



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

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## 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)

# 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:

$$E[Y(1) - Y(0) | A = 1]$$

- ▶ “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: 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



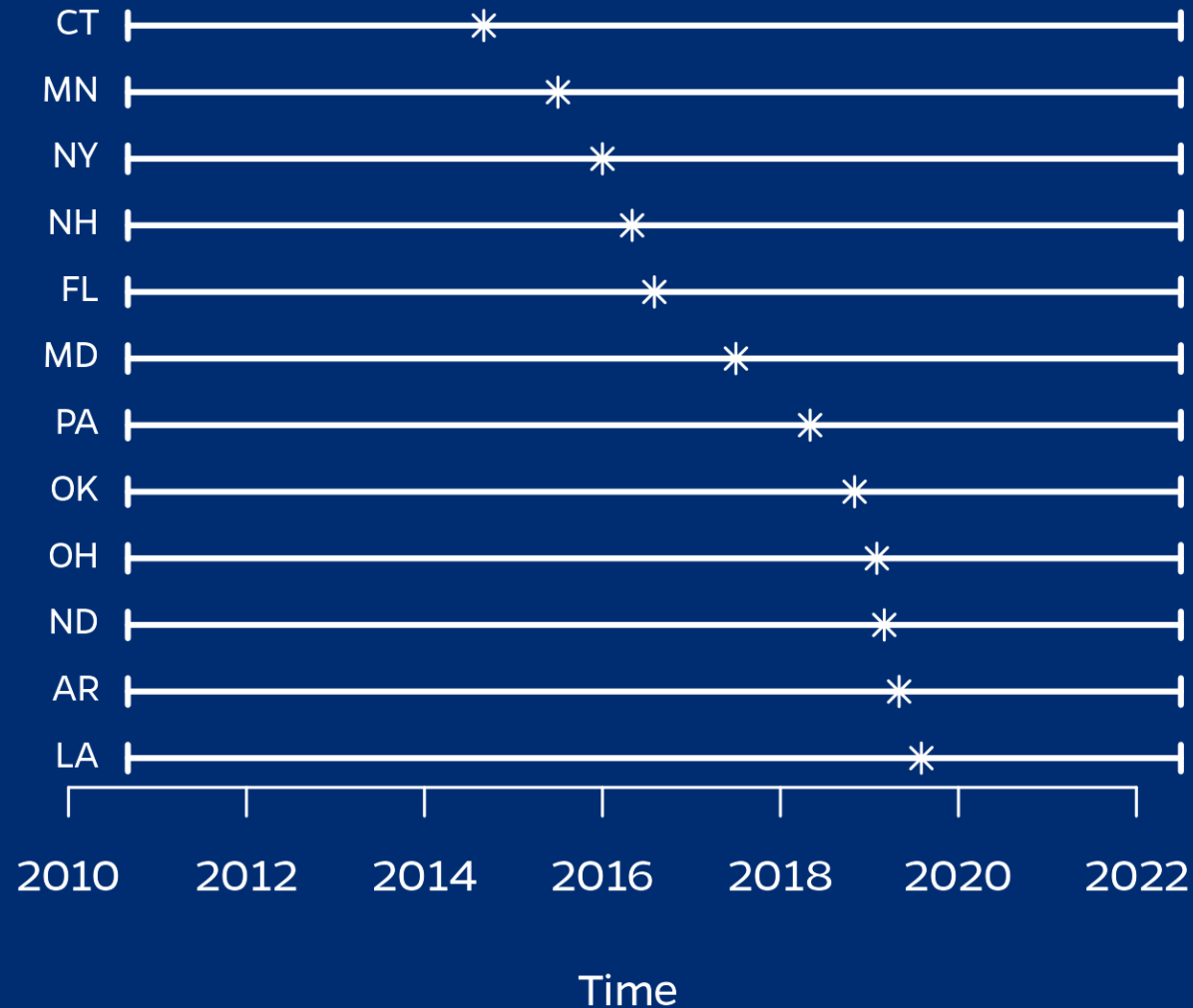
## Hypothetical Target Trial

- ▶ 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

