Target Trials in Policy Evaluation: A Case Study in Medical Cannabis Laws

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ORIGINAL RESEARCH

Effects of U.S. State Medical Cannabis Laws on Treatment of Chronic Noncancer Pain

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This work will appear in the July issue of *Annals of Internal Medicine*.

Please limit outside discussion of substantive findings until then!

Disclosures

I have a family member employed by a cannabis distributor in Michigan.

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The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Medical Cannabis: A Partial Solution?

- Cannabis industry and advocates have argued that medical cannabis could be a partial solution to the opioid overdose crisis [1]
  - Substitution of cannabis for opioids to treat chronic non-cancer pain
- Clinical guidelines do **not** recommend cannabis
- Chronic non-cancer pain is a qualifying condition for medical cannabis under all 38 existing state (+DC) programs [2]
- Some evidence of substitution of cannabis for prescription opioids among patients [3]

- **Question:** What are the effects of state medical cannabis laws on receipt of opioid and guideline-concordant non-opioid pain treatments for chronic non-cancer pain?

1. https://thecannabisindustry.org/combating-the-opioid-epidemic/
2. https://www.ncsl.org/health/state-cannabis-policy-enactment-database
3. Bicket MC, et al. *JAMA Network Open*. 2023.

Policy Evaluation is Hard

- Necessarily limited sample size
- Often high variability in definitions of treatment
  - "States are the laboratories of democracy" [1]
- Hard to isolate a policy's effects when other policies go into place around the same time

- **Partial solution:** Be very thoughtful about design! (surprise)

1. *New State Ice Co. v. Liebmann*, 285 U.S. 262 . *1932*

Trial Emulation Framework:
Estimand & Scientific Question

Hypothetical Target Trial

- Estimand is typically ATE:
$$E[Y(1) - Y(0)]$$
- "In general, what is the effect on outcomes of a state implementing a medical cannabis law versus not implementing a medical cannabis law?"

Our Policy Trial Emulation Analogue

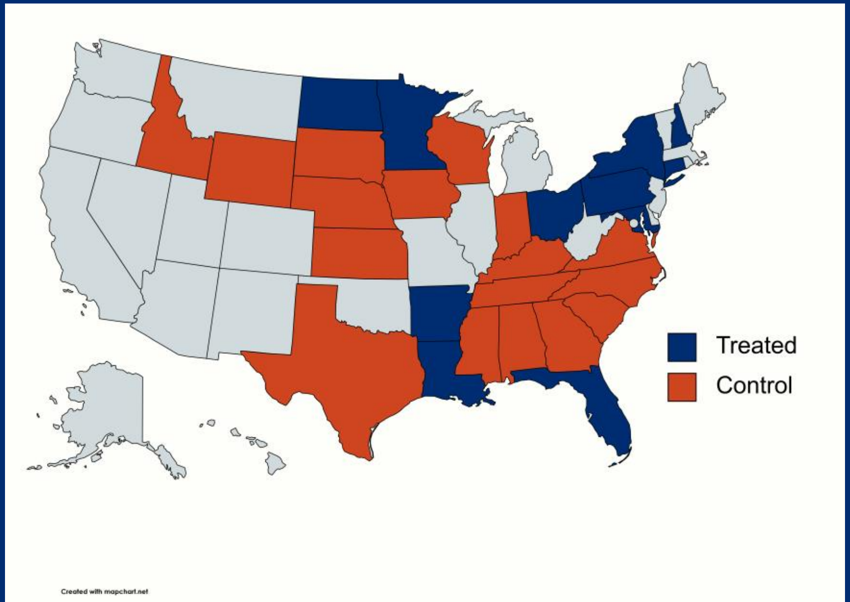
- Estimand is ATT:
$$E[Y(1) - Y(0) \mid A = 1]$$
- "Among states that implemented a medical cannabis law, what was the effect of the law on outcomes relative to what would have been observed had those states not implemented a medical cannabis law?"
- Only interested in studying policies on the books, rather than hypothetical policies

(ATT = ATE under random assignment or no treatment effect heterogeneity)

Trial Emulation Framework:
Units

Hypothetical Target Trial **AND** our Policy Trial Emulation Analogue

- **12 “treated” states** implemented a medical cannabis law between 2012 and 2019 and did not also implement a recreational cannabis program in that time.
- **17 “control” states** did not implement medical or recreational cannabis laws



Trial Emulation Framework:
Exposure & Outcomes

Hypothetical Target Trial **AND** our Policy Trial Emulation Analogue

- **Exposure:** Implementation of a medical cannabis law that includes chronic non-cancer pain diagnoses as qualifying conditions for receipt of medical cannabis
- **Outcomes:** Various measures of opioid and guideline-concordant non-opioid prescribing measured in time period after policy implementation (or lack of implementation)

