

UC Berkeley

UC Berkeley Electronic Theses and Dissertations

Title

Evaluating the health effects of policies using administrative and observational data sources

Permalink

<https://escholarship.org/uc/item/22b6w43t>

Author

Rowe, Christopher Lloyd

Publication Date

2020

Peer reviewed|Thesis/dissertation

Evaluating the health effects of policies using administrative and observational data sources

By

Christopher Lloyd Rowe

A dissertation submitted in partial satisfaction of the

requirements for the degree of

Doctor of Philosophy

in

Epidemiology

in the

Graduate Division

of the

University of California, Berkeley

Committee in charge:

Professor Jennifer Ahern, Chair

Professor Alan Hubbard

Professor Steven Raphael

Fall 2020

Evaluating the health effects of policies using administrative and observational data sources

Copyright 2020
By
Christopher Lloyd Rowe

Abstract

Evaluating the health effects of policies using administrative and observational data sources

By

Christopher Lloyd Rowe

Doctor of Philosophy in Epidemiology

University of California, Berkeley

Professor Jennifer Ahern, Chair

Understanding of the health effects of specific interventions is a key objective of epidemiology. Policies, whether implemented by governments or other institutions, have immense potential to influence population health and thus represent important study exposures for epidemiologists. However, because policies are often implemented without specific consideration of or plans for evaluation, there are two key challenges to any attempt to evaluate their effects: data availability and the methodological challenges associated with estimating causal effects using observational data. Fortunately, both the number and diversity of data sources that are available to health and other social science researchers are vast and constantly growing. In addition, there is a rich history of methodological advancement across multiple disciplines (most notably economics, statistics, political science, epidemiology, and biostatistics) pertaining to the evaluation of intervention effects in observational settings. The availability of large, novel data sources and a diverse set of methodological tools, combined with recent calls for a more “consequentialist” epidemiology that focuses as much on the effects of interventions as it does on understanding etiology, makes it an exciting time to be an epidemiologist. As such, the studies that constitute this dissertation aim to evaluate the health effects of three distinct sets of policies using diverse administrative and observational data sources and methods developed across multiple disciplines.

The first study evaluates the impacts of two national policies that aimed to expand access to buprenorphine for the treatment of opioid use disorder. The United States continues to grapple with an unprecedented opioid overdose epidemic and expanding access to medications for the treatment of opioid use disorder (MOUD), such as buprenorphine, is a key priority in the national response to the epidemic. This study uses comprehensive administrative data sources from California to evaluate the effects of 2016 policies expanding the buprenorphine waiver program on buprenorphine prescribing and opioid-related health outcomes.

The second study evaluates the impact of two clinic-level policies that aimed to reduce opioid prescribing at a safety-net clinic in 2013 and 2014 in San Francisco, CA. In addition to expanding access to MOUD, a concurrent strategy for addressing the opioid crisis has been to reduce unnecessary prescribing of opioid medications. However, there is ongoing concern that inflexible one-size-fits-all reductions in opioid prescribing could ultimately harm patients, and even result in transitions from prescription opioid use and dependence to heroin use and dependence. In 2013

and 2014, the clinic under study established standard protocols for dispensing opioid refills and conducting urine toxicology testing and a new committee facilitating opioid treatment decisions for complex patient cases. Using data from a retrospective cohort study of patients on long-term opioid therapy, this study evaluates the effects of these policies on opioid prescribing and use of heroin and opioid analgesics not prescribed to the patient.

The third study evaluates the impact of a major California criminal justice policy on mortality among state prisoners. In October 2011, California Assembly Bill 109 (AB109) sought to decrease the prison population by prospectively shifting the custodial responsibility of non-violent, non-serious, and non-sexual offenders from state prisons to county jails and probation departments. Leveraging several complementary data sources, this study evaluates the effects of AB109 on California state prisoner mortality.

Collectively, these studies contribute new evidence regarding the effects of these three sets of policies. Furthermore, two of the studies demonstrate the utility of administrative data sources for assessing the impacts of real-world interventions. As these data sources expand and become more organized, rigorous analyses that leverage their strengths and acknowledge their limitations will grow increasingly valuable as a tool for knowledge creation among epidemiologists and other applied researchers.

Table of Contents

<i>Acknowledgements</i>	<i>ii</i>
<i>Chapter 1: Introduction.....</i>	<i>1</i>
1.1 REFERENCES.....	2
<i>Chapter 2: Evaluating the effects of expanding the buprenorphine waiver program.....</i>	<i>3</i>
2.1 INTRODUCTION	3
2.2 METHODS	4
2.3 RESULTS.....	10
2.4 DISCUSSION	12
2.5 REFERENCES.....	14
2.6 FIGURES AND TABLES	21
<i>Chapter 3: Evaluating the effects of opioid prescribing policies on patient outcomes in a safety-net primary care clinic.....</i>	<i>34</i>
3.1 INTRODUCTION	34
3.2 METHODS	35
3.3 RESULTS.....	39
3.4 DISCUSSION	40
3.5 REFERENCES.....	42
3.6 FIGURES AND TABLES	46
<i>Chapter 4: Examining prisoner mortality following California’s historic Public Safety Realignment Act.....</i>	<i>58</i>
4.1 INTRODUCTION	58
4.2 METHODS	59
4.3 RESULTS.....	66
4.4 DISCUSSION	69
4.5 REFERENCES.....	72
4.6 FIGURES AND TABLES	76

Acknowledgements

This work would not have been possible without the support and generosity of so many.

It has been my great fortune to work under Dr. Jennifer Ahern during the course of my doctoral training. The care and rigor with which she practices science, her commitment and unflagging responsiveness to her students, and the opportunities she has cultivated for me delivered a level of training that I could not have obtained elsewhere or with an alternative advisor.

I am also incredibly grateful for the support of the other two members of my dissertation committee, Drs. Alan Hubbard and Steven Raphael. Dr. Hubbard's inputs on a variety of projects throughout my training have enabled me to develop a solid foundation of biostatistical knowledge, without which this and other work would not have been possible. Dr. Raphael has generously offered perspective and expertise from outside the disciplines of epidemiology and biostatistics, which has stretched me to think about empirical research in a way that transcends disciplinary traditions.

My colleagues and mentors at the San Francisco Department of Public Health, particularly Drs. Phillip Coffin, Glenn-Milo Santos, and Eric Vittinghoff, have been absolutely formative in my training as an applied research scientist. The knowledge they have imparted and the opportunities they have provided over the years paved my path to achieving this degree and onwards to wherever it leads.

Through coursework and mentorship, other UC Berkeley faculty members have had immense impact on my professional and intellectual development. Specifically, I am very grateful to Drs. Brenda Eskenazi, Patrick Bradshaw, Amani Allen, Maya Peterson, Mahasin Mujahid, and Art Reingold. Without their support, I would not have reached this juncture.

My fellow epidemiologists-in-training cultivated an environment of intellectual generosity and stimulation that has been critical to my training. I am continually amazed and inspired by their capabilities; they are a constant motivation to continue learning and to conduct more rigorous and impactful research. I cannot wait to see where they go and what they accomplish in the future.

I am forever indebted to my wife and muse, Leila Shooshani, for her unwavering support, her sincere commitment to my happiness and growth, and for so patiently giving audience to my innumerable lectures on the subject of this science that I love.

Lastly, I owe thanks of cosmic proportions to my parents, Steve and Cindy Rowe. I am here because of their unconditional love and support, the uncountable opportunities they have provided me, and the curiosity they have instilled in me. I am also grateful for the support of my brother, Ryan Rowe, whose own personal and professional journeys are a constant inspiration to continue exploring in pursuit of happiness and excitement.

Chapter 1: Introduction

The field of epidemiology is one of immense scope. According to the World Health Organization:

Epidemiology is the study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems.

First, regarding “health-related states or events”, the epidemiologist may be concerned with chronic diseases (e.g., cancer, diabetes, arthritis), communicable diseases (e.g., HIV, tuberculosis, influenza), mental disorders (e.g., depression, anxiety disorders, schizophrenia), states or events less easily categorized (e.g., violence, dog bites, pregnancy) or even the ultimate health state, death. Regarding “determinants”, the epidemiologist may be concerned with human behaviors (e.g., nutrition, substance use, sexual activity), social phenomena (e.g., racism, socioeconomic adversity, collective efficacy), environmental exposures (e.g., climate change, agricultural pesticides, air quality), transmission vectors (e.g., mosquitos, humans, ticks), or genetics. Beyond subject matter, the epidemiologist may be concerned with surveillance, etiology, prediction, methodological development, evaluation of interventions, or implementation science. Every corner of the field contributes, in one way or another, to the overall physical and mental health of humanity; no focus is inherently more valuable than another. However, some have voiced concerns that the field has focused too heavily on questions of etiology at the expense of diminished engagement with the application of this etiological knowledge to actually improve health outcomes. These concerns have been coupled with a call for a more “consequentialist” epidemiology that continues to engage with etiological inquiry but that also explicitly (not implicitly, as is usually done) informs the development of interventions and works to understand their true or hypothetical impact on population health.^{1–3} Rigorous evaluation of the impact of interventions is a critical component of this “consequentialist” epidemiology. Determining that a particular intervention is highly effective can inform its potential expansion or application to other places or populations, whereas determining that it is not effective, or that it is harmful, can inform its potential elimination or modification and stimulate the examination and development of alternatives.

Policies are a broad category of intervention that have immense potential to affect population health. Entities of all types develop and implement policies that, whether intended or not, can influence health. This can occur on an immense, national scale, such as with the Affordable Care Act, or on a more modest scale such as with the introduction of a new screening procedure in a single health clinic. Because policies that can affect health outcomes are constantly being implemented at different levels (e.g., national, state, city, clinic, etc.), in different places, and at different times, there are ample opportunities for evaluating their effects. However, because policies are typically implemented without specific consideration of or plans for their evaluation, there are two key challenges to any attempt to evaluate their effects. The first is data availability. Unless specific plans were arranged prior to the implementation of a policy, the investigator may face challenges identifying and obtaining relevant data that align with a specific research question. Fortunately, both the number and diversity of data sources that are either readily available or

available upon navigating a bit of bureaucracy are vast and constantly growing. For epidemiologists, some important examples of data sources that can be leveraged to evaluate policies are health-related administrative databases such as those that capture healthcare utilization, vital statistics, or drug prescriptions. The second key challenge is that policies are typically not randomized, and thus the rigorous evaluation of their effects presents nontrivial methodological challenges. Fortunately, there is a rich history of methodological advancement across multiple disciplines (most notably economics, statistics, political science, epidemiology, and biostatistics) pertaining to the evaluation of intervention effects in observational settings.

In the following chapters, methods from multiple disciplines and a variety of administrative and other observational data sources are leveraged to evaluate the health effects of three sets of policies. Chapter 2 evaluates the effects of two national policies aiming to expand access to treatment for opioid use disorder on various opioid-related health outcomes in California. Chapter 3 evaluates the effects of opioid prescribing policies on both intended and unintended health outcomes at a safety-net primary care clinic in San Francisco, CA. Chapter 4 evaluates the mortality effects of a major criminal justice policy that substantially reduced the California state prison population. Each of these policies were implemented at a different level (i.e., national, clinic, and state) and thus require unique considerations regarding data availability and analytic approach.

1.1 REFERENCES

1. Galea S. An argument for a consequentialist epidemiology. *Am J Epidemiol*. 2013;178(8):1185-1191. doi:10.1093/aje/kwt172
2. Keyes K, Galea S. What matters most: quantifying an epidemiology of consequence. *Ann Epidemiol*. 2015;25(5):305-311. doi:10.1016/j.annepidem.2015.01.016
3. Cates W Jr. Invited commentary: consequential(ist) epidemiology: let's seize the day. *Am J Epidemiol*. 2013;178(8):1192-1194. doi:10.1093/aje/kwt173

Chapter 2: Evaluating the effects of expanding the buprenorphine waiver program

2.1 INTRODUCTION

The United States continues to grapple with an unprecedented opioid overdose epidemic. Nearly half a million people have died from opioid-related drug overdoses since 1999.¹ Although the epidemic was initially driven by prescription opioids, it is now dominated by illicit opioids, specifically heroin and illicitly-made fentanyl and its analogs.^{2,3} Annual deaths involving heroin have increased more than five-fold since they started to rise in 2010 and deaths involving the class of drugs that includes illicitly-made fentanyl and its analogs increased ten-fold from 2013 to 2018.¹⁻³ These trends illustrate an evolving and increasingly complex epidemic that is now responsible for nearly 50,000 deaths per year.¹ Identifying effective strategies to address this ongoing crisis is critical.

Expanding access to treatment for opioid use disorder (OUD), which affects an estimated two million individuals in the U.S.,⁴ has been a key priority in the national response to the epidemic.⁵⁻⁹ Medications for opioid use disorder (MOUD) are the most effective treatment available for OUD and their superiority to non-pharmacologic approaches in decreasing opioid use and increasing treatment retention is well established.¹⁰⁻¹² There are three medications approved by the FDA for the long-term treatment for OUD: naltrexone, methadone, and buprenorphine.¹³ Of these, methadone and buprenorphine, which are themselves opioids, have the longest history of evidence establishing their effectiveness.^{10,11} Recovery from OUD is challenged by the euphoric and sedating effects of opioids (i.e., positive reinforcement) as well as severe physical and psychological withdrawal symptoms that accompany opioid detoxification and drug cravings that follow (i.e., negative reinforcement).¹³⁻¹⁵ Both methadone and buprenorphine facilitate OUD recovery by mitigating withdrawal symptoms and drug cravings while not producing euphoria among opioid-dependent individuals. In addition, both medications block the euphoric and sedating effects of other opioids that might be used concurrently. Despite their effectiveness, MOUD are extensively underutilized, with less than 40% of individuals with OUD accessing these medications.¹⁶⁻¹⁹ Although the reasons for this underutilization are varied and complex—including stigma among both patients and providers, inadequate insurance coverage, regulatory burdens, and lack of awareness, training, and institutional support among providers—several studies have identified significant gaps between the treatment need and capacity to provide MOUD at both the state and national levels.^{18,20-22}

While methadone for OUD can only be dispensed through highly structured and regulated opioid treatment programs, buprenorphine can be prescribed by qualified providers in non-specialty outpatient settings and dispensed by pharmacies, and thus represents an important avenue for

access. Specifically, since 2002, physicians (with either Doctor of Medicine [MD] or Doctor of Osteopathic Medicine [DO] degrees) who underwent eight hours of training and applied for a special waiver were permitted to prescribe buprenorphine for OUD to up to 30 patients, which was increased to 100 patients in 2006 for qualified providers. In 2016, two additional policy changes were made in an effort to expand buprenorphine prescribing capacity: (1) a final rule from the Substance Abuse and Mental Health Services Administration (SAMHSA) increased the patient limit from 100 to 275 for providers who prescribed buprenorphine to 100 patients for at least one year and met additional credential and practice criteria (hereafter MD/DO-275 waivers); and (2) the Comprehensive Addiction and Recovery Act (CARA) extended the ability to prescribe buprenorphine for OUD to nurse practitioners and physician assistants (hereafter NP/PA waivers).

To date, research has not examined the downstream effects of NP/PA or MD/DO-275 waivers. National studies have documented substantial increases in both the number of waived providers, including those with NP/PA and MD/DO-275 waivers, as well as the number of buprenorphine prescriptions in recent years, and found that increases have been uneven across states and counties.^{23–26} Multiple studies have highlighted the potential for NP/PA and 275-patient waivers to expand access to OUD treatment and help to close the current gap between capacity and demand. For example, although rural areas typically have fewer waived providers per capita,^{24,26} NPs and PAs accounted for more than half of new waivers in rural counties since 2017,²⁷ suggesting NP/PA waivers may be particularly effective in expanding rural access. In addition, the number of new MD/DO-275 waivers far exceeded federal projections, suggesting these waivers could translate to a significant expansion in buprenorphine prescribing.²³ Although one study examined and found a positive state-level association between the total number of waived providers and rates of buprenorphine prescribing among Medicaid enrollees prior to the 2016 policy changes,²⁸ no studies have investigated the associations between the number of NP/PA or MD/DO-275 waivers and population-level buprenorphine prescribing rates or opioid-related health outcomes. Each policy represents a distinct strategy for expanding access to buprenorphine: the NP/PA policy sought to expand the number of prescribers whereas the MD/DO-275 policy sought to expand the prescribing capacity of prescribers already focused on buprenorphine provision. Evaluating the impacts of these two policies can inform ongoing efforts to expand access to treatment for OUD.

Using several statewide administrative data sources from California, we examined the uptake of NP/PA and MD/DO-275 waivers both statewide and by county, as well as their association with buprenorphine prescribing and opioid-related mortality, emergency department visits, and hospitalizations.

2.2 METHODS

Overview and Data Sources

Our aim was to describe trends in the number and type of buprenorphine waivers in California from 2010-2018 and leverage variability at the county-level to examine associations between the number of NP/PA and MD/DO-275 waivers and both buprenorphine prescribing and opioid-related health outcomes from 2016-2018.