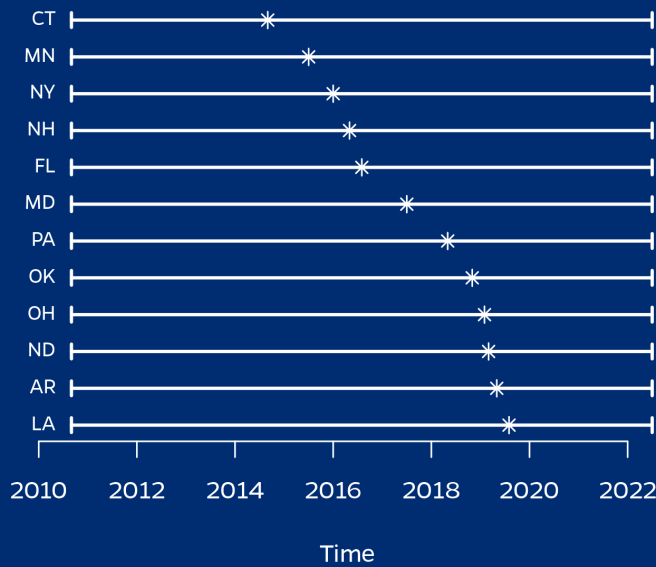
$$E[ Y(1) - Y(0) \mid A = 1 ]$$

*on average over the treated states.*

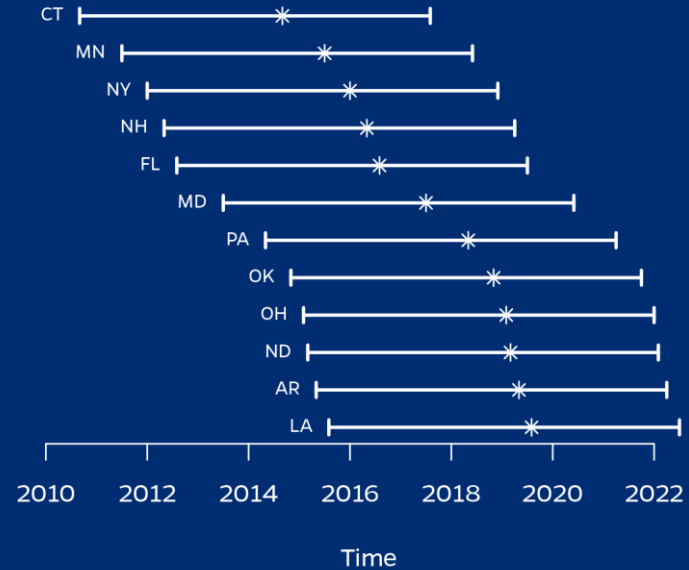
- ▶ Traditional policy evaluation method turns out to be *very biased* for this estimand under staggered adoption when treatment effect is time-varying (i.e., almost always) [1]
- ▶ *But:* it's okay when we look at one treated state at a time.



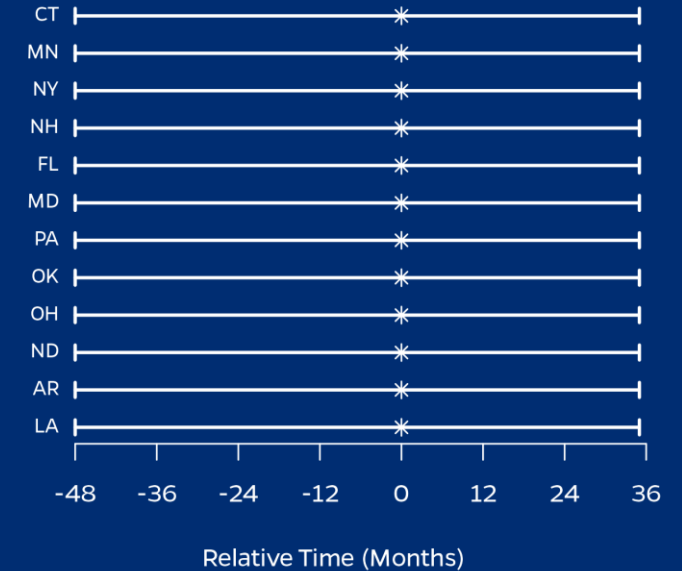
# “Stacking” (Serial Trial Emulation)