Trial Emulation Framework: Assignment Procedure

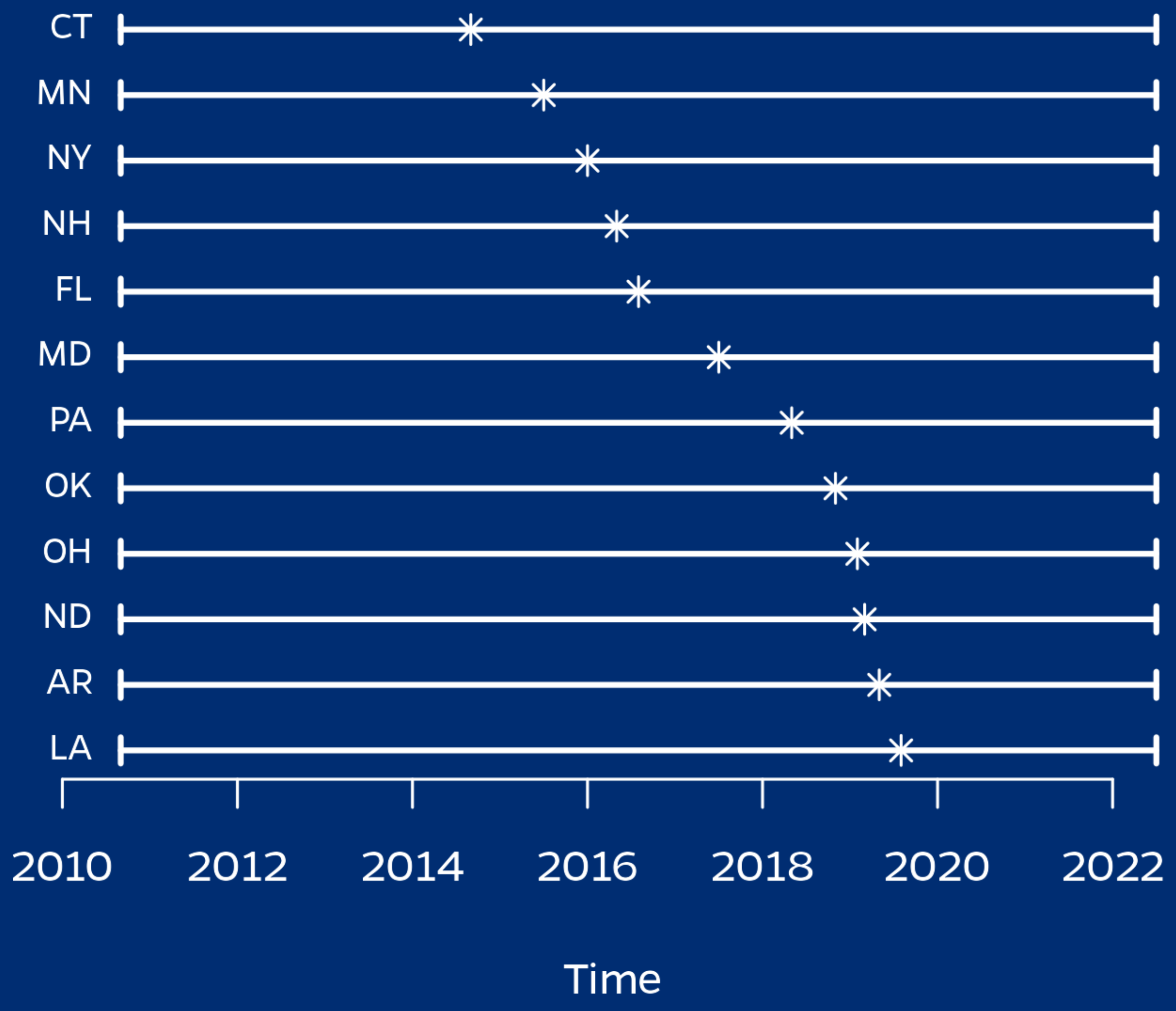
Hypothetical Target Trial

- Random assignment of states to implement or not implement a medical cannabis law after 4 years of baseline data collection.
- Unblinded: states will be aware of randomization status
- Essentially cluster-randomized (data from individuals within states)

Our Policy Trial Emulation Analogue

- Nonrandom policy adoption, possibly influenced by both known and unknown state-level characteristics

