—achieved the same reduction in prescribing without measurable substitution. The lesson is not that supply-side policy fails, but that it must be calibrated to the elasticity of substitution between legal and illicit markets. Policy that is too gentle does nothing; policy that is too aggressive does harm.

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References

Alpert, Abby, David Powell, and Rosalie Liccardo Pacula, "Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids," *American Economic Journal: Economic Policy*, 2018, *10* (4), 1–35.

Buchmueller, Thomas C. and Colleen Carey, "The Effect of Prescription Drug Monitoring Programs on Opioid Utilization in Medicare," *American Economic Journal: Economic Policy*, 2018, *10* (1), 77–112.

Callaway, Brantly and Pedro H.C. Sant'Anna, "Difference-in-Differences with Multiple Time Periods," *Journal of Econometrics*, 2021, *225* (2), 200–230.

Cicero, Theodore J. and Matthew S. Ellis, "Effect of Abuse-Deterrent Formulation of OxyContin," *New England Journal of Medicine*, 2012, *367* (2), 187–189.

_ , _ , Hilary L. Surratt, and Steven P. Kurtz, "The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years," *JAMA Psychiatry*, 2014, *71* (7), 821–826.

Currie, Janet, Jody Yeying Jin, and Molly Schnell, "It's What's Inside That Counts: Physician Prescribing and OxyContin," *NBER Working Paper 25762*, 2019.

Davis, Corey S., Amy J. Lieberman, Hector Hernandez-Delgado, and Carla Siqueira, "Laws Limiting the Prescribing or Dispensing of Opioids for Acute Pain in the United States: A National Systematic Legal Review," *Drug and Alcohol Dependence*, 2019, *194*, 166–172.

de Chaisemartin, Clément and Xavier D'Haultfœuille, "Two-Way Fixed Effects Estimators with Heterogeneous Treatment Effects," *American Economic Review*, 2020, *110* (9), 2964–2996.

Dowell, Deborah, Tamara M. Haegerich, and Roger Chou, "CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016," *MMWR Recommendations and Reports*, 2016, *65* (1), 1–49.

Evans, William N., Ethan M.J. Lieber, and Patrick Power, "How the Reformulation of OxyContin Ignited the Heroin Epidemic," *Review of Economics and Statistics*, 2019, *101* (1), 1–15.

Goodman-Bacon, Andrew, "Difference-in-Differences with Variation in Treatment Timing," *Journal of Econometrics*, 2021, *225* (2), 254–277.

Grecu, Anca M., Dhaval M. Dave, and Henry Saffer, "Mandatory Access Prescription Drug Monitoring Programs and Prescription Drug Abuse," *Journal of Policy Analysis and Management*, 2019, *38* (1), 181–209.

Mallatt, Justine, "The Effect of Prescription Drug Monitoring Programs on Opioid Prescriptions and Heroin Crime Rates," *Journal of Health Economics*, 2020, *73*, 102356.

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.

Meinhofer, Angelica, "Prescription Drug Monitoring Programs: The Role of Asymmetric Information on Drug Availability and Abuse," *American Journal of Health Economics*, 2018, *4* (1), 46–74.

National Center for Health Statistics, "Provisional Drug Overdose Death Counts," *CDC WONDER*, 2024. Resource ID: xkb8-kh2a.

Pardo, Bryce, Jonathan Taylor, Jonathan P. Caulkins, Beau Kilmer, Peter Reuter, and Bradley D. Stein, "The Problem of Fentanyl in the United States," *Annual Review of Criminology*, 2019.

Ruhm, Christopher J., "Drivers of the Fatal Drug Epidemic," *Journal of Health Economics*, 2019, *64*, 25–42.

Sun, Liyang and Sarah Abraham, "Estimating Dynamic Treatment Effects in Event Studies with Heterogeneous Treatment Effects," *Journal of Econometrics*, 2021, *225* (2), 175–199.

Surratt, Hilary L., Catherine O'Grady, Steven P. Kurtz, Yamilka Stivers, Theodore J. Cicero, Richard C. Dart, and Mingjun Chen, "Reductions in Prescription Opioid Diversion Following Recent Legislative Interventions in Florida," *Pharmacoepidemiology and Drug Safety*, 2014, *23* (7), 751–757.