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

We obtained administrative data that cover the entire state of California from several sources: (1) counts of buprenorphine waivers by type, month, and county were acquired through a Freedom of Information Act request from the Substance Abuse and Mental Health Services Administration, which manages the buprenorphine waiver program; (2) individual-level buprenorphine prescription data with unique patient and prescriber identifiers from the Controlled Substance Utilization Review and Evaluation System (CURES 2.0), California's controlled substance monitoring program maintained by the California Department of Justice; (3) individual-level opioid-related mortality data from the California Department of Public Health (CDPH); and (4) individual-level opioid-related emergency department visit and hospitalization data from the California Office of Statewide Health Planning and Development (OSHPD). All analysis measures were calculated by county and calendar quarter, which were selected to mitigate variability present at smaller geographic and temporal scales.

Exposures

Our two exposures of interest were the buprenorphine prescribing capacities associated with NP/PA and MD/DO-275 waivers. To capture these prescribing capacities, we calculated the patient prescribing capacity per 100,000 residents associated with all NP/PA and MD/DO-275 waivers separately. For example, if a county had one NP/PA 30-patient waiver and one NP/PA 100-patient waiver and a population of 150,000 residents, they would have an NP/PA waiver patient capacity rate of $((30 + 100)/150,000) * 100,000 = 86.7$ patients per 100,000 residents. Similarly, if a county had one 275-patient waiver and a population of 150,000 residents, they would have a MD/DO-275 waiver patient capacity rate of $(275/150,000) * 100,000 = 183.3$ patients per 100,000 residents. To capture all other prescribing capacity complementary to either NP/PA or MD/DO-275 waiver prescribing capacity, we calculated the total patient prescribing capacity rate and subtracted the NP/PA rate or MD/DO-275 rate, respectively.

The available waiver data had two key limitations. First, although SAHMSA maintains records of the date on which each waiver was first granted, the type of waiver (e.g., provider degree [MD, DO, NP, or PA] and patient limit [30, 100, or 275]), and the provider's current service address, they do not maintain historical address information. Thus, if a provider changed service addresses between the time they were granted their first waiver and when the data were obtained (March 2020), the duration of time providing service at the current address and any prior service addresses are unknown. Second, for 504 providers whose waivers had been retired, only the date on which the providers' waiver(s) were first granted, the type of waiver and patient limit(s), and the providers' most recent service address were available; the actual date of the retirement was not available. As of the time the data were obtained, only MD/DO-30 and MD/DO-100 waivers had been retired, which do not affect our primary exposures. In the main analysis, we assigned waivers to counties based on the providers' current county of practice and did not account for possible past moves or waiver retirements. However, both of these limitations were directly addressed in a sensitivity analysis described below.

Outcomes

Our seven outcomes were the rates of unique prescribers actively prescribing buprenorphine, unique patients receiving buprenorphine prescriptions, total number of buprenorphine

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

prescriptions, opioid-related health events (including deaths, emergency department visits, and hospitalizations), opioid-related deaths alone, opioid-related emergency department visits alone, and opioid-related hospitalizations alone.

We calculated the numbers and rates of unique buprenorphine prescribers, unique patients receiving buprenorphine prescriptions, and total buprenorphine prescriptions using data from CURES 2.0. All three measures were associated with counties based on the county of the prescribing provider. Each drug product in the CURES 2.0 data can be identified by a unique 11-digit National Drug Code number. Buprenorphine prescriptions were identified using resources developed and made publicly available by the Centers for Disease Control and Prevention.²⁹ Buprenorphine formulations prescribed for pain management and not treatment for OUD were excluded.

We calculated the overall number and rate of opioid-related health events as the sum of opioid-related deaths, emergency department visits, and hospitalizations.

We calculated the number and rate of opioid-related deaths using multiple cause of death files from the California Department of Public Health. To identify opioid-related deaths, we used the International Classification of Diseases, Tenth Revision (ICD10) underlying cause-of-death codes X40-X44 (unintentional), X60-X64 (suicide), X85 (homicide), or Y10-Y14 (undetermined intent) and multiple cause of death codes T40.0-T40.4 and T40.6, which correspond to opioids. Deaths that occurred outside of California were excluded.

We calculated the number and rate of both opioid-related emergency department visits and hospitalizations using ICD-10 diagnosis root codes T40.0-T40.4 and T40.6 (excluding codes with suffix “X6”, which corresponds to underdosing). We defined opioid-related encounters as those that include any of the aforementioned root codes as principal or secondary (i.e. “other”) diagnoses.

All three opioid-related health outcomes were associated with counties based on the county of residence of the decedent/patient because patients are more likely to receive buprenorphine prescriptions from providers practicing in their county of residence than the county in which they received emergency medical care or in which their death occurred, if different from their county of residence.

Descriptive Analysis

To examine the effects of the new policies on buprenorphine prescribing capacity statewide and by county, we generated several descriptive plots. First, we calculated both the number of new or upgraded buprenorphine waivers and the cumulative number of waivers in California by type and calendar quarter from 2010 to 2018. Second, we calculated the total patient prescribing capacity per 100,000 residents (across all waiver types) at the end of the first quarter of 2010 and the end of the fourth quarter of 2018 for each county. Third, we calculated the total patient prescribing capacity per 100,000 residents, segmented by waiver type, at the end of 2018 for each county.

Statistical Analysis

To examine the association between NP/PA and MD/DO-275 waiver capacity and each outcome, we fit Poisson regression models with county and quarter-year fixed effects and a population offset. Poisson models were used in favor of ordinary least squares because the outcomes were positively skewed counts of events, and coefficient estimates are robust to distributional misspecification, provided the conditional mean is correctly specified.³⁰ The county fixed effects control for all time invariant differences between counties, whereas quarter-year fixed effects control for all county invariant differences over time (i.e., the secular trend). Because we hypothesized a delay between the receipt of a waiver and the outcomes of interest, we employed a one quarter lag between independent and dependent variables. Specifically, we modeled the association between waiver capacity measured in one quarter and outcomes measured in the subsequent quarter, which ensures correct temporal ordering between our exposures and outcomes. Below, we refer to the quarter associated with the exposure as the exposure quarter and the subsequent quarter as the outcome quarter. Because the population denominator is incorporated into the outcome through the offset term, our dependent variables were included in the model as counts. Alternatively, our primary independent variables (NP/PA waiver capacity and MD/DO-275 waiver capacity) were included directly as rates.

In total, we fit 14 separate models, including all combinations of our two exposures (NP/PA waiver capacity and MD/DO-275 waiver capacity) and seven outcomes (unique buprenorphine prescribers, unique patients receiving buprenorphine prescriptions, buprenorphine prescriptions, all opioid-related health outcomes, opioid-related overdose deaths, opioid-related emergency department visits, and opioid-related hospitalizations). Models only included counties that had variability in both the exposure and outcome during the study period and the time period was limited to Q4 2016 through Q4 2018 for the NP/PA models and Q2 2016 through Q4 2018 for the MD-DO/275 models; the start of each time period corresponds to the quarter prior to introduction of each waiver type in California. Each model controlled for the buprenorphine prescribing capacity associated with all waiver types other than the exposure waiver type during the exposure quarter, unemployment rate (obtained from the Bureau of Labor Statistics and calculated as the mean monthly rate in each quarter) in the quarter prior to the exposure quarter, and the non-buprenorphine opioid prescription rate in the quarter prior to the exposure quarter. Each model also controlled for lagged values of the exposure to account for the possibility that our waiver-outcome relationships could be confounded by past numbers of waivers; specifically, the models controlled for the average value of the main exposure in the four prior quarters.

To control for county-level variability in the implementation of buprenorphine-related initiatives over time, each model included indicator variables corresponding to the implementation of three different California initiatives that aimed to expand access to buprenorphine for the treatment of OUD during the analysis period. Indicator variables captured the implementation of the Drug Medi-Cal Organized Delivery System,³¹ the California Hub and Spoke Program,³² and the California Health Care Foundation supported California Opioid Safety Coalitions Network.³³ For each initiative, we identified the month of implementation for each county and set the relevant indicator variable to 1 for the quarter of implementation and all subsequent quarters, and zero otherwise. Implementation months for each county are provided in Table 1. The NP/PA models

did not include an indicator variable for the California Opioid Safety Coalitions Network because it was initiated prior to the start of the analysis period for these models, thus any impacts of the program would be absorbed by the county fixed effects.

The introduction of the new waivers coincided with increasing fentanyl-related mortality in California and, due to its high potency and erratic adulteration of other illicit substances, fentanyl presents challenges for existing overdose prevention strategies (e.g., lay naloxone distribution).^{34,35} In addition, the timing and severity of increases in fentanyl-related mortality varied by county in California.³⁶ To control for possible confounding by the presence of fentanyl across counties and calendar quarters for each of the four health outcomes, these models controlled for the county-specific proportion of opioid overdose deaths involving fentanyl in the quarter prior to the exposure quarter.

In order to better capture the effects of a single new NP/PA or MD/DO-275 waiver, regression coefficients associated with NP/PA waiver capacity were scaled to correspond to a 30 patient capacity increase in a median-sized California county (186,620.5 residents), and those associated with MD/DO-275 waiver capacity were scaled to correspond to a 175-patient capacity increase. These numbers were selected because the majority of NP/PA waivers were new 30-patient limit waivers, and MD/DO-275 waivers correspond to a 175 patient increase from a 100-patient limit waiver. 95% confidence intervals were calculated using fully robust standard errors obtained from heteroscedasticity-consistent covariance matrices.^{37,38}

We thought that our exposure-outcome relationships could be confounded by prior values of the outcome (e.g., the number of waivers in the current quarter and the number of opioid-related overdose deaths in the subsequent quarter could both be affected by the number of opioid-related overdose deaths in a prior quarter). However, in fixed effects regression models, controlling for lagged dependent variables leads to inconsistent parameter estimates.^{30,39} Although this potential for uncontrolled confounding is a limitation of our analysis approach, it is unlikely that quarter-to-quarter fluctuations in buprenorphine prescribing and opioid-related health outcomes would have a strong influence on the number of new NP/PA and MD-275 waivers, as the opioid epidemic was well-established in California by time these waivers were introduced in 2016 and 2017.³⁶ In our view, confounding by unobserved and time-invariant differences between counties was a far more substantial concern than confounding by past outcomes, and thus we pursued the fixed effects approach.

Regression Model Specification

As described above, we examined the association between NP/PA and MD/DO-275 waivers and the rate of each outcome using Poisson regression models with county and quarter-year fixed effects, time-varying covariates, and a population offset. Our regression models were specified as follows:

$$Y_{it} \sim \text{Poisson}(\lambda = e^{\mu_{it}}) \text{ for counties } i = 1, \dots, N \text{ and quarters } t = 1, \dots, T$$

$$\begin{aligned} \text{where } \mu_{i,t} &= \log(E[Y_{i,t}|W_{i,t-1}, \mathbf{X}_{i,t-1}, P_{i,t}]) \\ &= \alpha_i + \gamma_t + \beta_1 W_{i,t-1} + \beta \mathbf{X}_{i,t-1} + \log(P_{i,t}) \end{aligned}$$

Where $Y_{i,t}$ is the outcome count for county i during quarter t ; α_i and γ_t are county and quarter fixed effects, respectively; $W_{i,t-1}$ is the waiver capacity rate associated with the waiver type of interest (NP/PA or MD/DO-275) for county i during quarter $t-1$; $\mathbf{X}_{i,t-1}$ is a vector of time-varying covariates for county i and indexed by quarter $t-1$; and $P_{i,t}$ is the population in county i during quarter t .

Our main results are estimates of β_1 for each combination of waiver type W (NP/PA or MD/DO-275) and outcome Y (buprenorphine prescribers, patients, and total prescriptions, total opioid-related health events, and opioid-related deaths, emergency department visits, and hospitalizations), and scaled as described above.

Sensitivity Analyses

To explore the associations between NP/PA and MD/DO-275 waiver capacities and our outcomes at a different timescale that would involve less variability in our measures, we also fit models using half-year periods (i.e., January to June, July to December) rather than quarters.

There is extensive variability in the population sizes of California's 58 counties (range = 1,094 – 10,101,104; median = 186,621; interquartile range = 47,868 – 704,863). To mitigate the influence of rate variability in smaller counties, we fit regression models among subsets of populous counties. Specifically, to avoid an arbitrary threshold, we sequentially obtained estimates when excluding counties with a mean population during the study period that was less than 10,000, 20,000, 30,000, 40,000, and 50,000 residents.

We also conducted a probabilistic sensitivity analysis to assess the sensitivity of our results to the two limitations of our waiver capacity measures: (1) the assumption that all providers practiced in the same county from the month in which they obtained their first waiver through the present; and (2) the fact that we did not account for waiver retirements.

For limitation (1), we used county-to-county migration data from the American Community Survey to estimate the probability that a provider moved to their present county for each month between January 2002 (the first month of the year in which the buprenorphine waiver program began) and March 2020 (when data were obtained and the providers were known to practice in their present county). Using these county- and month-specific probabilities, we simulated the month that each provider arrived in their present county. If a provider's simulated arrival month fell after the month in which they obtained their waiver, their waiver was not attributed to their present county until their simulated arrival month. If the simulated arrival month fell on or before the month during which they obtained their waiver, no change was made to the data. When a simulated arrival month fell after the month in which a provider obtained their waiver, we also simulated whether the provider moved from a different California county, and if so, the specific

county from which they came. In this scenario, the provider's waiver was associated with the simulated prior county from the original waiver date until the month that they moved to their present county.

For limitation (2), we randomly generated retirement months for the 504 retired waivers between the month of initial waiver receipt and March 2020, assuming that the probability of retiring each month increased linearly with calendar time.

For each set of simulated waiver data that incorporated stochastic moves and retirements, we generated measures and conducted analyses as described in the main text. We ran 1000 iterations and reported the 2.5% and 97.5% quantiles of the distributions of each effect estimate.

Randomization Inference

As an alternative approach to assessing the probability that our estimates were due to chance, we conducted a randomization inference procedure. The advantage of this approach to inference is that it does not rely on asymptotic theory, contrary to the fully robust standard errors that we report with our main estimates. Specifically, we randomly re-assigned each county's quarterly time series of waiver capacity rates (i.e., the waiver capacity rates associated with NP/PA and MD/DO-275 waivers as well as the corresponding other waiver capacity rates) to a different county, conducted analyses as described above, and recorded the t-statistics for the main associations of interest in each of the 14 models. The resulting distributions of t-statistics represent the distributions under the sharp null hypothesis; that is, that there was no association between exposure and outcome for any county-quarter. We conducted 1000 iterations and, for each of the 14 associations of interest, we reported the proportion of t-statistics under the sharp null hypothesis that were equal to or more extreme in absolute value than the observed t-statistic.

2.3 RESULTS

Buprenorphine Waivers in California

The cumulative number and number of new or upgraded buprenorphine waivers by type and calendar quarter from 2010 to 2018 in California are presented in Figures 1 and 2. The total patient prescribing capacity rate (across all waiver types) at the end of the first quarter of 2010 and the end of the fourth quarter of 2018 for each county are presented in Figure 3. The total patient prescribing capacity rates segmented by waiver type for each county at the end of 2018 are also presented in Figure 4.

The number of buprenorphine waivers increased substantially over the study period, with more rapid increases following the introduction of NP/PA and MD/DO-275 waivers, and there was extensive heterogeneity in the number and type of waivers across counties.

Associations between NP/PA and MD/DO-275 Waiver Capacity and Outcomes

Estimates for the covariate-adjusted associations between NP/PA and MD/DO-275 prescribing capacity rates and each of the seven outcomes are presented in Figure 5 and Table 2.

Each additional NP/PA waiver (scaled to correspond to a median-sized California county) was associated with a 1.5% increase in the rate of active buprenorphine prescribers (exponentiated Poisson regression coefficient = 1.015, 95% Confidence Interval = 1.007-1.024), a 1.4% increase in the rate of patients receiving buprenorphine prescriptions, (1.014, 1.007-1.020), and a 1.7% increase in the total buprenorphine prescriptions rate (1.017, 1.009-1.025) in the subsequent calendar quarter. When scaled to the median California population size and outcome rates in Q4 2018, these point estimates correspond to an average increase of 0.7 buprenorphine prescribers, 6.7 patients receiving buprenorphine and 11.7 buprenorphine prescriptions for each additional NP/PA waiver. Each additional MD/DO-275 waiver was associated with a 1.7% increase in the rate of patients receiving buprenorphine prescriptions, (1.017, 1.007-1.028) and a 2.7% increase in the total buprenorphine prescriptions rate (1.027, 1.016-1.039). These point estimates correspond to an average increase of 8.6 patients receiving buprenorphine and 18.7 buprenorphine prescriptions for each additional MD/DO-275 waiver. There was no association between MD/DO-275 waiver capacity and the rate of buprenorphine prescribers, which we expected given that MD/DO-275 waivers represent patient limit increases for providers who were already waived, as opposed to prescribing ability for new providers.

Each additional NP/PA waiver was associated with a 1.0% decrease in the opioid related emergency department visit rate (0.990, 0.980-1.000). This point estimate corresponds to an average decrease of 0.9 opioid-related ED visits for each additional NP/PA waiver. Otherwise, there were no clear associations between NP/PA or MD/DO-275 waiver capacity and opioid-related health outcomes for which 95% confidence intervals did not include the null.