Staggered Adoption of Medical Cannabis Laws



Staggered Adoption Causes Problems with Traditional Methods

- Research question in medical cannabis study is about an ATT

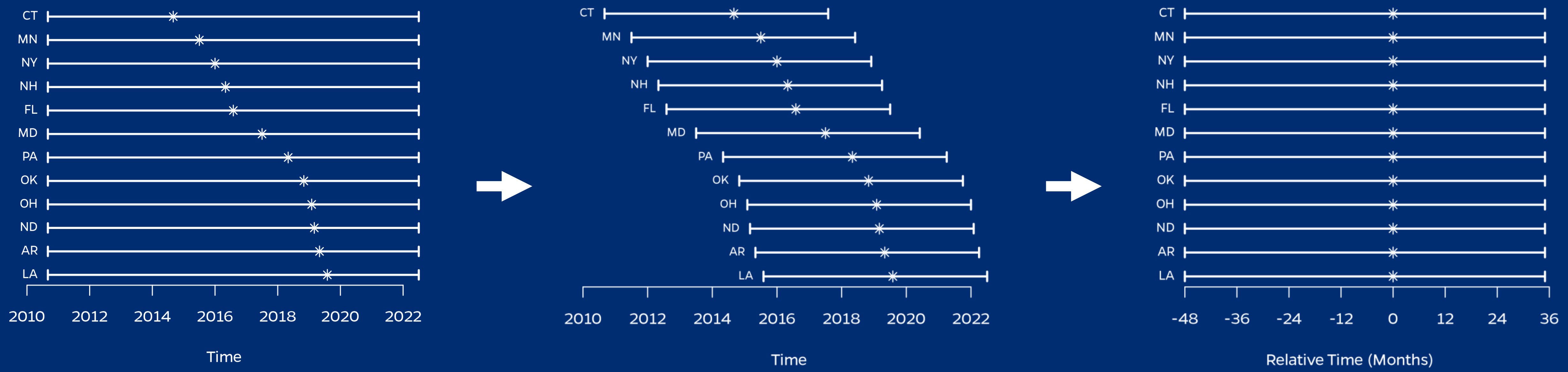
$$E[\,Y(1) - Y(0) \mid A = 1\,]$$

on average over the treated states.

- Traditional policy evaluation method turns out to be *very biased* for this estimand under staggered adoption when treatment effect is time-varying (i.e., almost always) [1]
- *But:* it's okay when we look at one treated state at a time.

1. Goodman-Bacon A. *J Econometrics. 2021.*

“Stacking” (Serial Trial Emulation)



Start with full data

Fix study periods

Anchor time at policy implementation

1. Hernán MA, Robins JM. *Am. J. Epidemiol*. 2016.
2. Ben-Michael E, Feller A, Stuart EA. *Epidemiology*. 2021.

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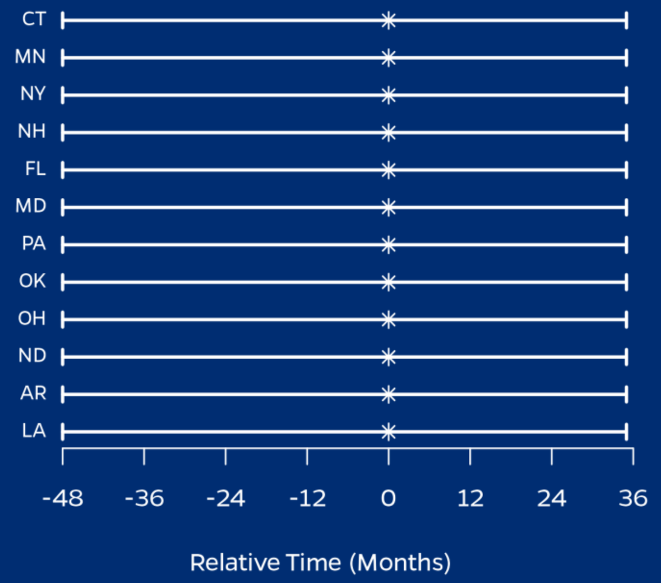


Anchor time at policy implementation

$$\left.\begin{array}{c}\widehat{ATT}_{CT}\\ \widehat{ATT}_{MN}\\ \widehat{ATT}_{NY}\\ \vdots\\ \widehat{ATT}_{AR}\\ \widehat{ATT}_{LA}\end{array}\right\} \quad \widehat{ATT}$$

Estimate state-specific effects

Aggregate state-specific effects (using, e.g., inverse-variance weighting)