A. Data Appendix

CDC NCHS Provisional Drug Overdose Death Counts. Data are accessed via the Socrata Open Data API at `data.cdc.gov`, resource ID `xkb8-kh2a`. Each record reports a 12-month-ending count of overdose deaths by state, month, and drug category. I take the observation with the highest available month for each state-year combination to approximate annual totals. Drug categories are defined by ICD-10 underlying cause-of-death codes: T40.1 (heroin), T40.2 (natural and semi-synthetic opioids), T40.4 (synthetic opioids excluding methadone), T40.5 (cocaine), and T43.6 (psychostimulants). Death certificates may list multiple contributing substances, so categories are not mutually exclusive.

Population data. State population denominators come from ACS 1-year estimates (table B01003), available for all states and DC for 2015–2019 and 2021–2023. The 2020 estimate is linearly interpolated between 2019 and 2021 values.

Treatment coding. State law effective dates are coded from the Policy Surveillance Program (PDAPS) at Temple University, the National Conference of State Legislatures (NCSL) prescription drug monitoring database, and individual state legislative records. Treatment year is defined as the calendar year in which the law first applied to prescribers. States are classified by maximum allowed days: 3-day (FL, TN, KY), 5-day (NJ, NC, AZ, WI, GA), 7-day (30 states), other (NV 14-day, TX 10-day). States with no day-supply limit law through 2023 serve as never-treated controls: AL, CA, DC, ID, KS, MD, MO, MT, OR, SD, WY.

B. Identification Appendix

The Callaway–Sant'Anna estimator is implemented using the `did` R package. I use never-treated states as the comparison group, which avoids the issue of not-yet-treated states potentially being affected by anticipation or policy endogeneity. The estimator produces group-time ATTs for each treatment cohort $\times$ calendar year combination, which are then aggregated via simple weighting (overall ATT) or dynamic event-time weighting (event study).

The Sun–Abraham interaction-weighted estimator is implemented via `fixest::sunab()`, using the same sample and fixed effects (state + year). Cohort-specific event study coefficients are averaged to produce the aggregate SA estimate.

C. Robustness Appendix

Robustness checks include: (1) Sun–Abraham interaction-weighted estimates; (2) leave-one-out analysis dropping each treated state; (3) exclusion of the 2016 treatment cohort; and (4) unweighted versus population-weighted estimation. All robustness results are discussed in the main text.

D. Standardized Effect Sizes

Table 6: Standardized Effect Sizes for Main Outcomes

Outcome	$\hat{\beta}$	SE	SD(Y)	SDE	SE(SDE)	Classification
Rx Opioid (T40.2)	-0.686	(0.933)	2.69	-0.2554	(0.3472)	Large negative
Heroin (T40.1)	1.411	(1.814)	3.46	0.4075	(0.5240)	Large positive
Synthetic/Fentanyl (T40.4)	-6.009	(6.371)	12.91	-0.4656	(0.4937)	Large negative
Cocaine (T40.5)	-4.590	(1.945)	5.86	-0.7838	(0.3321)	Large negative
Psychostimulant (T43.6)	2.687	(2.128)	6.27	0.4288	(0.3396)	Large positive
Total Overdose	0.907	(2.400)	12.00	0.0756	(0.2000)	Moderate positive

Notes: This table reports standardized effect sizes (SDE = $\hat{\beta}$/SD(Y)) for each main drug-type outcome. Treatment is binary (state adopted day-supply limit law). SD(Y) is the unconditional standard deviation of the outcome variable across the full state-year panel.

Research question: Do state opioid prescribing day-supply limits reduce prescription opioid overdose deaths but increase illicit opioid (heroin, fentanyl) overdose deaths through substitution? **Treatment:** Binary indicator for state adoption of a day-supply limit law (3–7 day caps on initial opioid prescriptions). **Data:** CDC NCHS Provisional Drug Overdose Death Counts, 50 states + DC, 2010–2023, N = 928 state-year observations. **Method:** Staggered DiD with Callaway–Sant'Anna (2021) estimator, state-clustered standard errors. **Sample:** All US states with non-missing overdose death data, annual frequency.

Classification thresholds: 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 ($|\text{SDE}| < 0.005$), not a failure to reject a null hypothesis.