Sensitivity Analyses

Estimates obtained using six-month time periods were largely consistent with the main estimates obtained using quarters, with the exception that the confidence intervals for the associations between NP/PA waiver capacity and the total buprenorphine prescription and opioid-related emergency department visit rates included the null (Table 3).

When excluding sparsely populated counties, estimates were largely unchanged (Table 4). However, each additional NP/PA waiver was associated with an 8-9% decrease in the opioid-related mortality rate when excluding counties with fewer than 20,000 to 50,000 residents (excluding counties with <10,000 residents: 0.939, 0.879-1.002; <20,000 residents: 0.917, 0.865-0.973, <30,000 residents: 0.915, 0.863-0.971; <40,000 residents: 0.913, 0.860-0.970; <50,000 residents: 0.912, 0.858-0.970). This point estimate corresponds to an average decrease of 0.2 opioid-related deaths (using the point estimate from the model excluding counties with fewer than 20,000 residents) per NP/PA waiver.

The results of our probabilistic sensitivity analysis were largely concordant with our main analysis (Table 5). Specifically, the 2.5% and 97.5% quantiles of estimates were both above the null for the associations between NP/PA waiver capacity and the buprenorphine prescriber, patient, and prescription rates and between MD/DO-275 waiver capacity and the buprenorphine patient and

prescription rates. The quantiles were both below the null for the association between NP/PA waiver capacity and the opioid-related emergency department visit rate.

Randomization Inference

The results of our randomization inference procedure were mostly consistent with inference using robust standard errors and are presented in Table 6 and Figure 6. For associations between NP/PA waiver capacity and the buprenorphine prescriber, patient, and prescription rates, 2.2%, 0.6%, and 0.8% of *t*-statistics under the sharp null hypothesis were more extreme than the observed *t*-statistics. For the association between MD/DO-275 waiver capacity and the buprenorphine prescription rate, 5.2% of sharp null *t*-statistics were more extreme than the observed *t*-statistic. The associations between MD/DO-275 waiver capacity and the buprenorphine patient rate and between NP/PA waiver capacity and the opioid-related ED visit rate were less robust, with 15.8% and 20.3% of sharp null *t*-statistics more extreme than the observed *t*-statistics, respectively.

2.4 DISCUSSION

We found that the number of waived providers and the overall buprenorphine prescribing capacity increased substantially in California following the implementation of new national policies allowing the MD/DO-275 and NP/PA waivers, and there was extensive variability across counties. We also found positive associations between both NP/PA and MD/DO-275 waivers and different measures of buprenorphine prescribing and negative associations between NP/PA waivers and opioid-related emergency department visits and, when excluding sparsely populated counties, opioid-related mortality. This is the first study to examine links between these novel types of buprenorphine waivers and buprenorphine prescribing and the first to examine links between any type of buprenorphine waiver and opioid-related health outcomes, which have implications for ongoing efforts to expand access to buprenorphine for the treatment of opioid use disorder.

NP/PA waivers were positively associated with the rate of buprenorphine prescribers, patients, and total prescriptions. This is consistent with a national 2017 study that found 75% of waived NPs and PAs reported prescribing buprenorphine since obtaining their waiver.⁴⁰ Although these findings highlight the potential for NPs and PA's to help fill existing treatment gaps, we also found substantial heterogeneity in the rates of NP/PA waivers across counties, which has also been reported across states at the national level.²⁷ Despite this variation, NP/PA waivers accounted for the majority of new waivers in rural U.S. counties through March 2019 and, in many cases, the first waived clinicians in such counties.²⁷ Our findings highlight the valuable contribution of NP's and PA's in filling the OUD treatment gap. However, to maximize impact of NP/PA waivers, future research should investigate whether the geographic heterogeneity in waiver rates is due to the distribution of NPs and PAs or other addressable factors (e.g., awareness or training constraints).

We also found that NP/PA waivers were associated with decreases in opioid-related emergency department visits and mortality; however, these findings were not robust to randomization inference, and the association with mortality was only present when excluding sparsely populated counties, so they should be interpreted with caution. Numerous studies have linked sustained OUD

treatment with methadone or buprenorphine with lower risk of opioid-related health encounters and mortality at the individual level,^{41–45} but studies demonstrating meaningful population-level effects are limited.⁴⁶ The translation of individual-level benefits to shifts in population-level outcomes depends on a variety of factors, including the number of individuals that receive sustained treatment in a given population. Medications for the treatment of OUD are extensively underutilized,^{16–18} but use, particularly that of buprenorphine, is increasing nationwide and our findings linking NP/PA waiver capacity to population-level health outcomes are promising. It is important for future work to investigate the characteristics of places (e.g., states, counties, smaller localities, health systems) where prescribing capacity translates most effectively to buprenorphine prescribing, retention in treatment, and improved health outcomes.

We found positive associations between MD/DO-275 waivers and both buprenorphine patients and prescriptions but found no associations between MD/DO-275 waivers and opioid-related health outcomes. Although not directly supported by our analysis, the presence of associations between NP/PA waivers and opioid-related health outcomes and the absence of those associations for MD/DO-275 waivers could suggest differences in treatment outcomes for patients prescribed buprenorphine by different types of providers with different prescribing limits. A recent study examined characteristics and prescribing practices by clinician type and patient limit,⁴⁰ but future research should explore patient outcomes in this context to identify potential differences and inform strategies to maximize patient benefits. MD/DO-275 waivers are uncommon relative to other waiver types, both nationally and in California.⁴⁷ The only other study to examine the abundance of these waivers found that growth through May 2018 exceeded initial projections,²³ but was uneven across the U.S. Although high-limit prescribers may not be relevant to all regions and settings, our findings do suggest that the increased limit permitted under the MD/DO-275 waivers are an important tool for expanding buprenorphine prescribing.

The introduction of NP/PA and MD/DO-275 waivers aimed to increase access to buprenorphine for OUD by increasing the number and prescribing capacity of buprenorphine prescribers, respectively. It is important to note that the supply and prescribing capacity of buprenorphine prescribers are only two of a wide array of constraints that inhibit broader utilization. Several studies have also highlighted a lack of education, training, and institutional support among providers,^{48–58} poor care coordination,^{48,51–55,57–59} inadequate reimbursement,^{51,54,58–61} stigma among both providers^{48,50,52,53,55,58,62} and patients,^{63,64} and lack of awareness among patients⁶⁵ as key barriers to buprenorphine treatment. As a consequence of these multi-faceted challenges, isolated efforts that address only single barriers are not likely to result in the large population-level increases in treatment utilization that are needed to combat the ongoing opioid crisis. For example, although Medicaid expansion has been linked to increased buprenorphine prescribing, one study found that this association may have been constrained by the number of waived providers.^{66,67} Despite the likely limited effectiveness of singular interventions, our findings suggest that the introduction of NP/PA and MD/DO-275 waivers had a meaningful effect on buprenorphine prescribing and possibly also on opioid-related health outcomes. These findings highlight the possibility that further expansion of buprenorphine prescribing, possibly by way of deregulation as has been advocated by some,^{68–70} could be an effective means to increase access.

Our study has several limitations. First, data were from administrative data sources, which are not collected for research purposes and may be subject to inaccuracies; however, leveraging these data are the only viable way to evaluate population-level effects and we have no specific reason to suspect the presence of systematic measurement error that would bias our findings. Second, our study is ecological in nature so we cannot confirm that the new NP/PA and MD/DO-275 waived providers contributed directly to subsequent changes in individual outcomes. Third, we could not confirm where each provider practiced between their waiver date and when the data were obtained in 2020 or whether they retired; however, we attempted to rigorously address this limitation in a sensitivity analysis, and our results were unchanged. Fourth, our analysis approach does not account for potential confounding by past outcomes, though we do not expect this to substantially bias our estimates. Fifth, our results are specific to the state of California and not necessarily generalizable to other states or the U.S. overall.

Despite these limitations, we employed a rigorous analysis approach that takes into account temporal ordering and controls for all time invariant and county invariant confounders as well as important time-varying confounders and found that NP/PA and MD/DO-275 waivers were associated with increased buprenorphine prescribing and NP/PA waivers were potentially associated with decreased opioid-related ED visits and mortality. These findings highlight the benefits of these relatively new waiver types and suggest that efforts to increase their adoption may lead to increased buprenorphine utilization and corresponding health benefits.

2.5 REFERENCES

1. Centers for Disease Control and Prevention National Center for Health Statistics. Multiple Cause of Death 1999-2018 on CDC WONDER Online Database, released 2019. Published online March 17, 2018. <http://wonder.cdc.gov/>
2. Hedegaard H, Minaño AM, Warner M. *Drug Overdose Deaths in the United States, 1999-2018*. National Center for Health Statistics; 2020.
3. Wilson N, Kariisa M, Seth P, Smith H, Davis NL. Drug and Opioid-Involved Overdose Deaths - United States, 2017-2018. *MMWR Morb Mortal Wkly Rep*. 2020;69(11):290-297. doi:10.15585/mmwr.mm6911a4
4. Substance Abuse and Mental Health Services Administration. *Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health*. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2019. <https://www.samhsa.gov/data/>
5. Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies--tackling the opioid-overdose epidemic. *The New England journal of medicine*. 2014;370(22):2063-2066. doi:10.1056/NEJMp1402780
6. President's Commission on Combating Drug Addiciton and the Opioid Crisis. *Draft Interim Report*. Office of National Drug Control Policy; 2017. Accessed August 8, 2010. <https://www.whitehouse.gov/sites/whitehouse.gov/files/ondcp/commission-interim-report.pdf>

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

7. Behavioral Health Coordinating Committee PDAS. *Addressing Prescription Drug Abuse in the United States: Current Activities and Future Opportunities*. United States Department of Health and Human Services; 2013. Accessed August 8, 2010. https://www.cdc.gov/drugoverdose/pdf/hhs_prescription_drug_abuse_report_09.2013.pdf
8. National Governors Association. *Governors' Priorities for Addressing the Nation's Opioid Crisis*.; 2016. Accessed August 15, 2017. <https://www.nga.org/files/live/sites/NGA/files/pdf/2016/1602PrioritiesOpioidCrisis.pdf>
9. American Medical Association Opioid Task Force. *Task Force Recommendations*.; 2014. Accessed August 15, 2017. <https://www.ama-assn.org/delivering-care/reversing-opioid-epidemic>
10. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *The Cochrane database of systematic reviews*. 2009;(3):CD002209. doi:10.1002/14651858.CD002209.pub2
11. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *The Cochrane database of systematic reviews*. 2014;(2):CD002207. doi:10.1002/14651858.CD002207.pub4
12. Connery HS. Medication-assisted treatment of opioid use disorder: review of the evidence and future directions. *Harvard review of psychiatry*. 2015;23(2):63-75. doi:10.1097/HRP.0000000000000075
13. Bart G. Maintenance medication for opiate addiction: the foundation of recovery. *J Addict Dis*. 2012;31(3):207-225. doi:10.1080/10550887.2012.694598
14. Koob GF, Volkow ND. Neurocircuitry of addiction. *Neuropsychopharmacology*. 2010;35(1):217-238. doi:10.1038/npp.2009.110
15. Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry*. 2016;3(8):760-773. doi:10.1016/S2215-0366(16)00104-8
16. Wu LT, Zhu H, Swartz MS. Treatment utilization among persons with opioid use disorder in the United States. *Drug and alcohol dependence*. 2016;169:117-127. doi:10.1016/j.drugalcdep.2016.10.015
17. Lembke A, Chen JH. Use of Opioid Agonist Therapy for Medicare Patients in 2013. *JAMA Psychiatry*. 2016;73(9):990. doi:10.1001/jamapsychiatry.2016.1390
18. Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment. *American journal of public health*. 2015;105(8):e55-63. doi:10.2105/AJPH.2015.302664
19. Saloner B, Karthikeyan S. Changes in Substance Abuse Treatment Use Among Individuals With Opioid Use Disorders in the United States, 2004-2013. *JAMA*. 2015;314(14):1515. doi:10.1001/jama.2015.10345

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

20. Rosenblatt RA, Andrilla CH, Catlin M, Larson EH. Geographic and specialty distribution of US physicians trained to treat opioid use disorder. *Annals of family medicine*. 2015;13(1):23-26. doi:10.1370/afm.1735
21. Knudsen HK. The Supply of Physicians Waivered to Prescribe Buprenorphine for Opioid Use Disorders in the United States: A State-Level Analysis. *J Stud Alcohol Drugs*. 2015;76(4):644-654.
22. Sigmon SC. Access to treatment for opioid dependence in rural America: challenges and future directions. *JAMA Psychiatry*. 2014;71(4):359-360. doi:10.1001/jamapsychiatry.2013.4450
23. Knudsen HK, Lin LA, Lofwall MR. Adoption of the 275-patient buprenorphine treatment waiver for treating opioid use disorder: A state-level longitudinal analysis. *Subst Abus*. Published online July 11, 2019;1-10. doi:10.1080/08897077.2019.1635959
24. Andrilla CHA, Moore TE, Patterson DG, Larson EH. Geographic Distribution of Providers With a DEA Waiver to Prescribe Buprenorphine for the Treatment of Opioid Use Disorder: A 5-Year Update. *J Rural Health*. 2019;35(1):108-112. doi:10.1111/jrh.12307
25. Olfson M, Zhang VS, Schoenbaum M, King M. Trends in Buprenorphine Treatment in the United States, 2009-2018. *JAMA*. 2020;323(3):276-277. doi:10.1001/jama.2019.18913
26. Ghertner R. U.S. trends in the supply of providers with a waiver to prescribe buprenorphine for opioid use disorder in 2016 and 2018. *Drug Alcohol Depend*. 2019;204:107527. doi:10.1016/j.drugalcdep.2019.06.029
27. Barnett ML, Lee D, Frank RG. In Rural Areas, Buprenorphine Waiver Adoption Since 2017 Driven By Nurse Practitioners And Physician Assistants. *Health Aff (Millwood)*. 2019;38(12):2048-2056. doi:10.1377/hlthaff.2019.00859
28. Wen H, Hockenberry JM, Pollack HA. Association of Buprenorphine-Waivered Physician Supply With Buprenorphine Treatment Use and Prescription Opioid Use in Medicaid Enrollees. *JAMA Netw Open*. 2018;1(5):e182943. doi:10.1001/jamanetworkopen.2018.2943
29. National Center for Injury Prevention and Control. CDC compilation of benzodiazepines, muscle relaxants, stimulants, zolpidem, and opioid analgesics with oral morphine milligram equivalent conversion factors, 2018 version. Published online 2018. <https://www.cdc.gov/drugoverdose/resources/data.html>
30. Wooldridge JM. Distribution-free estimation of some nonlinear panel data models. *Journal of Econometrics*. 1999;90(1):77-97. doi:10.1016/S0304-4076(98)00033-5
31. California Department of Health Care Services. Drug Medi-Cal Organized Delivery System.
32. Miele GM, Caton L, Freese TE, et al. Implementation of the hub and spoke model for opioid use disorders in California: Rationale, design and anticipated impact. *J Subst Abuse Treat*. 2020;108:20-25. doi:10.1016/j.jsat.2019.07.013

33. Public Health Institute. *Tackling an Epidemic: An Assessment of the California Opioid Safety Coalitions Network*.; 2017. <http://www.phi.org/wp-content/uploads/migration/uploads/application/files/bt93oju0nrnbsmjhpdw692ljgu0d27ttdpzxmbclj7cxq99alz.pdf>
34. Fairbairn N, Coffin PO, Walley AY. Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic. *Int J Drug Policy*. 2017;46:172-179. doi:10.1016/j.drugpo.2017.06.005
35. Raheemullah A, Andruska N. Fentanyl analogue overdose: Key lessons in management in the synthetic opioid age. *J Opioid Manag*. 2019;15(5):428-432. doi:10.5055/jom.2019.0531
36. California Department of Public Health. California Opioid Overdose Surveillance Dashboard. Published April 27, 2020. Accessed May 11, 2020. <https://skylab.cdph.ca.gov/ODdash/>
37. Huber PJ. The behavior of maximum likelihood estimates under nonstandard conditions. *Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability*. 1967;1(1):221-233.
38. White H. A Heteroskedasticity-Consistent Covariance Matrix Estimator and a Direct Test for Heteroskedasticity. *Econometrica*. 1980;48(4):817. doi:10.2307/1912934
39. Nickell S. Biases in Dynamic Models with Fixed Effects. *Econometrica*. 1981;49(6):1417. doi:10.2307/1911408
40. Jones CM, McCance-Katz EF. Characteristics and prescribing practices of clinicians recently waived to prescribe buprenorphine for the treatment of opioid use disorder. *Addiction*. 2019;114(3):471-482. doi:10.1111/add.14436
41. Krawczyk N, Mojtabei R, Stuart EA, et al. Opioid agonist treatment and fatal overdose risk in a state-wide US population receiving opioid use disorder services. *Addiction*. Published online February 24, 2020. doi:10.1111/add.14991
42. Samples H, Williams AR, Crystal S, Olfson M. Impact Of Long-Term Buprenorphine Treatment On Adverse Health Care Outcomes In Medicaid: The impact of longer treatment on health care outcomes for opioid use disorder within a key population of Medicaid enrollees. *Health Affairs*. 2020;39(5):747-755. doi:10.1377/hlthaff.2019.01085
43. Pearce LA, Min JE, Piske M, et al. Opioid agonist treatment and risk of mortality during opioid overdose public health emergency: population based retrospective cohort study. *BMJ*. Published online March 31, 2020:m772. doi:10.1136/bmj.m772
44. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ*. 2017;357:j1550. doi:10.1136/bmj.j1550