1. Hernán MA, Robins JM. *Am. J. Epidemiol.* 2016.
2. Ben-Michael E, Feller A, Stuart EA. *Epidemiology*. 2021.

Trial Emulation Framework:
Data Collection Units

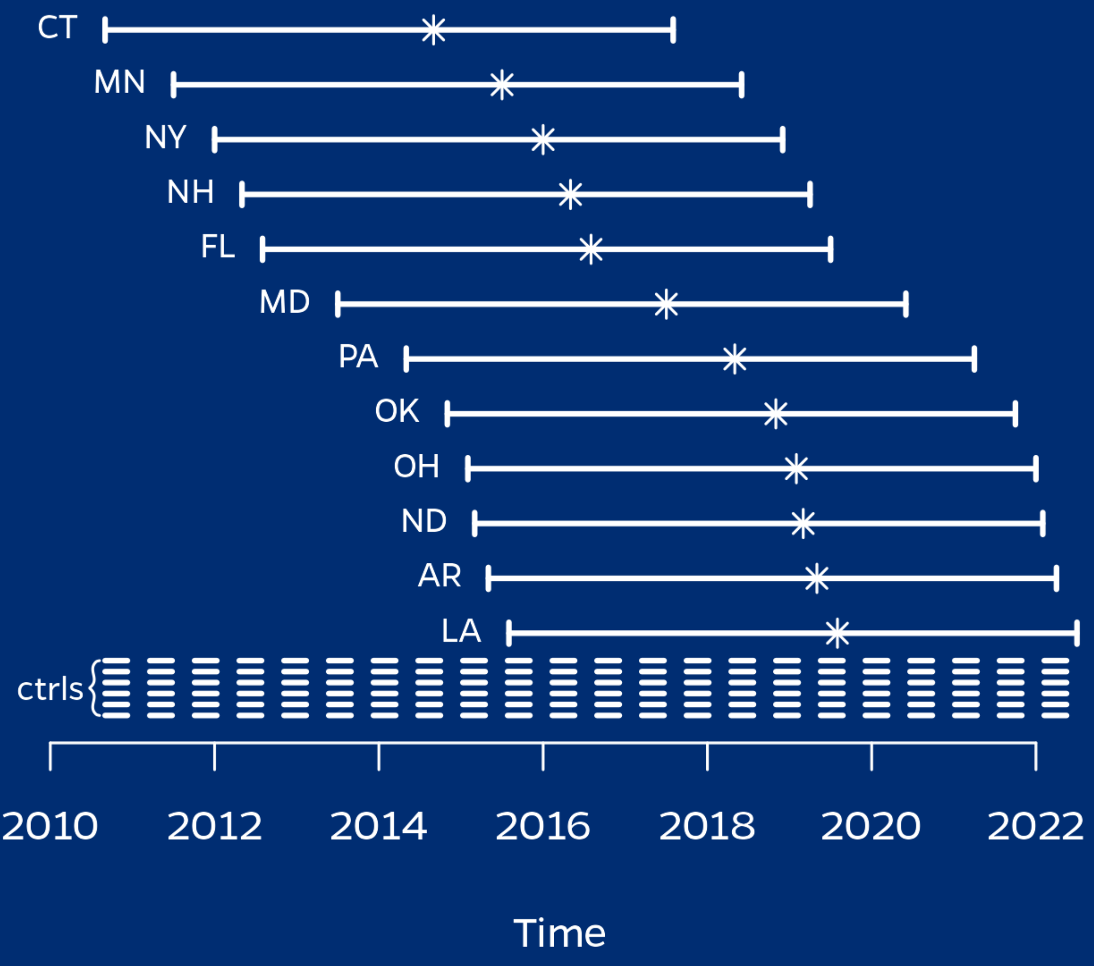
Hypothetical Target Trial

- People living in exposed & unexposed states with a chronic non-cancer pain diagnosis in the 4 years prior to policy implementation.
- Ideally people would not be allowed to move across states, wouldn't die, and would contribute complete data
  - Avoid compositional changes over time

Our Policy Trial Emulation Analogue

- People living in the treated state or one of the untreated states with a chronic non-cancer pain diagnosis in treated state's 4-year pre-law period
- Continuously enrolled in commercial health insurance for entire 7-year study period
  - Avoid compositional changes over time
  - No reason to believe enrollment is related to implementation of cannabis law