Start with full data



Fix study periods

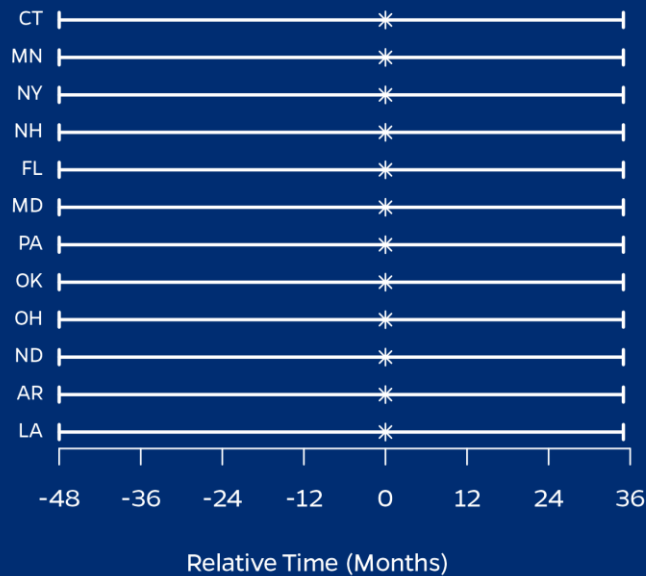


Anchor time at policy implementation

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



# “Stacking” (Serial Trial Emulation)



$$\begin{aligned} & \widehat{ATT}_{CT} \\ & \widehat{ATT}_{MN} \\ & \widehat{ATT}_{NY} \\ & \vdots \\ & \widehat{ATT}_{AR} \\ & \widehat{ATT}_{LA} \end{aligned}$$