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

45. Williams AR, Samples H, Crystal S, Olfson M. Acute Care, Prescription Opioid Use, and Overdose Following Discontinuation of Long-Term Buprenorphine Treatment for Opioid Use Disorder. *AJP*. 2020;177(2):117-124. doi:10.1176/appi.ajp.2019.19060612
46. Schwartz RP, Gryczynski J, O'Grady KE, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. *American journal of public health*. 2013;103(5):917-922. doi:10.2105/AJPH.2012.301049
47. Substance Abuse and Mental Health Services Administration. Practitioner and Program Data. Published March 4, 2020. Accessed May 4, 2020. <https://www.samhsa.gov/medication-assisted-treatment/training-materials-resources/practitioner-program-data>
48. Cunningham CO, Kunins HV, Roose RJ, Elam RT, Sohler NL. Barriers to Obtaining Waivers to Prescribe Buprenorphine for Opioid Addiction Treatment Among HIV Physicians. *J GEN INTERN MED*. 2007;22(9):1325-1329. doi:10.1007/s11606-007-0264-7
49. Cunningham CO, Sohler NL, McCoy K, Kunins HV. Attending physicians' and residents' attitudes and beliefs about prescribing buprenorphine at an urban teaching hospital. *Fam Med*. 2006;38(5):336-340.
50. DeFlavio JR, Rolin SA, Nordstrom BR, Kazal LA Jr. Analysis of barriers to adoption of buprenorphine maintenance therapy by family physicians. *Rural Remote Health*. 2015;15:3019.
51. Barry DT, Irwin KS, Jones ES, et al. Integrating buprenorphine treatment into office-based practice: a qualitative study. *J Gen Intern Med*. 2009;24(2):218-225. doi:10.1007/s11606-008-0881-9
52. Gordon AJ, Kavanagh G, Krumm M, et al. Facilitators and barriers in implementing buprenorphine in the Veterans Health Administration. *Psychol Addict Behav*. 2011;25(2):215-224. doi:10.1037/a0022776
53. Mendoza S, Rivera-Cabrero AS, Hansen H. Shifting blame: Buprenorphine prescribers, addiction treatment, and prescription monitoring in middle-class America. *Transcult Psychiatry*. 2016;53(4):465-487. doi:10.1177/1363461516660884
54. Netherland J, Botsko M, Egan JE, et al. Factors affecting willingness to provide buprenorphine treatment. *J Subst Abuse Treat*. 2009;36(3):244-251. doi:10.1016/j.jsat.2008.06.006
55. Yang A, Arfken CL, Johanson C-E. Steps physicians report taking to reduce diversion of buprenorphine. *Am J Addict*. 2013;22(3):184-187. doi:10.1111/j.1521-0391.2012.00335.x
56. van Boekel LC, Brouwers EPM, van Weeghel J, Garretsen HFL. Stigma among health professionals towards patients with substance use disorders and its consequences for healthcare delivery: systematic review. *Drug Alcohol Depend*. 2013;131(1-2):23-35. doi:10.1016/j.drugalcdep.2013.02.018

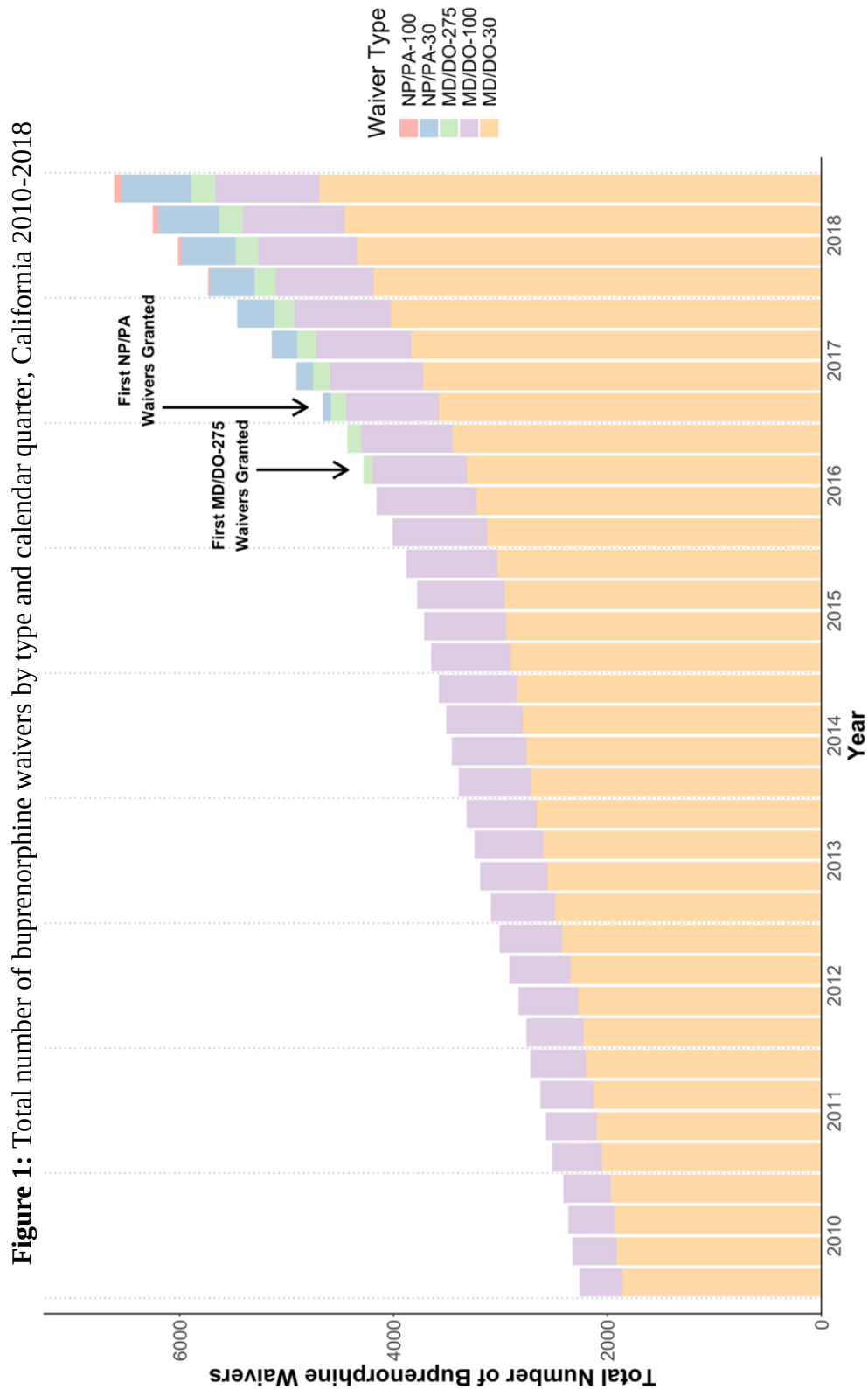
CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

57. Hutchinson E, Catlin M, Andrilla CH, Baldwin LM, Rosenblatt RA. Barriers to primary care physicians prescribing buprenorphine. *Annals of family medicine*. 2014;12(2):128-133. doi:10.1370/afm.1595
58. Haffajee RL, Bohnert ASB, Lagisetty PA. Policy Pathways to Address Provider Workforce Barriers to Buprenorphine Treatment. *Am J Prev Med*. 2018;54(6 Suppl 3):S230-S242. doi:10.1016/j.amepre.2017.12.022
59. Quest, BS TL, Merrill, MD JO, Roll, PhD J, Saxon, MD AJ, Rosenblatt, MD, MPH RA. Buprenorphine therapy for opioid addiction in rural Washington: The experience of the early adopters. *JOM*. 2012;8(1):29-38. doi:10.5055/jom.2012.0093
60. Arfken CL, Johanson C-E, di Menza S, Schuster CR. Expanding treatment capacity for opioid dependence with office-based treatment with buprenorphine: National surveys of physicians. *Journal of Substance Abuse Treatment*. 2010;39(2):96-104. doi:10.1016/j.jsat.2010.05.004
61. Gunderson EW, Levin FR, Kleber HD, Fiellin DA, Sullivan LE. Evaluation of a Combined Online and in Person Training in the Use of Buprenorphine. *Substance Abuse*. 2006;27(3):39-45. doi:10.1300/J465v27n03_06
62. Kissin W, McLeod C, Sonnefeld J, Stanton A. Experiences of a national sample of qualified addiction specialists who have and have not prescribed buprenorphine for opioid dependence. *Journal of addictive diseases*. 2006;25(4):91-103. doi:10.1300/J069v25n04_09
63. Link BG, Struening EL, Rahav M, Phelan JC, Nuttbrock L. On stigma and its consequences: evidence from a longitudinal study of men with dual diagnoses of mental illness and substance abuse. *Journal of health and social behavior*. 1997;38(2):177-190.
64. Luoma JB, Twohig MP, Waltz T, et al. An investigation of stigma in individuals receiving treatment for substance abuse. *Addictive behaviors*. 2007;32(7):1331-1346. doi:10.1016/j.addbeh.2006.09.008
65. Roman PM, Abraham AJ, Knudsen HK. Using medication-assisted treatment for substance use disorders: evidence of barriers and facilitators of implementation. *Addict Behav*. 2011;36(6):584-589. doi:10.1016/j.addbeh.2011.01.032
66. Gertner AK, Robertson AG, Jones H, Powell BJ, Silberman P, Domino ME. The effect of Medicaid expansion on use of opioid agonist treatment and the role of provider capacity constraints. *Health Serv Res*. Published online March 12, 2020. doi:10.1111/1475-6773.13282
67. Saloner B, Levin J, Chang H-Y, Jones C, Alexander GC. Changes in Buprenorphine-Naloxone and Opioid Pain Reliever Prescriptions After the Affordable Care Act Medicaid Expansion. *JAMA Netw Open*. 2018;1(4):e181588. doi:10.1001/jamanetworkopen.2018.1588

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

68. Fiscella K, Wakeman SE, Beletsky L. Buprenorphine Deregulation and Mainstreaming Treatment for Opioid Use Disorder: X the X Waiver. *JAMA Psychiatry*. 2019;76(3):229. doi:10.1001/jamapsychiatry.2018.3685
69. Davis CS, Carr DH. Legal and policy changes urgently needed to increase access to opioid agonist therapy in the United States. *Int J Drug Policy*. 2019;73:42-48. doi:10.1016/j.drugpo.2019.07.006
70. Stancliff S, Greene D, Zucker HA. Why 24 State and Territorial Health Officials Support Buprenorphine Deregulation. *Am J Public Health*. 2019;109(12):1678-1679. doi:10.2105/AJPH.2019.305370

2.6 FIGURES AND TABLES



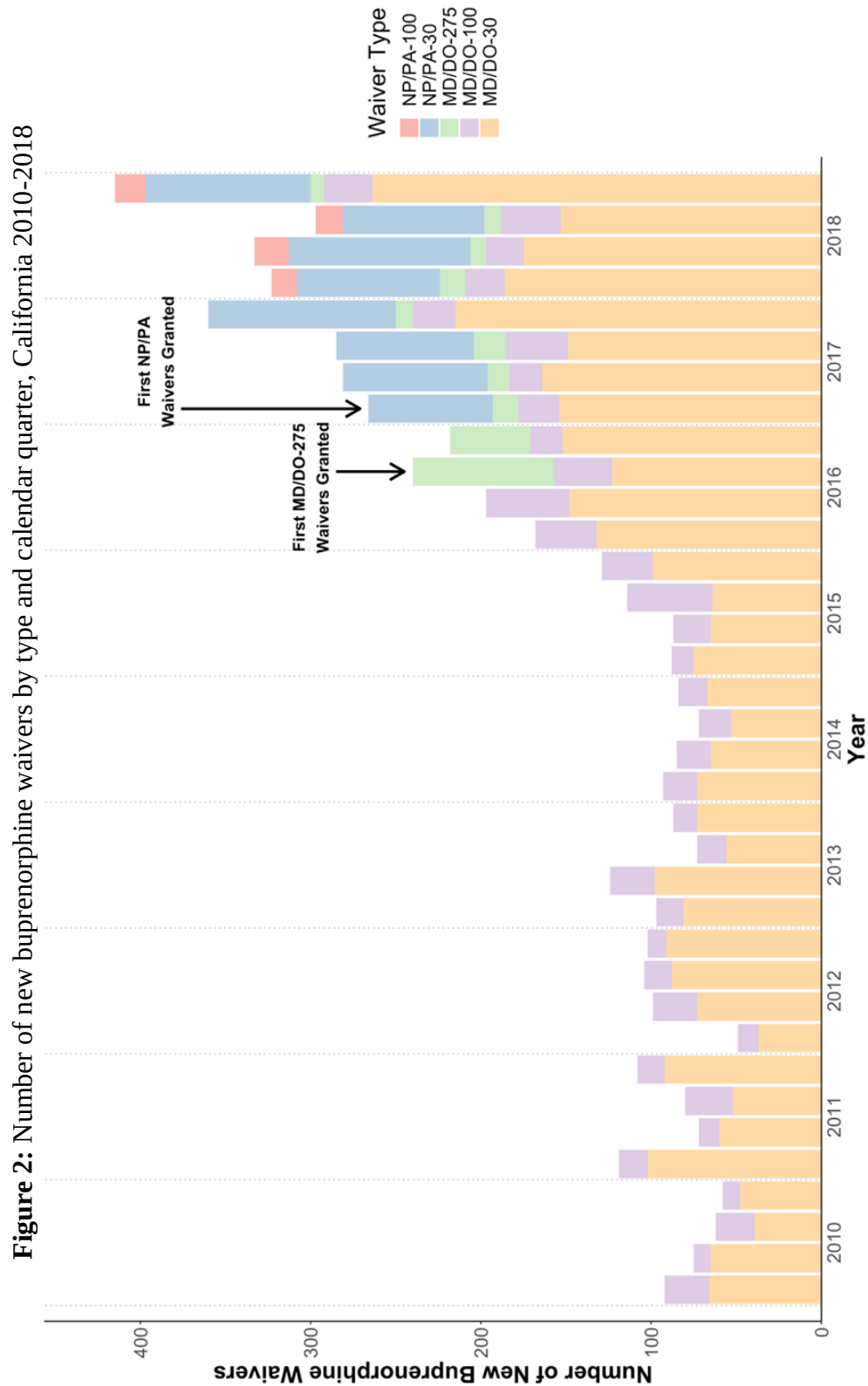
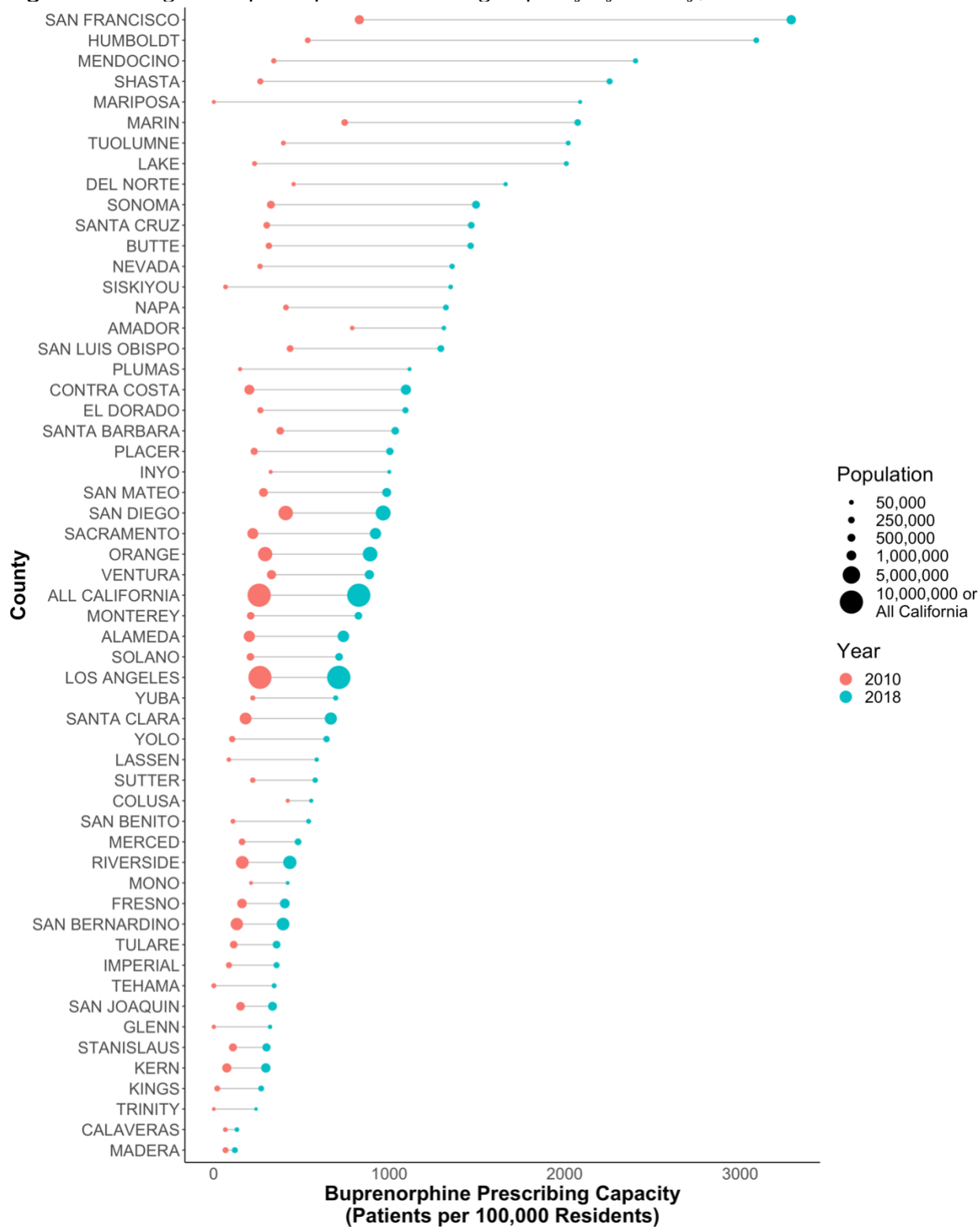