State Cohort Construction:
Anchoring Time for Controls



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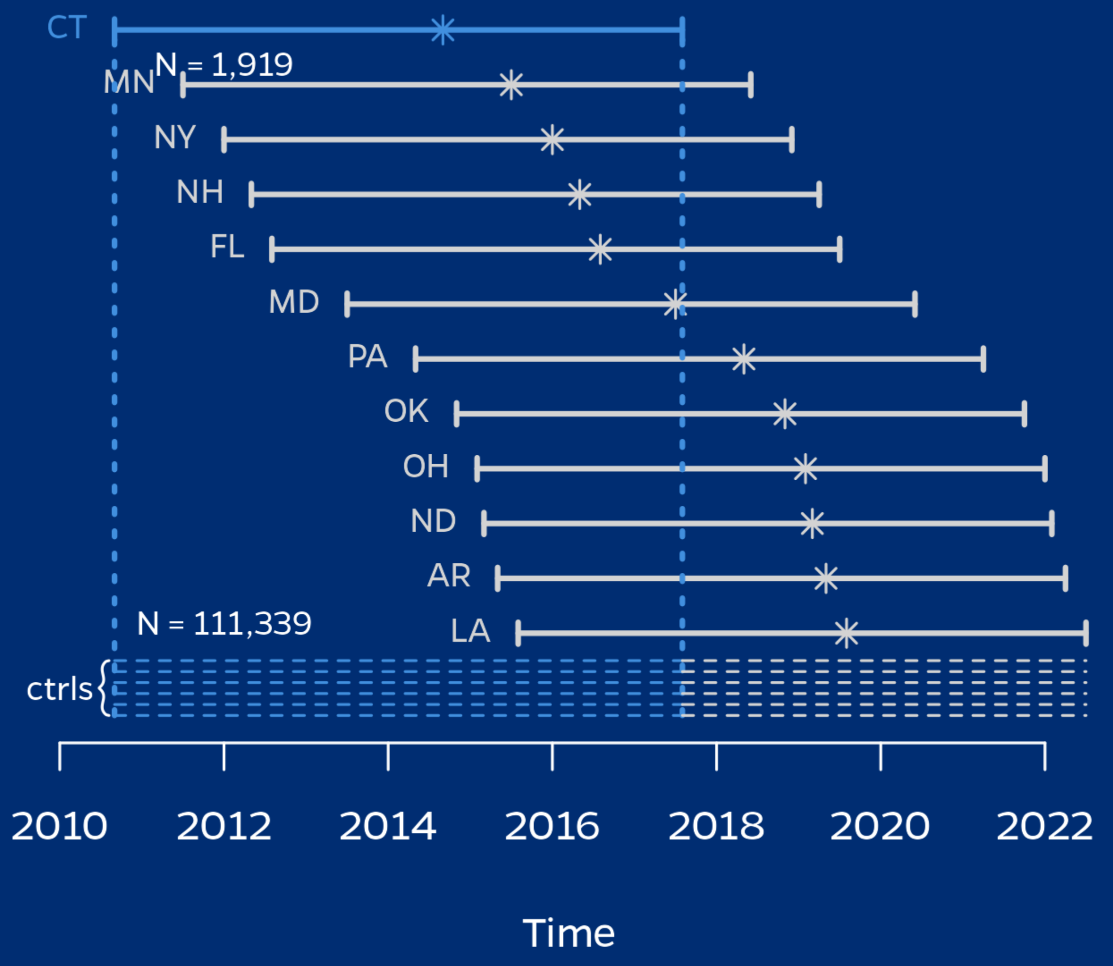