$$\widehat{ATT}$$

Anchor time at policy implementation

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



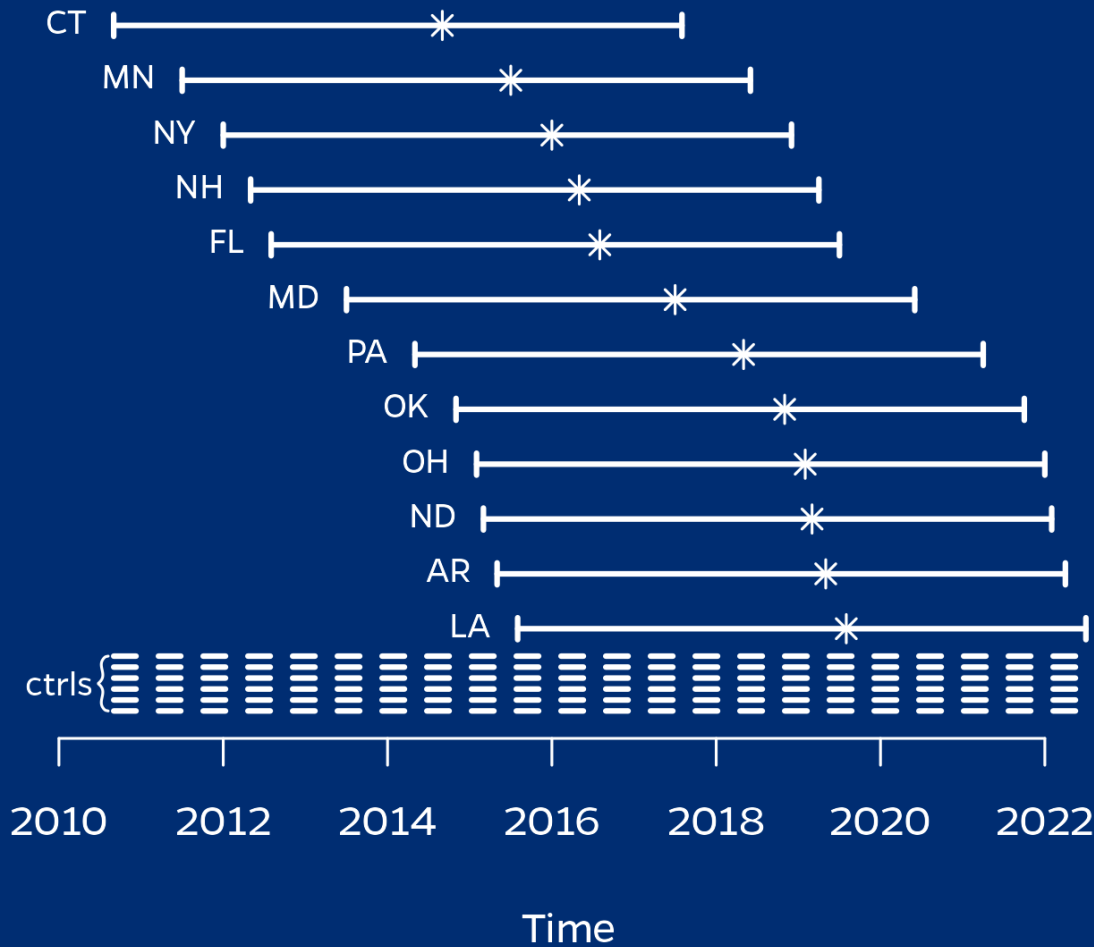
## Hypothetical Target Trial

- ▶ 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

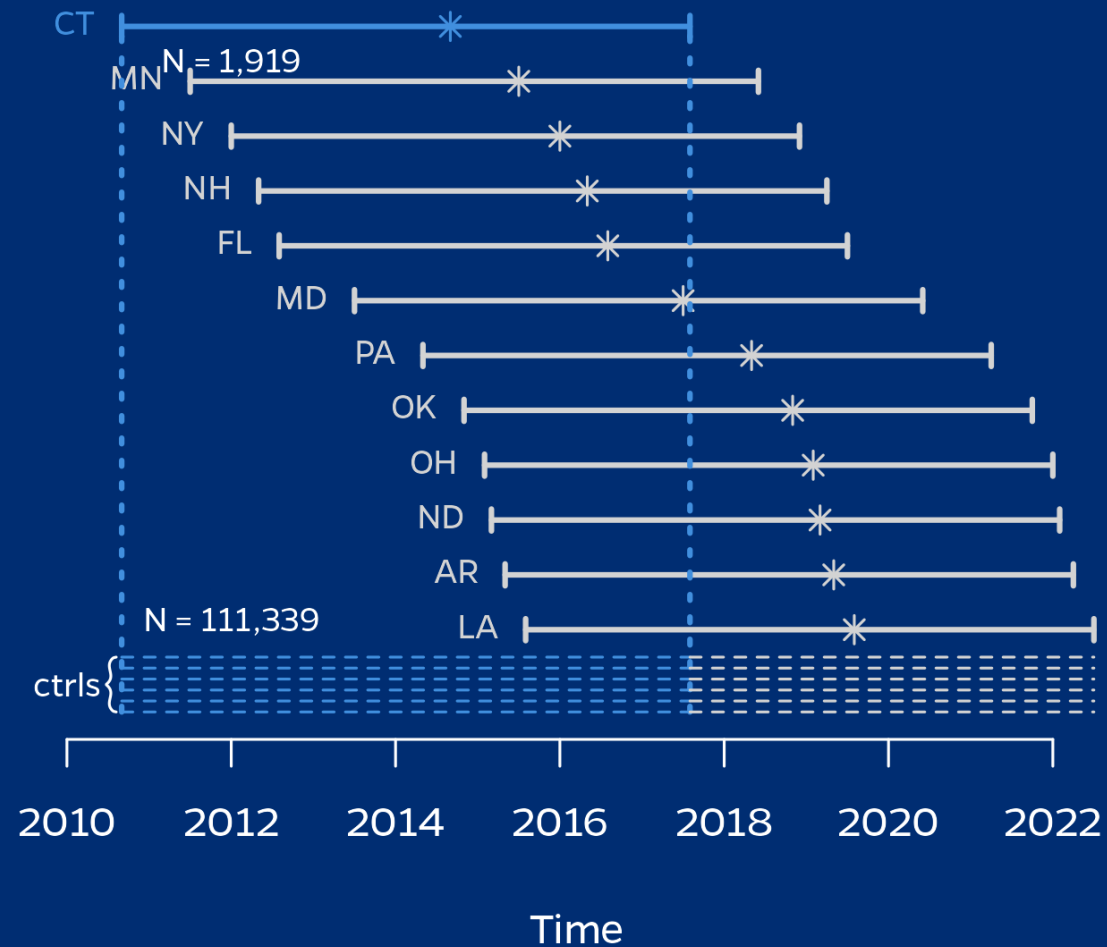
## Our Policy Trial Emulation Analogue

- ▶ 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