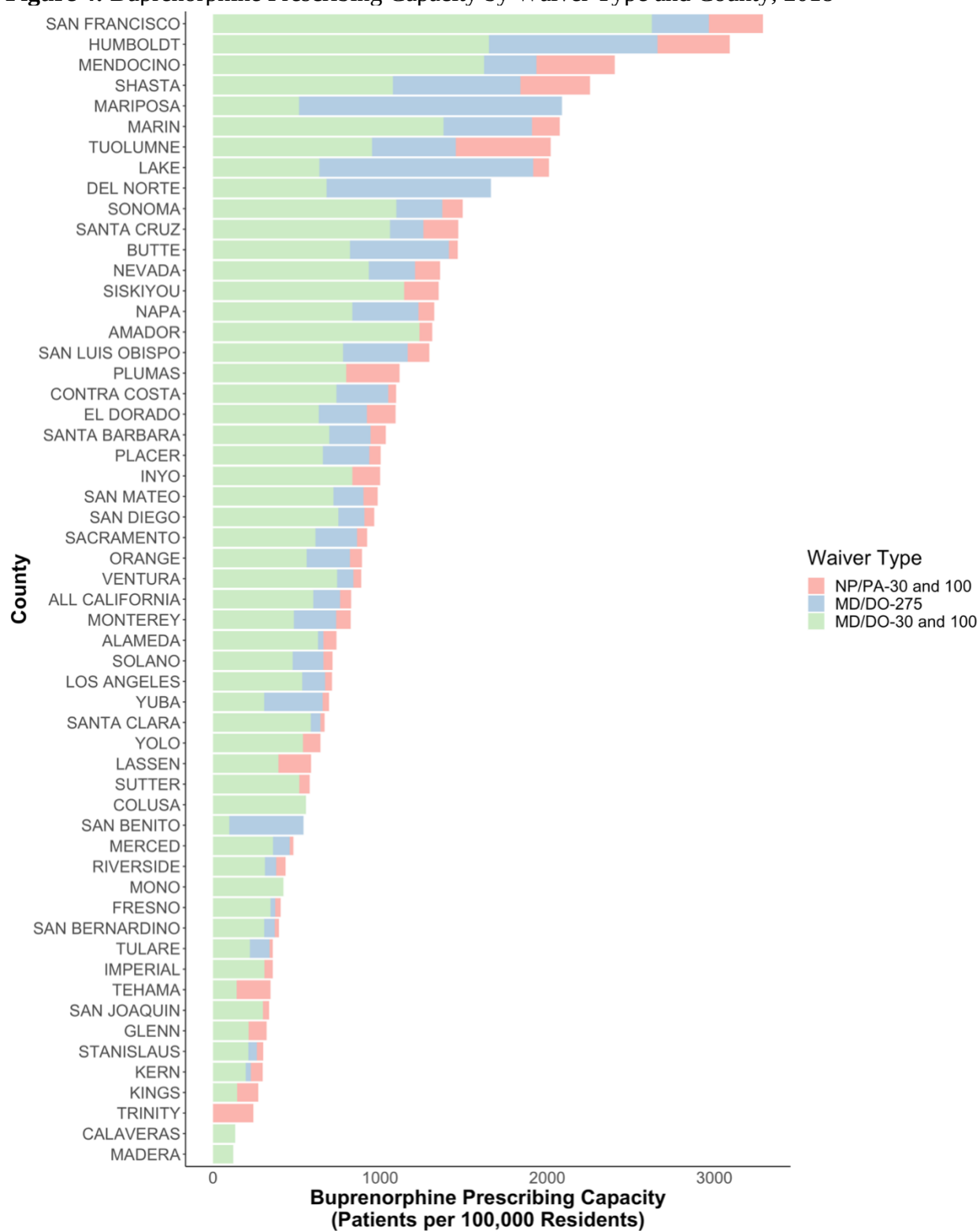
Figure 3: Change in Buprenorphine Prescribing Capacity by County, California 2010-2018*



*Excludes three counties (Alpine, Sierra, Modoc) with Q1 2010 population less than 10,000.

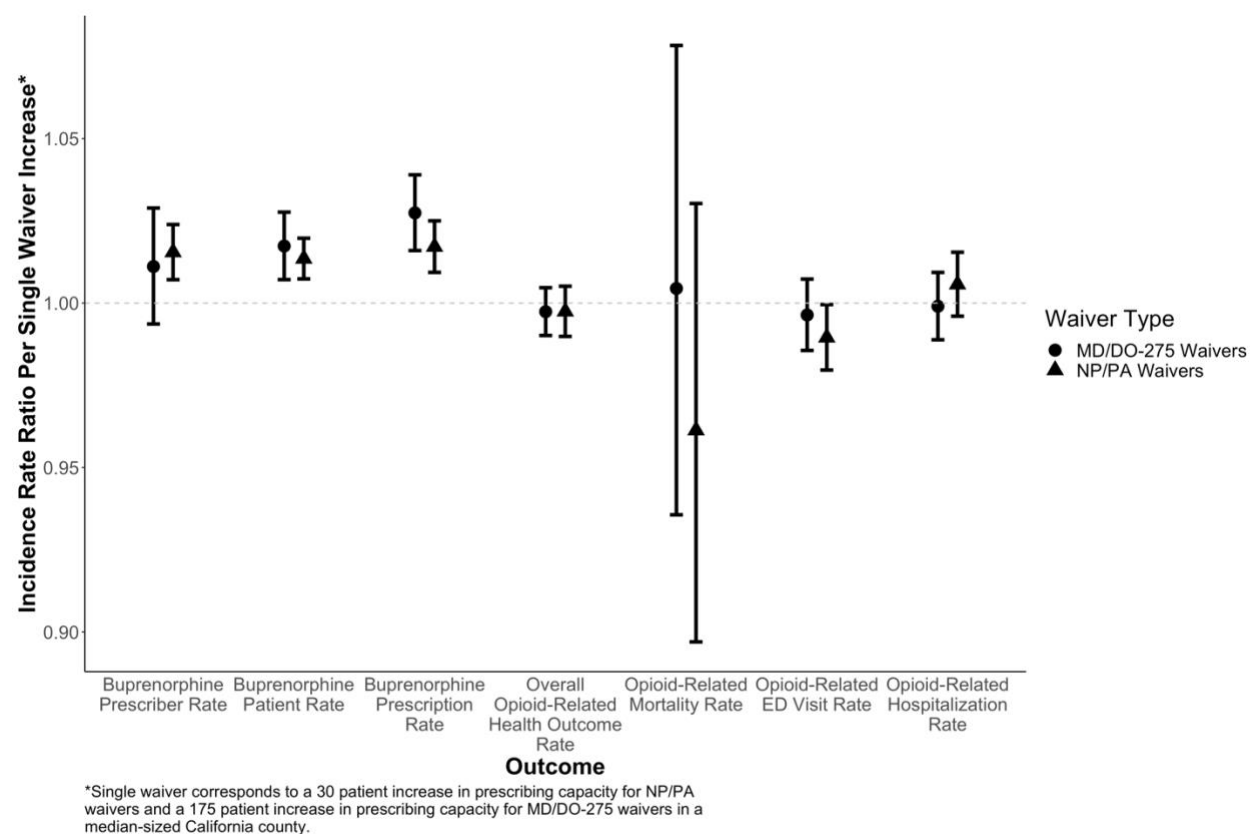
CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

Figure 4: Buprenorphine Prescribing Capacity by Waiver Type and County, 2018*



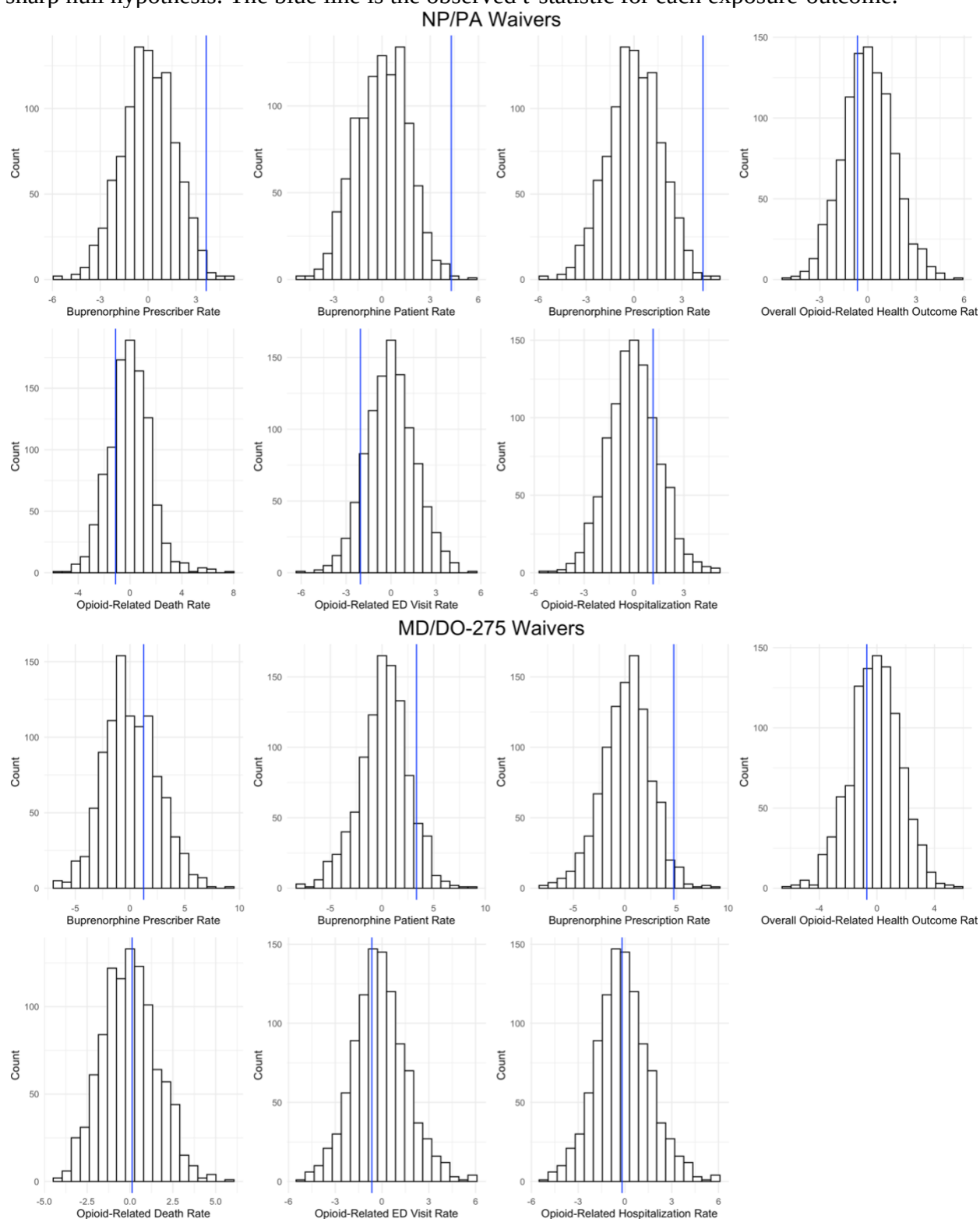
*Excludes three counties (Alpine, Sierra, Modoc) with Q1 2010 population less than 10,000.

Figure 5: Fixed effects Poisson regression results estimating associations between waiver capacities and buprenorphine prescribing and opioid-related health outcomes, California, 2016-2018



CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

Figure 6: Randomization inference results. The distributions are those of t-statistics under the sharp null hypothesis. The blue line is the observed t-statistic for each exposure-outcome.



CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

Table 1: California county implementation months for three buprenorphine-related initiatives controlled for in main analysis

County	Implementation Dates		
	Drug Medi-Cal Organized Delivery System	California Hub and Spoke Program	California Healthcare Foundation Supported California Opioid Safety Coalitions Network*
Alameda	July 2018		November 2015
Alpine			
Amador			
Butte		August 2017	
Calaveras			
Colusa			
Contra Costa	July 2017	August 2017	November 2015
Del Norte			
El Dorado		August 2017	
Fresno		August 2017	
Glenn			
Humboldt		August 2017	November 2015
Imperial	July 2018		
Inyo			
Kern			
Kings		August 2017	
Lake		August 2017	November 2015
Lassen		August 2017	November 2015
Los Angeles	July 2017	August 2017	November 2015
Madera			
Marin	April 2017	August 2017	November 2015
Mariposa			
Mendocino		August 2017	November 2015
Merced			
Modoc			November 2015
Mono			
Monterey	July 2018		
Napa	December 2017		November 2015
Nevada	July 2018	August 2017	November 2015
Orange	July 2018		November 2015
Placer	November 2018	August 2017	November 2015
Plumas		August 2017	November 2015
Riverside	February 2017	August 2017	
Sacramento		August 2017	
San Benito			
San Bernardino	March 2018	August 2017	
San Diego	July 2018	August 2017	
San Francisco	July 2017	August 2017	
San Joaquin	July 2018	August 2017	
San Luis Obispo	January 2018		November 2015

CHAPTER 2: THE BUPRENORPHINE WAIVER PROGRAM

San Mateo	February 2017		
Santa Barbara	December 2018		
Santa Clara	June 2017		November 2015
Santa Cruz	January 2018	August 2017	November 2015
Shasta		August 2017	November 2015
Sierra		August 2017	November 2015
Siskiyou		August 2017	November 2016 [†]
Solano		August 2017	
Sonoma			November 2015
Stanislaus			
Sutter			
Tehama		August 2017	
Trinity		August 2017	
Tulare			
Tuolumne		August 2017	November 2015
Ventura	December 2018		
Yolo	July 2018	August 2017	November 2015
Yuba		August 2017	

*Because the California Health Care supported Opioid Safety Network Coalitions Network was initiated prior to the time period included in the analysis models for all counties except for Siskiyou county, the corresponding policy indicator variables are subsumed by the county fixed effects for all counties except for Siskiyou.

[†]The coalition in Siskiyou county did not begin until "late 2016".

Table 2: Fixed effects Poisson regression results using quarter periods (main analysis results)

Exposure	Outcome Rate	IRR*	(95% CI)	Number of Counties Included [†]	Number of Quarters Per County [‡]	Total Observations
NP/PA Waivers	Buprenorphine Prescribers	1.015	(1.007-1.024)	48	8	384
	Buprenorphine Patients	1.014	(1.007-1.020)	48	8	384
	Buprenorphine Prescriptions	1.017	(1.009-1.025)	48	8	384
	All Opioid-Related Health Outcomes	0.997	(0.990-1.005)	49	8	392
	Opioid-Related Deaths	0.961	(0.897-1.030)	49	8	392
	Opioid-Related ED Visits	0.990	(0.980-1.000)	49	8	392
MD/DO- 275 Waivers	Opioid-Related Hospitalizations	1.006	(0.996-1.015)	49	8	392
	Buprenorphine Prescribers	1.011	(0.994-1.029)	38	10	380
	Buprenorphine Patients	1.017	(1.007-1.028)	38	10	380
	Buprenorphine Prescriptions	1.027	(1.016-1.039)	38	10	380
	All Opioid-Related Health Outcomes	0.997	(0.990-1.005)	39	10	390
	Opioid-Related Deaths	1.004	(0.936-1.078)	39	10	390
	Opioid-Related ED Visits	0.996	(0.986-1.007)	39	10	390
	Opioid-Related Hospitalizations	0.999	(0.989-1.009)	39	10	390

*Incidence rate ratios (IRRs) correspond to a 30 patient increase in prescribing capacity for NP/PA and a 175 patient increase in prescribing capacity for MD/DO-275 waivers in a median-sized California county.

[†]Models only included counties that experienced variability in both the exposure and outcome.

[‡]NP/PA Waiver models include outcome quarters from Q1 2017 through Q4 2018; MD/DO-275 waiver models include outcome quarters from Q3 2016 through Q4 2018. The starting quarters were selected such that the first exposure quarter corresponds to the quarter prior to the introduction of each waiver type.