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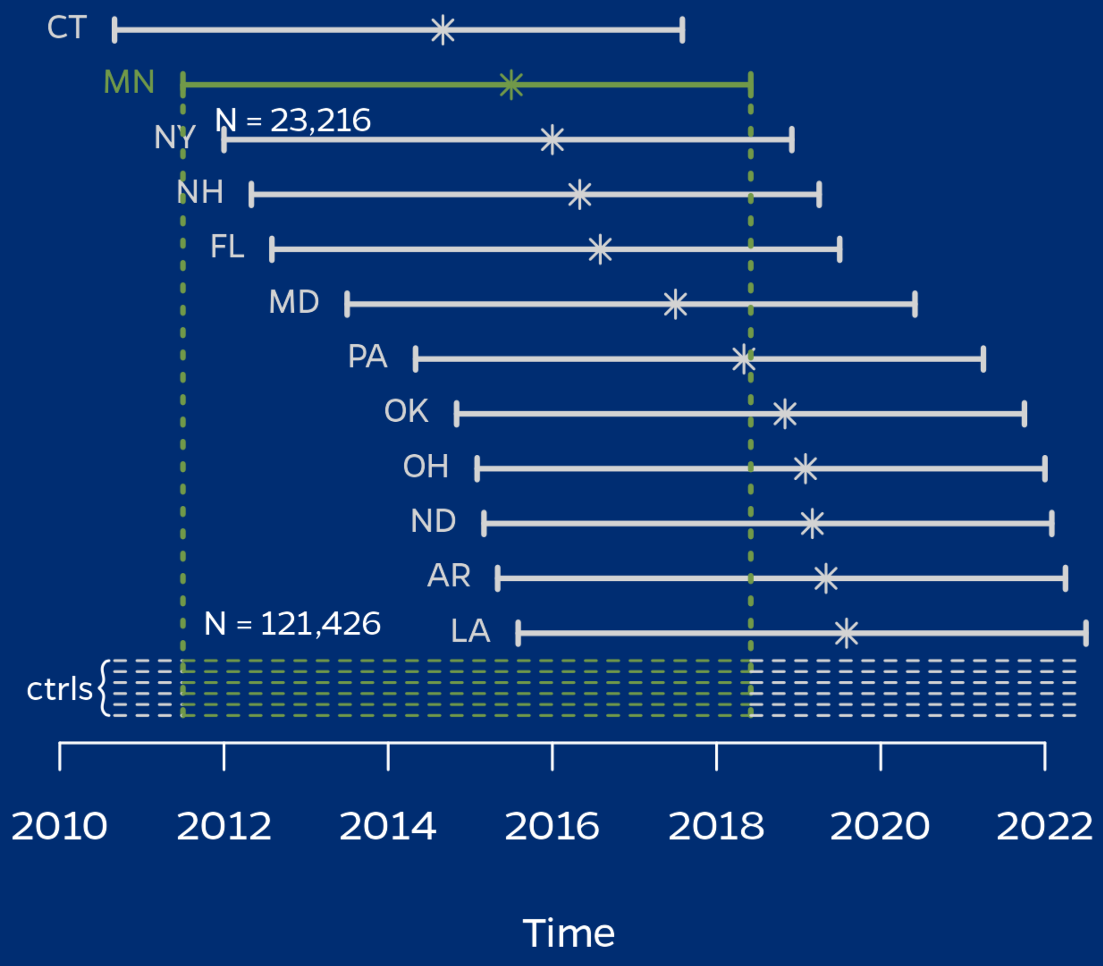

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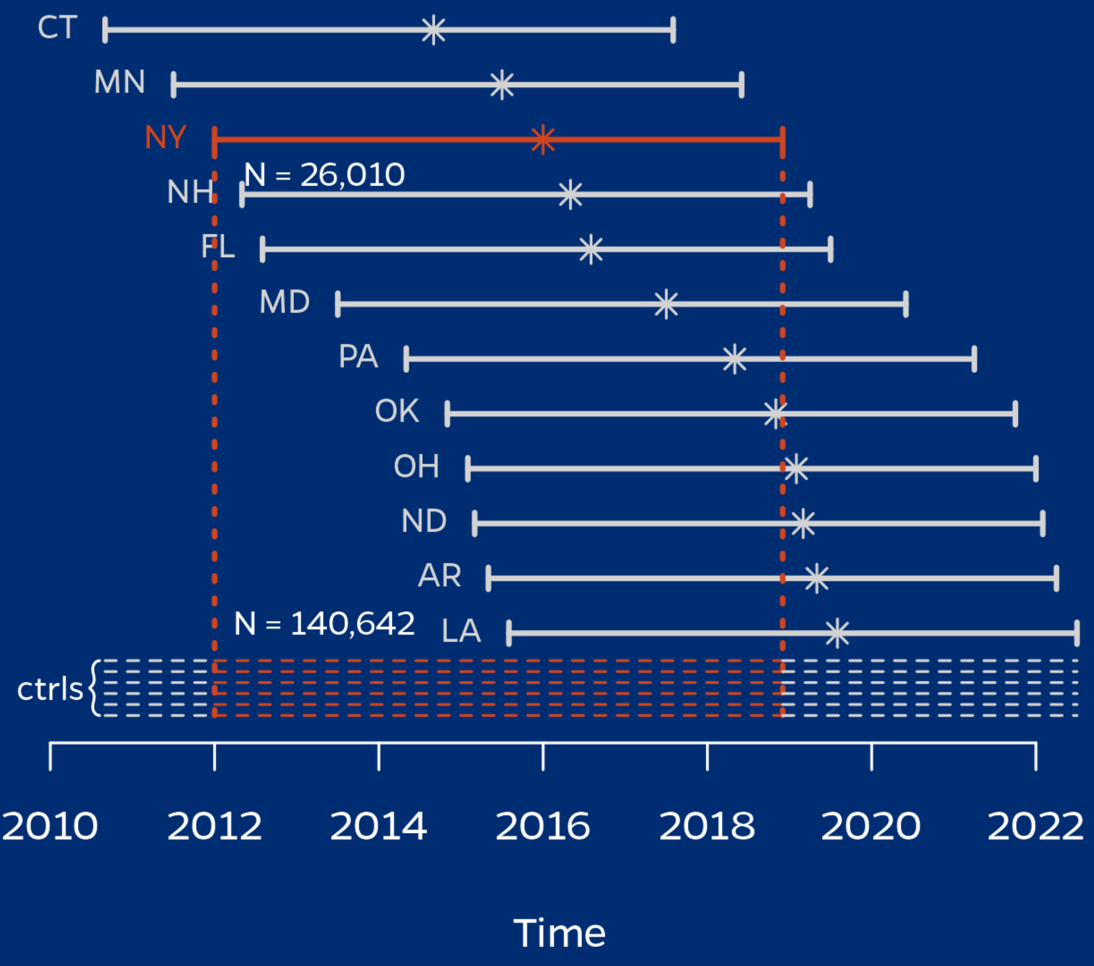