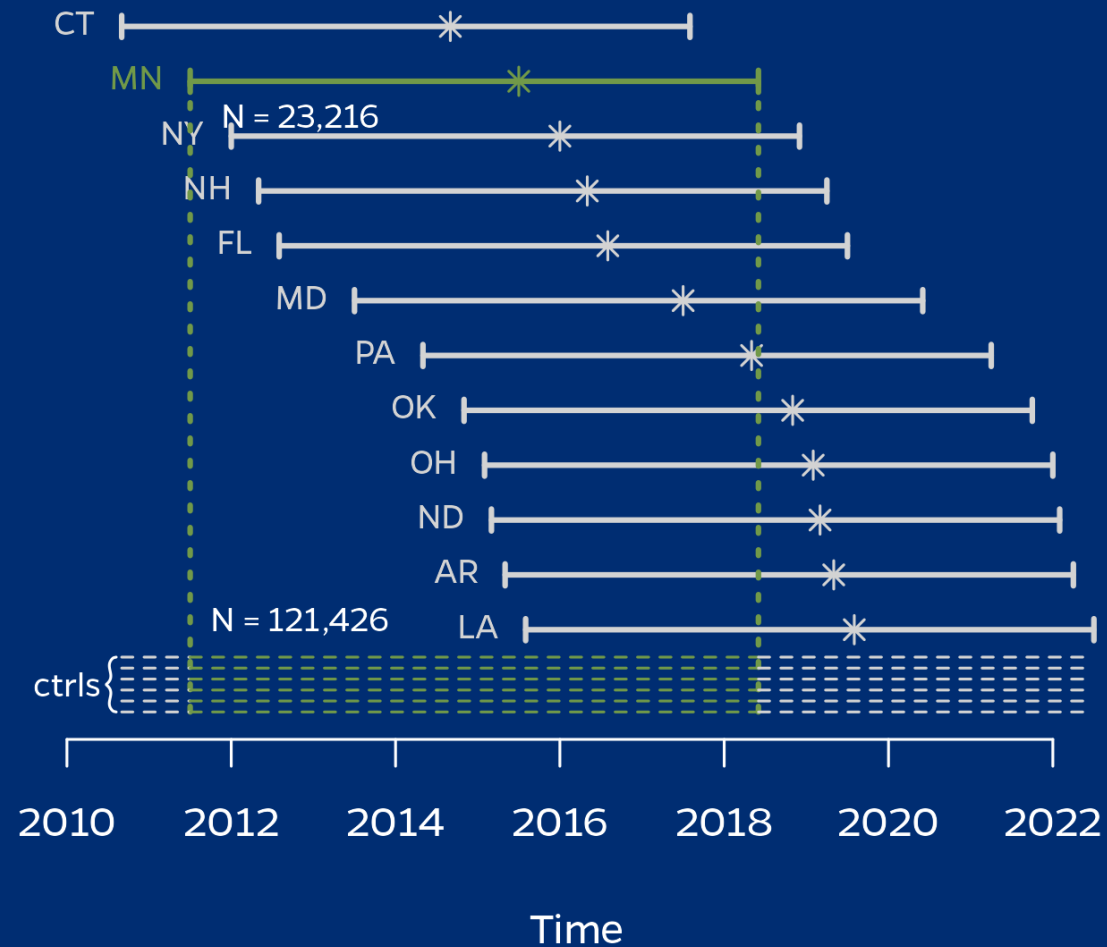


# State Cohort Construction: Anchoring Time for Controls

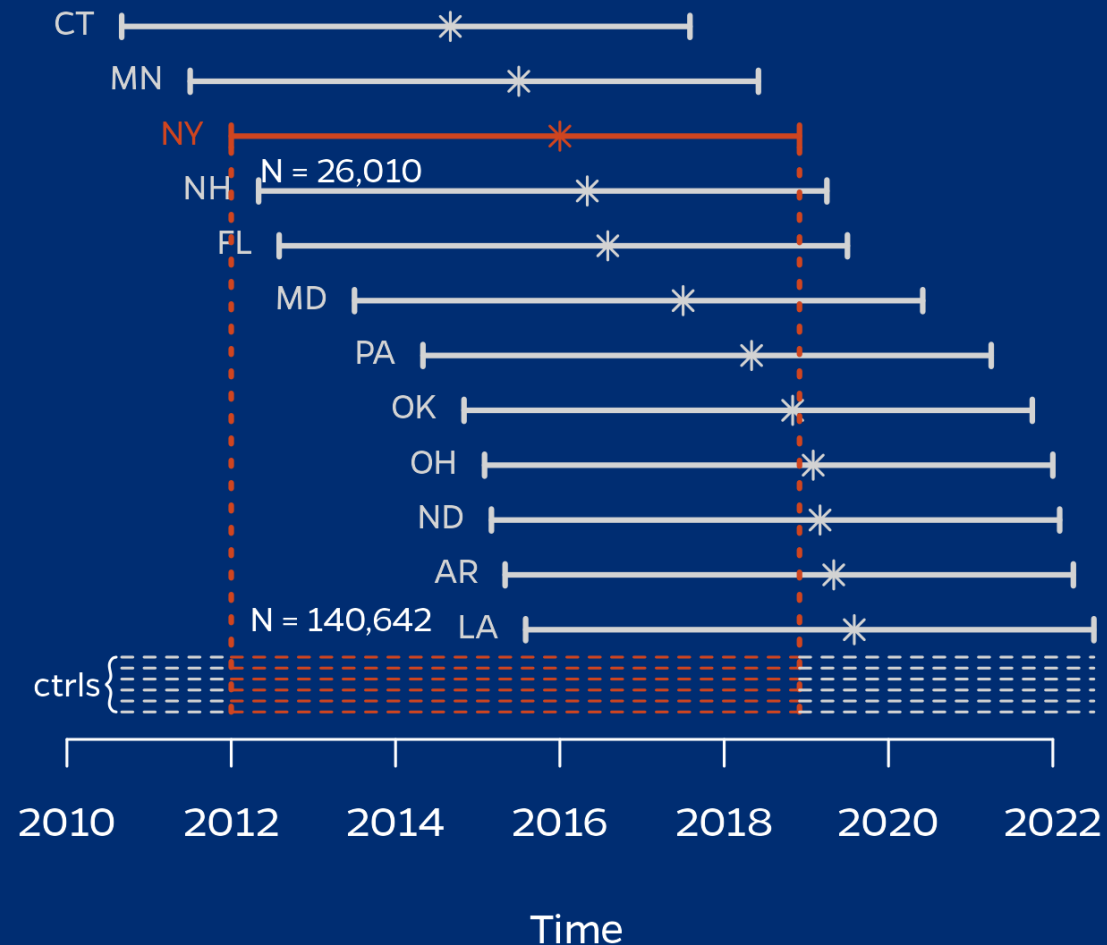




# State Cohort Construction: Anchoring Time for Controls



# State Cohort Construction: Anchoring Time for Controls



# 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]



# 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)

A large, faint graphic on the left side of the slide. It features a stylized flame at the top and a globe with latitude and longitude lines below it, all in a lighter shade of blue than the background.

# Acknowledgements

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

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