Table 3: Fixed effects Poisson regression results using half-year periods (sensitivity analysis)

Exposure	Outcome Rate	IRR*	(95% CI)
NP/PA Waivers	Buprenorphine Prescribers	1.015	(1.005-1.026)
	Buprenorphine Patients	1.012	(1.002-1.021)
	Buprenorphine Prescriptions	1.011	(1.000-1.023)
	All Opioid-Related Health Outcomes	0.994	(0.985-1.003)
	Opioid-Related Deaths	0.960	(0.909-1.014)
	Opioid-Related ED Visits	0.992	(0.979-1.005)
	Opioid-Related Hospitalizations	0.997	(0.986-1.007)
MD/DO-275 Waivers	Buprenorphine Prescribers	1.003	(0.983-1.023)
	Buprenorphine Patients	1.015	(1.002-1.027)
	Buprenorphine Prescriptions	1.020	(1.005-1.035)
	All Opioid-Related Health Outcomes	0.998	(0.990-1.006)
	Opioid-Related Deaths	0.996	(0.934-1.062)
	Opioid-Related ED Visits	0.994	(0.982-1.005)
	Opioid-Related Hospitalizations	1.003	(0.993-1.014)

*Incidence rate ratios (IRRs) correspond to a 30 patient increase in prescribing capacity for NP/PA and a 175 patient increase in prescribing capacity for MD/DO-275 waivers in a median-sized California county.

Table 4: Fixed effects Poisson regression results excluding sparsely populated counties (sensitivity analysis)*

Exposure	Outcome Rate	Excluding Counties With <10,000 Residents		Excluding Counties With <20,000 Residents		Excluding Counties With <30,000 Residents	
		IRR	(95% CI)	IRR	(95% CI)	IRR	(95% CI)
NP/PA Waivers	Buprenorphine Prescribers	1.016	(1.007-1.025)	1.015	(1.006-1.025)	1.016	(1.006-1.025)
	Buprenorphine Patients	1.013	(1.007-1.019)	1.013	(1.006-1.019)	1.012	(1.006-1.019)
	Buprenorphine Prescriptions	1.016	(1.008-1.024)	1.016	(1.008-1.025)	1.016	(1.008-1.024)
	All Opioid-Related Health Outcomes	0.996	(0.988-1.005)	0.997	(0.987-1.007)	0.996	(0.987-1.006)
	Opioid-Related Deaths	0.939	(0.879-1.002)	0.917	(0.865-0.973)	0.915	(0.863-0.971)
	Opioid-Related ED Visits	0.986	(0.974-0.998)	0.987	(0.974-1.001)	0.988	(0.974-1.001)
MD/DO- 275 Waivers	Opioid-Related Hospitalizations	1.007	(0.996-1.017)	1.007	(0.995-1.018)	1.005	(0.994-1.017)
	Buprenorphine Prescribers	1.011	(0.994-1.029)	1.011	(0.994-1.028)	1.012	(0.994-1.031)
	Buprenorphine Patients	1.017	(1.007-1.028)	1.017	(1.007-1.027)	1.018	(1.007-1.029)
	Buprenorphine Prescriptions	1.027	(1.016-1.039)	1.027	(1.016-1.038)	1.029	(1.017-1.040)
	All Opioid-Related Health Outcomes	0.999	(0.988-1.009)	0.999	(0.989-1.010)	0.999	(0.988-1.010)
	Opioid-Related Deaths	1.004	(0.936-1.078)	0.996	(0.928-1.070)	0.985	(0.915-1.061)
NP/PA Waivers	Opioid-Related ED Visits	0.996	(0.979-1.013)	0.997	(0.979-1.015)	0.995	(0.977-1.014)
	Opioid-Related Hospitalizations	1.002	(0.988-1.015)	1.002	(0.988-1.016)	1.003	(0.989-1.017)
NP/PA Waivers	Buprenorphine Prescribers	1.016	(1.007-1.025)	1.016	(1.007-1.026)		
	Buprenorphine Patients	1.012	(1.005-1.018)	1.013	(1.006-1.019)		
	Buprenorphine Prescriptions	1.015	(1.007-1.024)	1.016	(1.008-1.024)		
	All Opioid-Related Health Outcomes	0.996	(0.987-1.006)	0.996	(0.987-1.006)		
	Opioid-Related Deaths	0.913	(0.86-0.970)	0.912	(0.858-0.970)		
	Opioid-Related ED Visits	0.988	(0.975-1.002)	0.988	(0.974-1.002)		
MD/DO- 275 Waivers	Opioid-Related Hospitalizations	1.005	(0.994-1.017)	1.006	(0.994-1.017)		
	Buprenorphine Prescribers	1.012	(0.994-1.031)	1.012	(0.994-1.031)		
	Buprenorphine Patients	1.018	(1.007-1.029)	1.018	(1.007-1.029)		
	Buprenorphine Prescriptions	1.029	(1.017-1.040)	1.029	(1.017-1.040)		
	All Opioid-Related Health Outcomes	0.999	(0.988-1.010)	0.999	(0.988-1.010)		
	Opioid-Related Deaths	0.985	(0.915-1.061)	0.985	(0.915-1.061)		
NP/PA Waivers	Opioid-Related ED Visits	0.995	(0.977-1.014)	0.995	(0.977-1.014)		

Opioid-Related Hospitalizations	1.003 (0.989-1.017)	1.003 (0.989-1.017)
*The NP/PA models included 47, 44, 43, 42, and 41 counties when excluding counties with fewer than 10, 20, 30, 40, and 50 thousand residents; The MD/DO-275 models included 38, 37, 36, and 36 counties when excluding counties with fewer than 10, 20, 30, 40, and 50 thousand residents.		
†Incidence rate ratios (IRRs) correspond to a 30 patient increase in prescribing capacity for NP/PA and a 175 patient increase in prescribing capacity for MD/DO-275 waivers in a median-sized California county.		

Table 5: 2.5% and 97% quantiles for probabilistic sensitivity analysis estimates.

Exposure	Outcome Rate	Quantile	
		2.5%	97.5%
NP/PA Waivers	Buprenorphine Prescribers	1.010	1.021
	Buprenorphine Patients	1.008	1.018
	Buprenorphine Prescriptions	1.011	1.024
	All Opioid-Related Health Outcomes	0.993	1.003
	Opioid-Related Deaths	0.935	1.001
	Opioid-Related ED Visits	0.984	0.997
	Opioid-Related Hospitalizations	1.000	1.012
MD/DO- 275 Waivers	Buprenorphine Prescribers	0.993	1.025
	Buprenorphine Patients	1.006	1.023
	Buprenorphine Prescriptions	1.013	1.034
	All Opioid-Related Health Outcomes	0.992	1.003
	Opioid-Related Deaths	0.950	1.051
	Opioid-Related ED Visits	0.987	1.002
	Opioid-Related Hospitalizations	0.992	1.007

Table 6: Randomization inference results: proportion of sharp null t-statistics more extreme than observed t-statistic

Exposure	Outcome Rate	%
NP/PA Waivers	Buprenorphine Prescribers	2.2
	Buprenorphine Patients	0.6
	Buprenorphine Prescriptions	0.8
	All Opioid-Related Health Outcomes	69.0
	Opioid-Related Deaths	44.3
	Opioid-Related ED Visits	20.3
	Opioid-Related Hospitalizations	43.3
MD/DO- 275 Waivers	Buprenorphine Prescribers	62.5
	Buprenorphine Patients	15.8
	Buprenorphine Prescriptions	5.2
	All Opioid-Related Health Outcomes	68.0
	Opioid-Related Deaths	93.1
	Opioid-Related ED Visits	67.8
	Opioid-Related Hospitalizations	90.4

Chapter 3: Evaluating the effects of opioid prescribing policies on patient outcomes in a safety-net primary care clinic

3.1 INTRODUCTION

The United States continues to grapple with an unprecedented opioid overdose epidemic. Nearly half a million people have died from opioid-related drug overdoses since 1999, including close to 50,000 deaths annually in recent years.¹ Although the crisis is now dominated by illicit opioids such as heroin and fentanyl, nearly one third of opioid overdose deaths involved prescription opioids in 2018.^{2,3}

Opioid stewardship measures aiming to limit supply and mitigate harms associated with prescription opioids in primary care settings have been a major component of the national response to the epidemic.^{4–11} Most prominently, the Centers for Disease Control and Prevention (CDC) released guidelines for prescribing opioids for chronic pain in 2016, which was linked to a national reduction in opioid prescribing.^{12,13} Despite well-documented declines in opioid prescribing,^{14–16} the rate of prescribing in the U.S. remains substantially higher than any other nation and varies widely throughout the country.^{17–19} In addition, little is known about the effectiveness of specific components of the CDC guidelines or of other prescribing-related policies in reducing opioid prescribing or their effects on other patient outcomes, intended or unintended.²⁰ Several studies have linked reduction or discontinuation of prescribed opioids to adverse patient outcomes, including dropping out of care,²¹ initiation of illicit opioid use²², and death by overdose and suicide.^{23–25} In light of these risks, critical examination of the effects of specific policies on opioid prescribing and other patient outcomes is needed to identify the safest and most effective strategies moving forward.

In 2013-2014, a safety-net primary care clinic in San Francisco, California implemented two new policies and established a new committee in an effort to promote more judicious opioid prescribing. Specifically, the clinic implemented policies restricting opioid prescription refills under certain circumstances and standardizing the regular use of urine toxicology testing and established a new committee to discuss treatment decisions for complex patient cases involving opioid therapy. Understanding the effects of these interventions on opioid prescribing and on unintended negative outcomes can inform opioid prescribing policies and practices in the future.

In this study, we used a retrospective cohort study design to evaluate the combined effects of these two policies and committee on opioid prescribing, use of heroin, and use of opioid analgesics not prescribed to the patient.

3.2 METHODS

Parent Study

Data were from a retrospective cohort study of 602 publicly-insured patients who were prescribed opioids for chronic non-cancer pain in San Francisco's safety-net health network.²² To be eligible, participants had to be at least 18 years of age, able to communicate in English, and prescribed opioids for at least three months from 2013-2015. Potential participants were identified through patient registries maintained by each network clinic and primary care providers were contacted for permission to contact patients directly. Participants who were contacted and agreed to participate were seen for a single in-person visit in 2017 or 2018, which included an in-depth interview to collect retrospective substance use patterns (including heroin and non-prescribed opioid analgesics) and other demographic and behavioral information. Separately, opioid prescription and other clinical measures were manually abstracted from participants' medical charts.

Policies Under Study

The interventions were established at the clinic within a one-year period from July 1, 2013 to July 1, 2014. The purpose of the two policies was to define uniform procedures related to opioid prescribing so as to "clarify expectations and improve safety for patients and staff, reduce risks and harms from opioids, and reduce staff anxiety." The first policy addressed opioid refills and the second policy addressed the use of urine toxicology testing. The new committee was called the "yellow flag" committee in reference to yellow flag behaviors, which are potentially concerning behaviors in the context of opioid prescribing (e.g., repeated requests for dose escalations, presenting to clinic while intoxicated). The purpose of the yellow flag committee, which began meeting in early 2014, was to establish a formal system for multidisciplinary group discussion of treatment plans for patients who were prescribed opioids under complex or challenging circumstances (e.g., patients with substance use histories, those prescribed particularly high opioid dosages, or those with a history of yellow flag behaviors).

Opioid Refill Policy: Effective July 1, 2013, the opioid refill policy established uniform procedures for refilling opioid medications. Specifically, the policy outlined procedures for refilling opioid medications when patients requested early or late refills or reported lost or stolen opioid medications or prescriptions. The policy established a limit of one early or late refill in a 12-month period and outlined requirements for increased monitoring and a detailed treatment plan assessment (including possible dose modification) in the case of multiple early or late refill requests or for patients who have exhibited yellow flag behavior.

Urine Toxicology Policy: Effective July 1, 2014, the urine toxicology policy established uniform procedures for requesting urine samples from patients for toxicological testing, interpreting results, and taking action based on results. The policy required that all patients prescribed chronic opioids be asked to submit a urine sample for toxicology testing prior to initiating therapy and at least once per 12 months while continuing therapy. The policy outlined procedures for when urine toxicology

CHAPTER 3: OPIOID PRESCRIBING POLICIES

results were inconsistent with prescribed medications (e.g., negative for the prescribed opioid, or positive for cocaine, methamphetamine, or non-prescribed opioids), including a detailed assessment of the patient's treatment plan and possible opioid discontinuation with a taper.

Yellow Flag Committee: The “yellow flag” committee, which was conceived in late 2013 and officially began meeting in early 2014, was designed to discuss treatment plans for the following types of patients: those on opioids whose use has become problematic for the patient, provider, or staff; those with three or more “yellow flag” behaviors; those with a behavioral agreement for disruptive or violent behavior related to opioids; and those on opioids who are at higher risk for overdose or death (e.g., patients with overdose in the past 12 months, patients on high dose opioids [>400 morphine milligram equivalents per day or $>100\text{mg}$ methadone per day]). The committee did not review every case falling into the above categories, which would not have been feasible due to volume, but sought to identify and review the most complex patient cases involving opioids, which typically fell into one of these categories. Any staff member at the clinic could also request a case review by the committee as well, regardless of reason. Committee composition included a provider (always a medical doctor, but sometimes also a nurse practitioner or physician assistant, who was not the primary care provider), nursing staff and behavioral health staff. The committee was not explicitly tasked with decreasing the opioid dose for patients on high doses, but generally did provide recommendations to maximize non-opioid treatments and consider decreasing doses, especially in high-risk cases.

These two policies and the committee will hereafter be referred to as the interventions.

Clinics Under Study

The clinic that implemented the interventions (hereafter referred to as the treated clinic) predominately provides primary care to adults experiencing homelessness, residents of permanent supportive housing, and other members of San Francisco's downtown neighborhoods, which are characterized by concentrated socioeconomic disadvantage and elevated rates of drug overdose mortality.^{26–28}

To evaluate the impacts of the interventions among patients at the treated clinic, we leveraged the experience of patients at a control clinic that is part of the same network as the treated clinic but that did not implement the interventions. Specifically, we used patients at a clinic that provides integrated primary and specialty care to the network's HIV-infected patients. The control clinic is unique among the network's clinics in that, during a time of both national and local reductions in opioid prescribing, it did not implement formal policies to reduce prescribing, whereas other clinics in the network did. In addition, the control clinic is partially managed by a local university and is not subject to the same oversight as other clinics in the network.

Analysis Sample

The analysis was restricted to 151 patients who were prescribed opioids and receiving care from the treated clinic and an additional 122 patients who were prescribed opioids and receiving care from the control clinic at the time of the first policy change (July 1, 2013). Patients in the analysis sample were required to have started receiving care from the network on January 1, 2012 or earlier; all retrospective study measures were collected starting in January 1, 2012, so this restriction ensured that all patients had complete follow-up during the full pre-policy period (i.e., January 1,

CHAPTER 3: OPIOID PRESCRIBING POLICIES

2012 through June 30, 2013). Measures from the pre-policy period were used to assess trends in outcomes during the pre-policy period as well as to generate baseline covariates for estimating patient propensity scores, both described in greater detail below.

Measures and Data Sources

Clinical measures were manually abstracted from electronic medical charts by trained staff who were blinded to all other study data. Measures included opioid prescription data (opioid type, dose, quantity per 30 days), exposure to opioid stewardship activities (controlled substance monitoring program [CSMP] checks, controlled substance agreements, and “yellow flag” behaviors documented by the provider), and emergency department visits and their opioid-relatedness.

Self-reported use frequency of heroin, non-prescribed opioid analgesics, cocaine, methamphetamine, and alcohol was collected for each calendar quarter (i.e., January-March, April-June, etc.) from 2012 until the date of the study visit through an in-person historical reconstruction interview procedure described elsewhere.²² Demographic information (e.g., age, education) was also collected at the study visit.

Study Outcomes

Six study outcomes were assessed for each patient for the one-year pre-policy period (July 1, 2012 – June 30, 2013), the implementation period (July 1, 2013 – June 30, 2014), and a three additional post-policy periods (July 1, 2014 – June 30, 2015; July 1, 2015 – June 30, 2016; July 1, 2016 – June 30, 2017). The implementation period and three additional post-policy periods will hereafter be referred to as the first, second, third, and fourth post-policy periods.

Outcomes included whether the patient had an active opioid prescription on the last day of each period, and their mean daily opioid dose in morphine milligram equivalents (MME),^{29,30} any heroin use and use frequency, and any non-prescribed opioid analgesic use and use frequency during each period. To avoid counting temporary discontinuations of opioid prescriptions, a patient was only considered to not be on opioids at the end of each period if they were not prescribed opioids on the last day of a period and were not prescribed opioids for a period of at least three months. Use frequency of heroin and non-prescribed opioid analgesics was operationalized as sequential integers ranging from 0 to 6 corresponding to none, once, intermittently, less than weekly or weekly, multiple times per week, and daily or nearly daily.