Trial Emulation Framework: Analytic Strategy

Hypothetical Target Trial

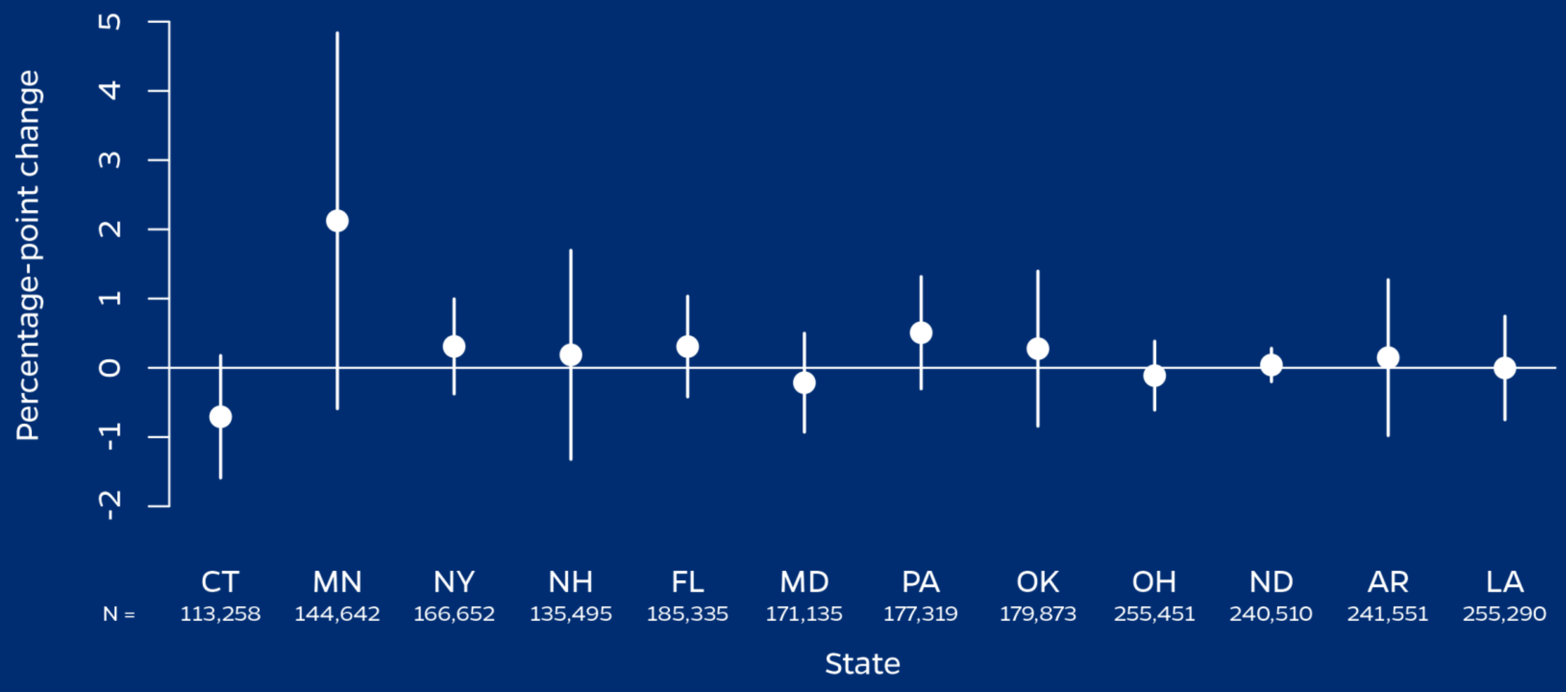
- "Traditional" modeling approach for cluster-randomized trial with longitudinal outcome
- Effect estimation unconfounded due to randomization