Statistical Analysis

The associations between the new policies and each of the six outcomes were assessed using a conditional difference-in-differences approach.³¹

The key assumption underlying the standard difference in differences approach in our context is that the change in outcome from pre- to post-policy periods in the control clinic represents the change that would have occurred in the treated clinic had the policies under study not been implemented (i.e., the secular trend). If this assumption holds, the difference in differences estimate can be interpreted as an unbiased estimate of the effect of the policies on the outcome under study. Although the parallel trends assumption is fundamentally untestable, its plausibility

can be assessed by examining treated and control clinic outcome trends during the pre-policy period. Although not guaranteed, parallel outcome trends during the pre-policy period may suggest that the trends would have remained parallel through the post-policy period had the policies not been implemented. Thus, we plotted the mean outcomes over time during the pre-policy period as well as separate linear regression fits using the individual-level outcomes for each clinic (Figure 1). Because there were only 18 months in the pre-policy period, we plotted outcomes and fit the regression lines using calendar quarter as the timescale. As a result, the unit of time utilized in assessing pre-policy outcome trends is smaller than that used in the main analysis (i.e., years), which may result in greater outcome variability in the pre-policy assessment.

Because visual inspection of these pre-policy outcome trends during the pre-policy period suggested possible violations of the parallel trends assumption, we used a generalization of the difference-in-differences design that relies on the weaker “conditional parallel trends” assumption. The conditional parallel trends assumption posits that any differences in outcome trends in the absence of treatment are the result of differences in observed baseline covariates between the treated and the control group. This approach uses propensity score weighting to balance covariates that may be associated with differential outcome dynamics among the treated and control groups.

As derived and presented elsewhere,³¹ the conditional difference-in-differences estimates for each post-policy period are calculated as follows:

$$\frac{1}{n} \sum_{i=1}^n \left(\frac{(Y_{i,2} - Y_{i,1})}{P(T = 1)} \times \frac{(T_i - P(T = 1|X_i))}{(1 - P(T = 1|X_i))} \right)$$

Where $Y_{i,2}$ is the outcome for patient i in period 2 (i.e., a post-policy period) and $Y_{i,1}$ is the outcome for patient i in period 1 (i.e., the pre-policy period). T_i is the treatment indicator for patient i , which is equal to 1 if the patient was a patient of the treated clinic and 0 otherwise. $P(T = 1|X_i)$ is the estimated propensity score and $P(T = 1)$ is the empirical proportion of treated clinic patients among the entire sample.

We used logistic regression to estimate propensity scores and included independent variables that we hypothesized may impact trends in our outcomes. Specifically, we included gender, race/ethnicity, age, education, and the following measures corresponding to the 18 month pre-policy period from January 1, 2012 through June 30, 2013: use of heroin, use of non-prescribed opioid analgesics, use of alcohol, use of methamphetamine, use of cocaine, any emergency department visits, any opioid-related emergency department visits, any pain agreements, any CSMP checks, any yellow flag behavior indicated by the physician, and mean opioid dose.

We then applied the conditional difference-in-differences weighting estimator to each outcome and post-policy period and calculated 95% bootstrap confidence intervals using the percentile method with 2000 iterations.

Sensitivity Analysis

Because matching on pre-period outcome levels can bias difference-in-difference estimates when pre-period outcome levels are correlated with treatment assignment,³² we conducted a sensitivity analysis in which we excluded the relevant pre-period outcome as an independent variable in the propensity score models. Specifically, we excluded mean opioid dose when estimating the propensity scores for the opioid prescription outcomes, heroin use for the heroin use outcomes, and non-prescribed opioid analgesic use for the non-prescribed opioid analgesic use outcomes.

3.3 RESULTS

Sample Characteristics

The analysis includes 151 (55%) treated clinic patients and 122 (45%) control clinic patients. Treated clinic patients were more likely to be older (mean age of 52.5 among treated clinic patients vs. 49.9 among control clinic patients), female (34% vs. 21%), non-Hispanic white (38% vs. 30%) and to have had experience with opioid stewardship activities in the pre-policy period (controlled substance agreements: 20% vs. 8%; yellow flag behaviors: 33% vs. 25%; CSMP checks: 6% vs. 1%) relative to control clinic patients. Detailed patient characteristics by clinic are presented in Table 1.

Conditional Differences-in-Differences Estimates

There was no evidence that the interventions were associated with whether patients were prescribed opioids at the end of each period (Figure 2). However, the interventions were associated with a reduction in mean opioid dose in the first three post-policy years (Year 1 conditional difference-in-differences estimate: -52.0 MME [95% confidence interval: -109.9, -10.6]; Year 2: -106.2 MME [-195.0, -34.6]; Year 3: -98.6 MME [-198.7, -23.9]; Year 4: -72.6 MME [-160.4, 3.6]) (Figure 3).

There was no evidence that the interventions were associated with heroin use or use frequency (Figures 4-5).

Although 95% confidence intervals included the null, estimates suggested a possible positive association between the interventions and non-prescribed opioid analgesic use (Year 3: 5.2 absolute percentage points [-0.1, 11.2]) and use frequency (Year 3: 0.21 ordinal frequency scale points [0.00, 0.47]) in the third post-policy year (Figures 6-7).

All conditional difference-in-differences estimates and 95% confidence intervals are reported in Table 2.

Sensitivity Analysis

The results of our sensitivity analysis, for which we excluded pre-policy outcome levels as independent variables when estimating propensity scores, were largely consistent with the main results and are presented in Table 3.

3.4 DISCUSSION

We found that the implementation of opioid refill and urine toxicology policies and the establishment of a committee to discuss complex patient cases were associated with reductions in opioid dose and were suggestive of increases in non-prescribed opioid analgesic use. There was no evidence that the interventions were associated with changes in the overall proportion of patients prescribed opioids or in heroin use.

The interventions were associated with over a 100 MME reduction (40% relative change from the pre-intervention dose), which brought the mean opioid dose among treated clinic patients below 200 MME, a dose deemed high risk and targeted for reduction by policies at the Veterans Administration Health System.⁴⁸ The interventions under study did not have the explicit aim of reducing patients' opioid dose but rather aimed to mitigate problematic patient behavior and improve safety. Our findings suggest that policies guided by this strategy may provide an effective approach for reducing opioid prescribing.

The dose reductions were greatest in the second and third post-policy years but were largely attenuated by the fourth year. The slower pace of dose reductions among control clinic patients suggest that secular trends in opioid prescribing may have caught up to reductions achieved by the interventions. Although the control clinic did not implement specific opioid prescribing policies, our study period overlaps with several trends and policies that likely affected prescribing trends at both the treated and control clinics. There were national reductions in prescribed opioid dose during this time,^{15,16} which were likely driven by an increasing awareness of the risks associated with prescription opioids³⁵⁻³⁹ and further influenced by the release of the CDC's prescribing guidelines in 2016.¹³ In addition, there were several state and local changes aiming to promote safer opioid prescribing during this period. Specifically, the Medical Board of California adopted its own prescribing guidelines in 2014,⁴⁰ which were similar to the CDC's opioid prescribing guidelines and may have led to reductions in opioid prescribing across California. Also, the network that includes the clinics under study formed a pain management workgroup in 2012 to promote responsible prescribing across all the network's clinics. Lastly, the managed care organization that oversees the management of the majority of Medicaid clients in San Francisco implemented dose and quantity limits on opioid prescribing in 2014. Our results suggest that these changes, among others, were sufficient to gradually reduce prescribed opioid dose without the explicit interventions implemented at the treated clinic, though not with the rapidity achieved by the interventions.

There was no association between the interventions and a decrease in the proportion of patients prescribed opioids. However, to participate in the parent study, patients were required to complete an in-person visit in either 2017 or 2018, which may have systematically excluded patients who had dropped out of care, died, or been otherwise difficult to locate since the interventions were implemented in 2013-2014. Opioid discontinuation and dose reductions have been linked to both dropping out of care²¹ and mortality,²³⁻²⁵ suggesting the possibility that opioid-discontinued patients may be under-represented in our sample. An unpublished quality improvement analysis conducted at the treated clinic found a 52% reduction in the number of patients on chronic opioids from 2012 to 2015, which is substantially larger than the 15% reduction observed among our treated clinic sample over a similar timeframe.⁴¹ This difference suggests that patients who had

their opioids discontinued are under-represented in our treated clinic sample; unfortunately, we have no way to make a similar assessment for our control clinic sample. However, under the assumption that undersampling of opioid-discontinued patients occurred at the same rate across the treated and control clinics, our estimate of a true effect would be biased towards the null. Thus, our null effect estimate for this measure should be interpreted with caution. To mitigate the threat of such biases, it is important that future studies evaluate opioid prescribing policies using entire populations of interest or truly representative samples.

The results were suggestive of a positive association between the interventions and use of non-prescribed opioid analgesics, although confidence intervals included the null. Because of the challenges involved with collecting measures of substance use, studies examining the relationship between changes in prescribed opioid dose and subsequent substance use are limited. However, this finding is consistent with a study among the entire parent study sample that found that opioid dose discontinuations were associated with more frequent use of both heroin and non-prescribed opioid analgesics, and opioid dose reductions were associated with any use of non-prescribed opioid analgesics.²² It is also worth noting that the treated clinic implemented an integrative pain management program to advance the use of multimodal pain treatments in 2016, which was associated with self-reported improvements in pain, social satisfaction, and mental health outcomes among participating patients.⁴² It is plausible that this program and its benefits could have attenuated any adverse impacts of the interventions on non-prescribed opioid use. Regardless, our findings highlight the importance of carefully weighing the potential benefits and harms associated with reducing or discontinuing opioid therapy for individual patients.⁴³

The present study has several limitations. First, our convenience sample may not be representative of the entire patient population among the two clinics over the course of the study period, as was suggested in the context of our opioid discontinuation outcome. Second, although our opioid prescription measures were abstracted from medical charts, our measures of illicit opioid use were obtained via retrospective self-report and thus vulnerable to various reporting biases. Third, the patients under study are socioeconomically disadvantaged relative to the general population and thus the estimated impacts of these policies may not be generalizable to other patient populations. Fourth, the validity of the conditional difference-in-differences estimator depends on the assumption that any differences in outcome trends not attributable to the treatment are attributable to baseline characteristics that we observed and incorporated into our analysis, which is not directly testable. Related to this, our analytic approach and choice of control group also assume that outcome trends are independent of HIV-status, conditional on other observed patient characteristics. Although levels of outcomes may differ by HIV-status, we have no reason to expect trends in outcomes to differ after accounting for other demographic and clinical characteristics.

Despite these limitations, the present study offers a rigorous evaluation of the effects of specific opioid prescribing policies on opioid prescribing and illicit opioid use. We found that policies addressing concerning behavior, such as multiple early refill requests or abnormal urine toxicology results, and a patient-centered committee designed to facilitate challenging treatment decisions were associated with a substantial reduction in mean opioid dose and possibly with an increase in non-prescribed opioid analgesic use. Such empirical evidence is essential for informing the path

forward as we continue to seek a balance between reducing opioid prescribing and minimizing harms for affected patients.

3.5 REFERENCES

1. Centers for Disease Control and Prevention National Center for Health Statistics. Multiple Cause of Death 1999-2018 on CDC WONDER Online Database, released 2019. Published online March 17, 2018. <http://wonder.cdc.gov/>
2. Hedegaard H, Minaño AM, Warner M. *Drug Overdose Deaths in the United States, 1999-2018*. National Center for Health Statistics; 2020.
3. Wilson N, Kariisa M, Seth P, Smith H, Davis NL. Drug and Opioid-Involved Overdose Deaths - United States, 2017-2018. *MMWR Morb Mortal Wkly Rep*. 2020;69(11):290-297. doi:10.15585/mmwr.mm6911a4
4. Strickler GK, Zhang K, Halpin JF, Bohnert ASB, Baldwin GT, Kreiner PW. Effects of mandatory prescription drug monitoring program (PDMP) use laws on prescriber registration and use and on risky prescribing. *Drug Alcohol Depend*. 2019;199:1-9. doi:10.1016/j.drugalcdep.2019.02.010
5. Shev AB, Wintemute GJ, Cerda M, Crawford A, Stewart SL, Henry SG. Prescription Drug Monitoring Program: Registration and Use by Prescribers and Pharmacists Before and After Legal Mandatory Registration, California, 2010-2017. *Am J Public Health*. 2018;108(12):1669-1674. doi:10.2105/AJPH.2018.304704
6. Kay C, Wozniak E, Ching A, Bernstein J. Pain Agreements and Healthcare Utilization in a Veterans Affairs Primary Care Population: A Retrospective Chart Review. *Pain Ther*. 2018;7(1):121-126. doi:10.1007/s40122-018-0098-5
7. Penko J, Mattson J, Miaskowski C, Kushel M. Do patients know they are on pain medication agreements? Results from a sample of high-risk patients on chronic opioid therapy. *Pain Med*. 2012;13(9):1174-1180. doi:10.1111/j.1526-4637.2012.01430.x
8. Pergolizzi JV, Curro FA, Col N, et al. A multicentre evaluation of an opioid patient-provider agreement. *Postgrad Med J*. 2017;93(1104):613-617. doi:10.1136/postgradmedj-2016-134607
9. Mahajan G. Role of Urine Drug Testing in the Current Opioid Epidemic. *Anesth Analg*. 2017;125(6):2094-2104. doi:10.1213/ANE.0000000000002565
10. Pergolizzi J, Pappagallo M, Stauffer J, et al. The role of urine drug testing for patients on opioid therapy. *Pain Pract*. 2010;10(6):497-507. doi:10.1111/j.1533-2500.2010.00375.x
11. Von Korff M, Dublin S, Walker RL, et al. The Impact of Opioid Risk Reduction Initiatives on High-Dose Opioid Prescribing for Patients on Chronic Opioid Therapy. *J Pain*. 2016;17(1):101-110. doi:10.1016/j.jpain.2015.10.002

12. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep*. 2016;65(1):1-49. doi:10.15585/mmwr.rr6501e1
13. Bohnert ASB, Guy GP Jr, Losby JL. Opioid Prescribing in the United States Before and After the Centers for Disease Control and Prevention’s 2016 Opioid Guideline. *Ann Intern Med*. 2018;169(6):367-375. doi:10.7326/M18-1243
14. Fenton JJ, Agnoli AL, Xing G, et al. Trends and Rapidity of Dose Tapering Among Patients Prescribed Long-term Opioid Therapy, 2008-2017. *JAMA Netw Open*. 2019;2(11):e1916271. doi:10.1001/jamanetworkopen.2019.16271
15. Guy GP, Zhang K, Bohm MK, et al. Vital Signs: Changes in Opioid Prescribing in the United States, 2006-2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(26):697-704. doi:10.15585/mmwr.mm6626a4
16. Strickler GK, Kreiner PW, Halpin JF, Doyle E, Paulozzi LJ. Opioid Prescribing Behaviors - Prescription Behavior Surveillance System, 11 States, 2010-2016. *MMWR Surveill Summ*. 2020;69(1):1-14. doi:10.15585/mmwr.ss6901a1
17. Schieber LZ, Guy GP, Seth P, et al. Trends and Patterns of Geographic Variation in Opioid Prescribing Practices by State, United States, 2006-2017. *JAMA Netw Open*. 2019;2(3):e190665. doi:10.1001/jamanetworkopen.2019.0665
18. International Narcotics control Board. *Narcotic Drugs 2019, Estimated World Requirements for 2020, Statistics for 2018*. <https://www.incb.org/>
19. Centers for Disease Control and Prevention. U.S. Opioid Prescribing Rate Maps. Accessed March 27, 2020. <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html>
20. Frank JW, Lovejoy TI, Becker WC, et al. Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy: A Systematic Review. *Ann Intern Med*. 2017;167(3):181-191. doi:10.7326/M17-0598
21. Perez HR, Buonora M, Cunningham CO, Heo M, Starrels JL. Opioid Taper Is Associated with Subsequent Termination of Care: a Retrospective Cohort Study. *J Gen Intern Med*. 2020;35(1):36-42. doi:10.1007/s11606-019-05227-9
22. Coffin PO, Rowe C, Oman N, et al. Illicit opioid use following changes in opioids prescribed for chronic non-cancer pain. Fischer G, ed. *PLoS ONE*. 2020;15(5):e0232538. doi:10.1371/journal.pone.0232538
23. James JR, Scott JM, Klein JW, et al. Mortality After Discontinuation of Primary Care-Based Chronic Opioid Therapy for Pain: a Retrospective Cohort Study. *J Gen Intern Med*. 2019;34(12):2749-2755. doi:10.1007/s11606-019-05301-2