Our Policy Trial Emulation Analogue

- Stacked effect estimation
- Must account for potential confounders
  - Idiosyncratic in "difference-in-differences" setups
- We used the **augmented synthetic control method** [1]

1. Ben-Michael E, Rothstein J, Feller A. *J Am Stat Assoc.* 2021.

Medical Cannabis Study Results: Proportion Receiving Opioid Prescriptions



State-specific effects of medical cannabis laws on

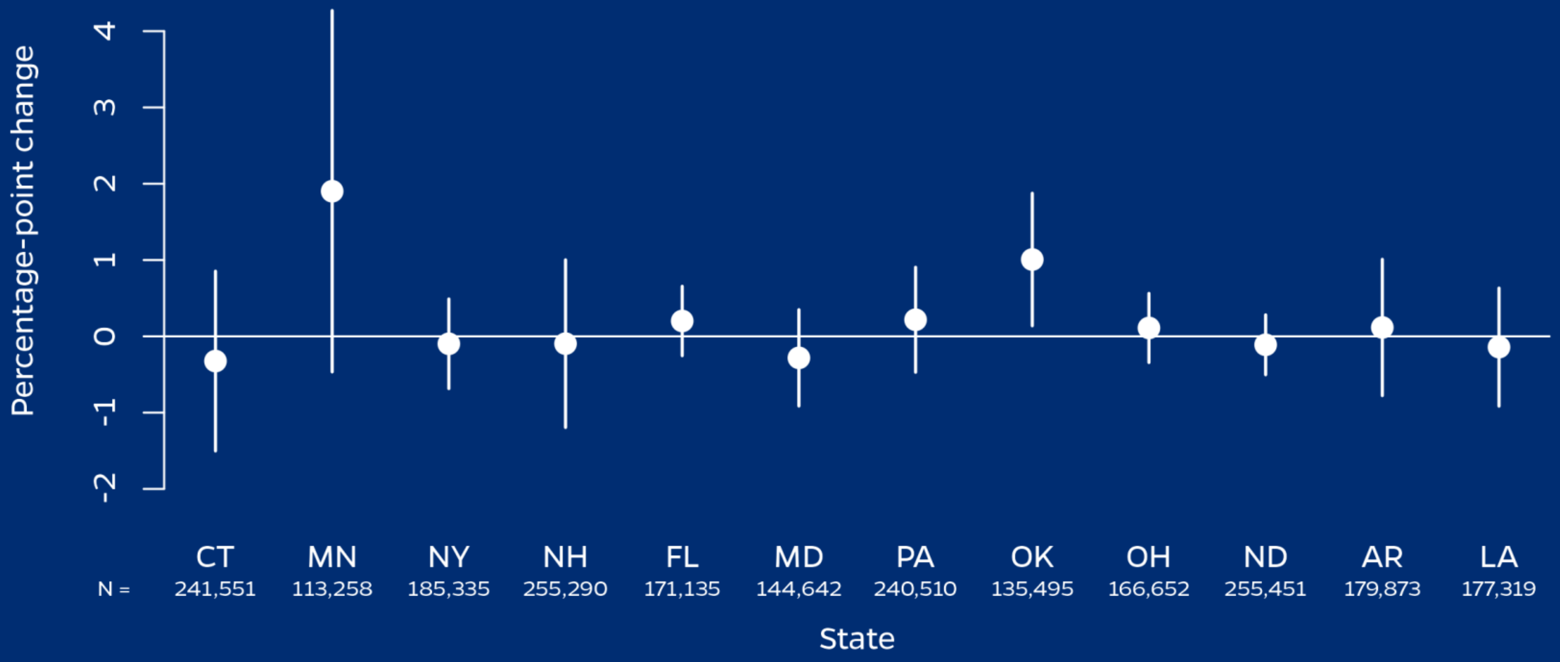
the proportion of chronic non-cancer pain patients receiving *__any opioid prescription__* in a given month,

on average over the first 3 years of law implementation.

Inverse-variance weighted aggregate effect:
0.05 (-0.12, 0.21) pct points

1. McGinty EE, et al. *Ann Internal Med*. To Appear.

Medical Cannabis Study Results:
Proportion Receiving Non-Opioid Prescriptions



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Recap

- Trial emulation provides a nice framework for good study design
  - Careful consideration of estimand, baseline, analysis
- Avoids issues with traditional kitchen-sink modeling approaches in policy evaluation
  - State-specific estimates are useful!
- Can go further: might allow changing control pool if comparison states implement confounding policies (i.e., different controls for each treated state)

Acknowledgements

Co-authors: Beth McGinty, Kayla Tormohlen, Mark Bicket, Alex McCourt, Lainie Rutkow, Sarah White, Liz Stuart

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