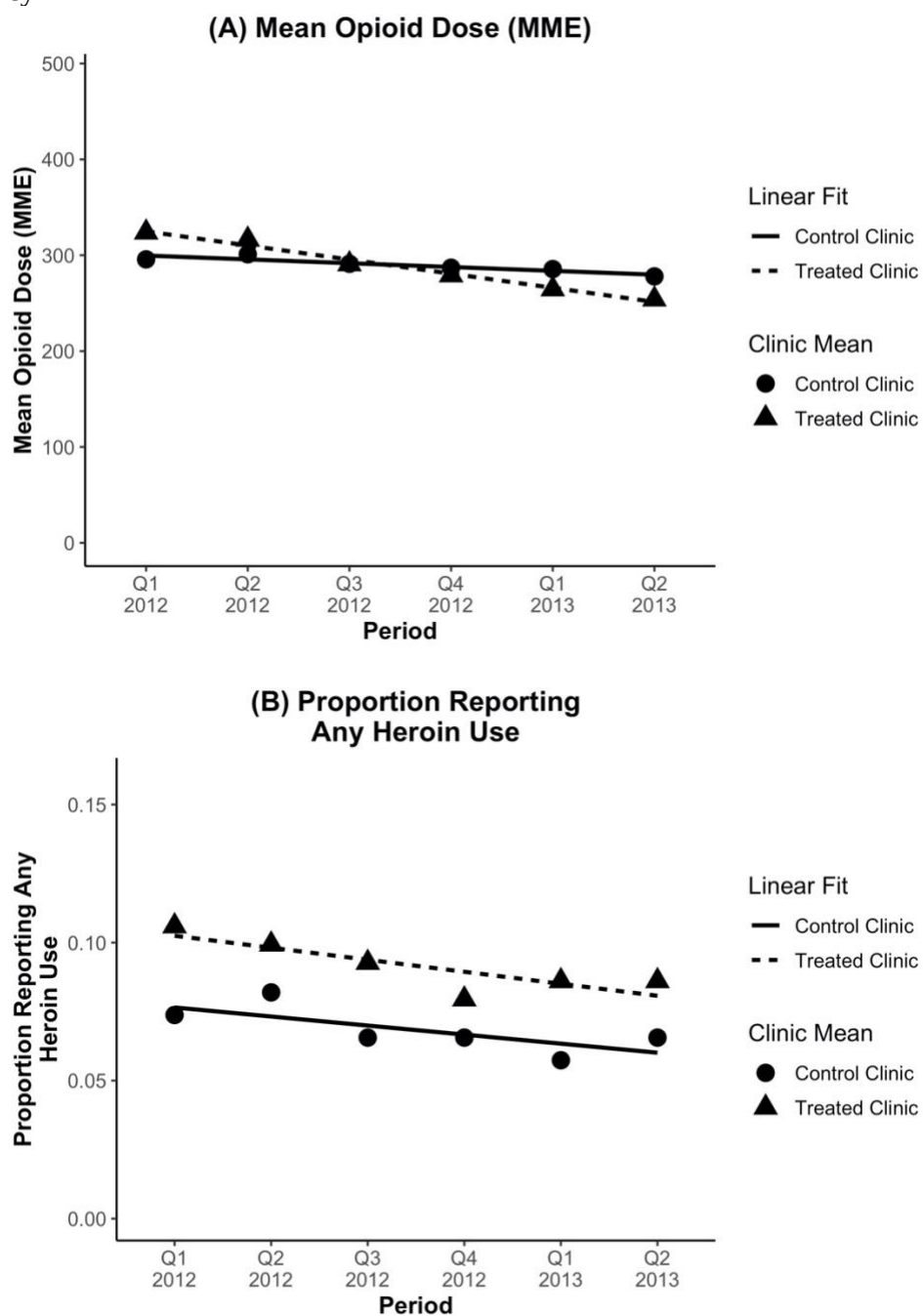
24. Oliva EM, Bowe T, Manhapra A, et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *BMJ*. 2020;368:m283. doi:10.1136/bmj.m283
25. Demidenko MI, Dobscha SK, Morasco BJ, Meath THA, Ilgen MA, Lovejoy TI. Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users. *Gen Hosp Psychiatry*. 2017;47:29-35. doi:10.1016/j.genhosppsych.2017.04.011
26. Davidson PJ, McLean RL, Kral AH, Gleghorn AA, Edlin BR, Moss AR. Fatal heroin-related overdose in San Francisco, 1997-2000: a case for targeted intervention. *J Urban Health*. 2003;80(2):261-273. doi:10.1093/jurban/jtg029
27. Visconti AJ, Santos G-M, Lemos NP, Burke C, Coffin PO. Opioid Overdose Deaths in the City and County of San Francisco: Prevalence, Distribution, and Disparities. *J Urban Health*. 2015;92(4):758-772. doi:10.1007/s11524-015-9967-y
28. Chang JS. Health in the Tenderloin: A resident-guided study of substance use, treatment, and housing. *Soc Sci Med*. 2017;176:166-174. doi:10.1016/j.socscimed.2017.01.014
29. Centers for Disease Control and Prevention. Calculating Total Daily Dose of Opioids for Safer Dosage. Published online August 28, 2019. Accessed May 12, 2020. https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf
30. Von Korff M, Korff MV, Saunders K, et al. De facto long-term opioid therapy for noncancer pain. *Clin J Pain*. 2008;24(6):521-527. doi:10.1097/AJP.0b013e318169d03b
31. Abadie A. Semiparametric Difference-in-Differences Estimators. *Review of Economic Studies*. 2005;72:1-19.
32. Daw JR, Hatfield LA. Matching and Regression to the Mean in Difference-in-Differences Analysis. *Health Serv Res*. 2018;53(6):4138-4156. doi:10.1111/1475-6773.12993
33. Westanmo A, Marshall P, Jones E, Burns K, Krebs EE. Opioid Dose Reduction in a VA Health Care System--Implementation of a Primary Care Population-Level Initiative. *Pain Med*. 2015;16(5):1019-1026. doi:10.1111/pme.12699
34. Lin LA, Bohnert ASB, Kerns RD, Clay MA, Ganoczy D, Ilgen MA. Impact of the Opioid Safety Initiative on opioid-related prescribing in veterans. *Pain*. 2017;158(5):833-839. doi:10.1097/j.pain.0000000000000837
35. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*. 2010;152(2):85-92. doi:10.7326/0003-4819-152-2-201001190-00006
36. Bohnert ASB, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305(13):1315-1321. doi:10.1001/jama.2011.370

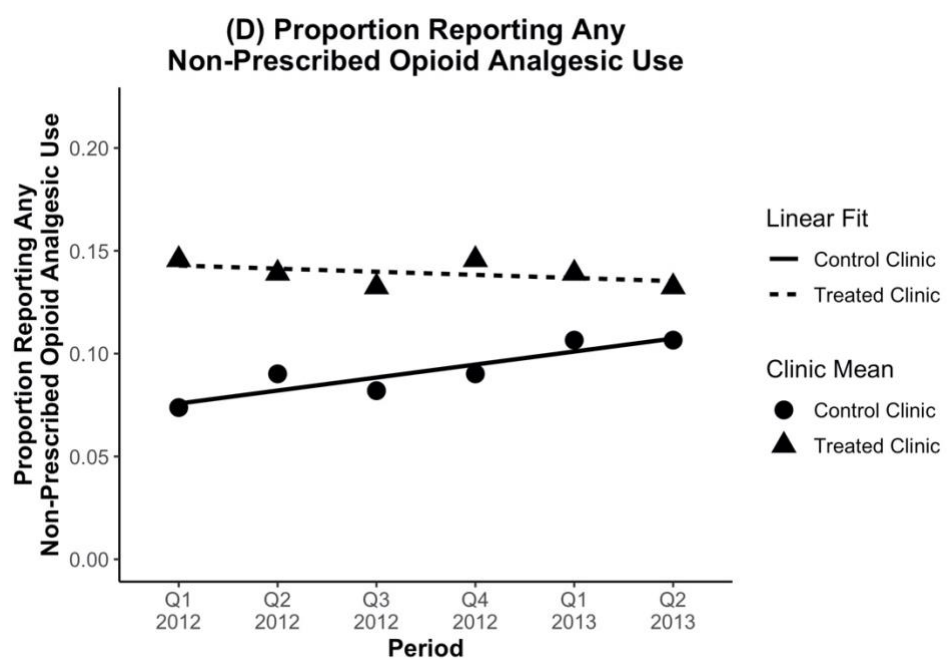
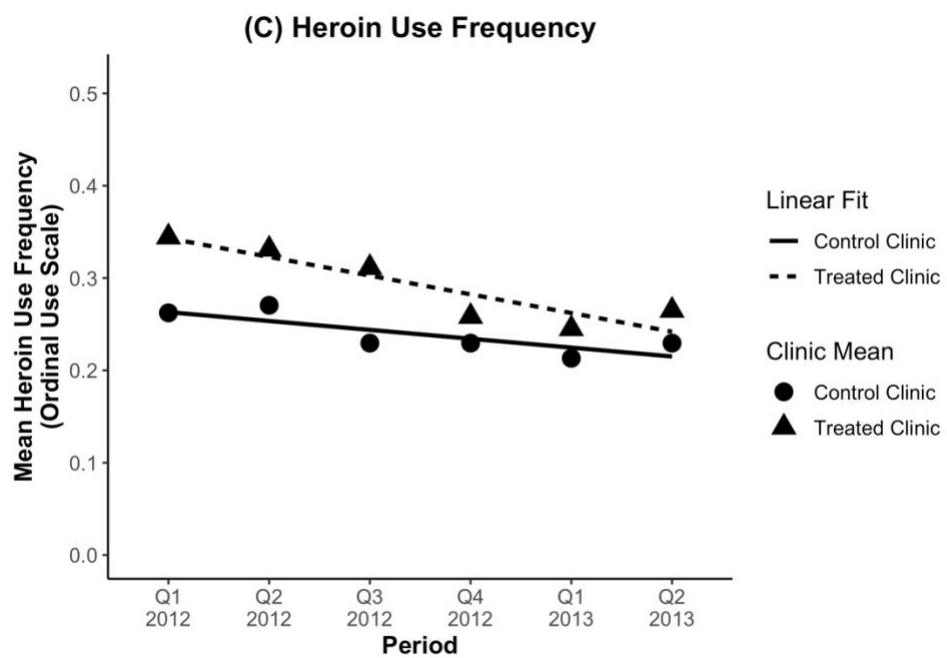
CHAPTER 3: OPIOID PRESCRIBING POLICIES

37. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*. 2011;171(7):686-691. doi:10.1001/archinternmed.2011.117
38. Centers for Disease Control and Prevention (CDC). Vital signs: overdoses of prescription opioid pain relievers---United States, 1999--2008. *MMWR Morb Mortal Wkly Rep*. 2011;60(43):1487-1492.
39. Okie S. A flood of opioids, a rising tide of deaths. *N Engl J Med*. 2010;363(21):1981-1985. doi:10.1056/NEJMp1011512
40. Medical Board of California. *Guidelines For Prescribing Controlled Substances For Pain*.; 2014.
41. Eagen K. *Personal Communication*.; 2020.
42. Chao MT, Hurstak E, Leonoudakis-Watts K, et al. Patient-Reported Outcomes of an Integrative Pain Management Program Implemented in a Primary Care Safety Net Clinic: a Quasi-experimental Study. *J GEN INTERN MED*. 2019;34(7):1105-1107. doi:10.1007/s11606-019-04868-0
43. Dowell D, Haegerich T, Chou R. No Shortcuts to Safer Opioid Prescribing. *N Engl J Med*. 2019;380(24):2285-2287. doi:10.1056/NEJMp1904190

3.6 FIGURES AND TABLES

Figure 1: Pre-policy outcome trends for (A) mean opioid dose (B) any heroin use, (C) heroin use frequency, (D) any non-prescribed opioid analgesic use, and (E) non-prescribed opioid analgesic use frequency





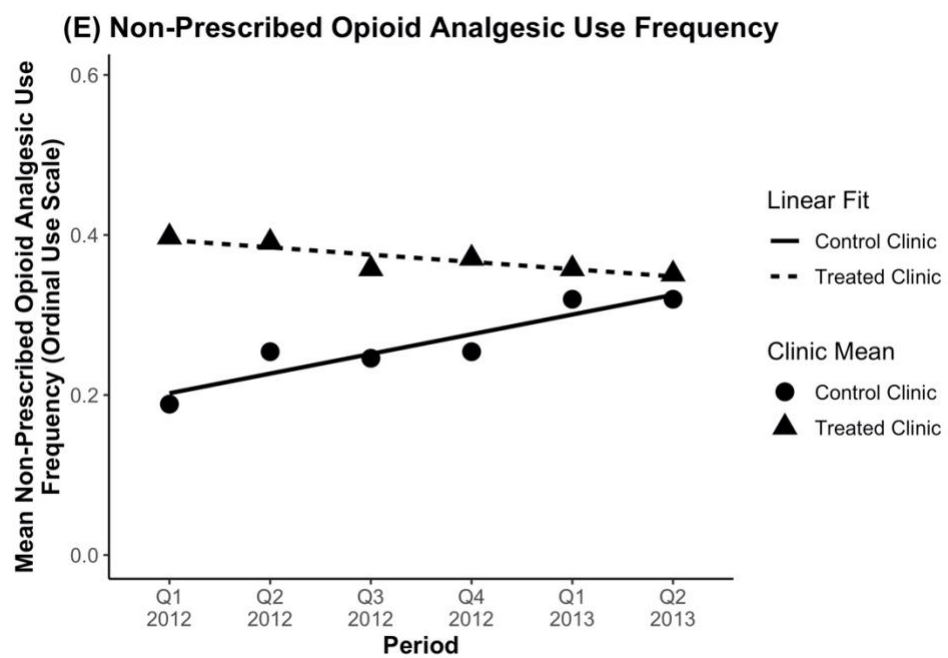


Figure 2: (A) Outcome trends by clinic and (B) conditional difference in differences estimates for the binary opioid prescription outcome

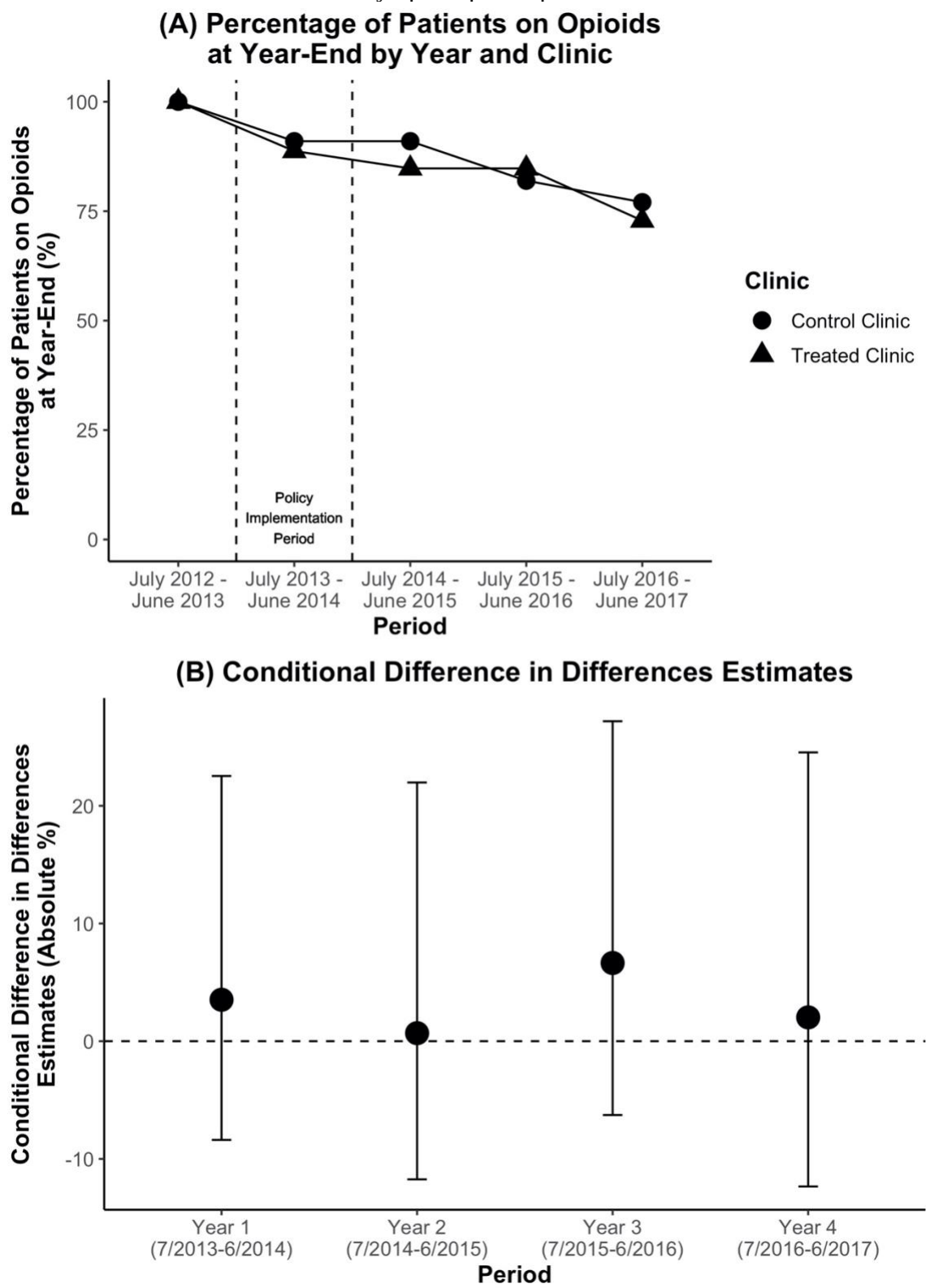


Figure 3: (A) Outcome trends by clinic and (B) conditional difference in differences estimates for the mean opioid dose outcome

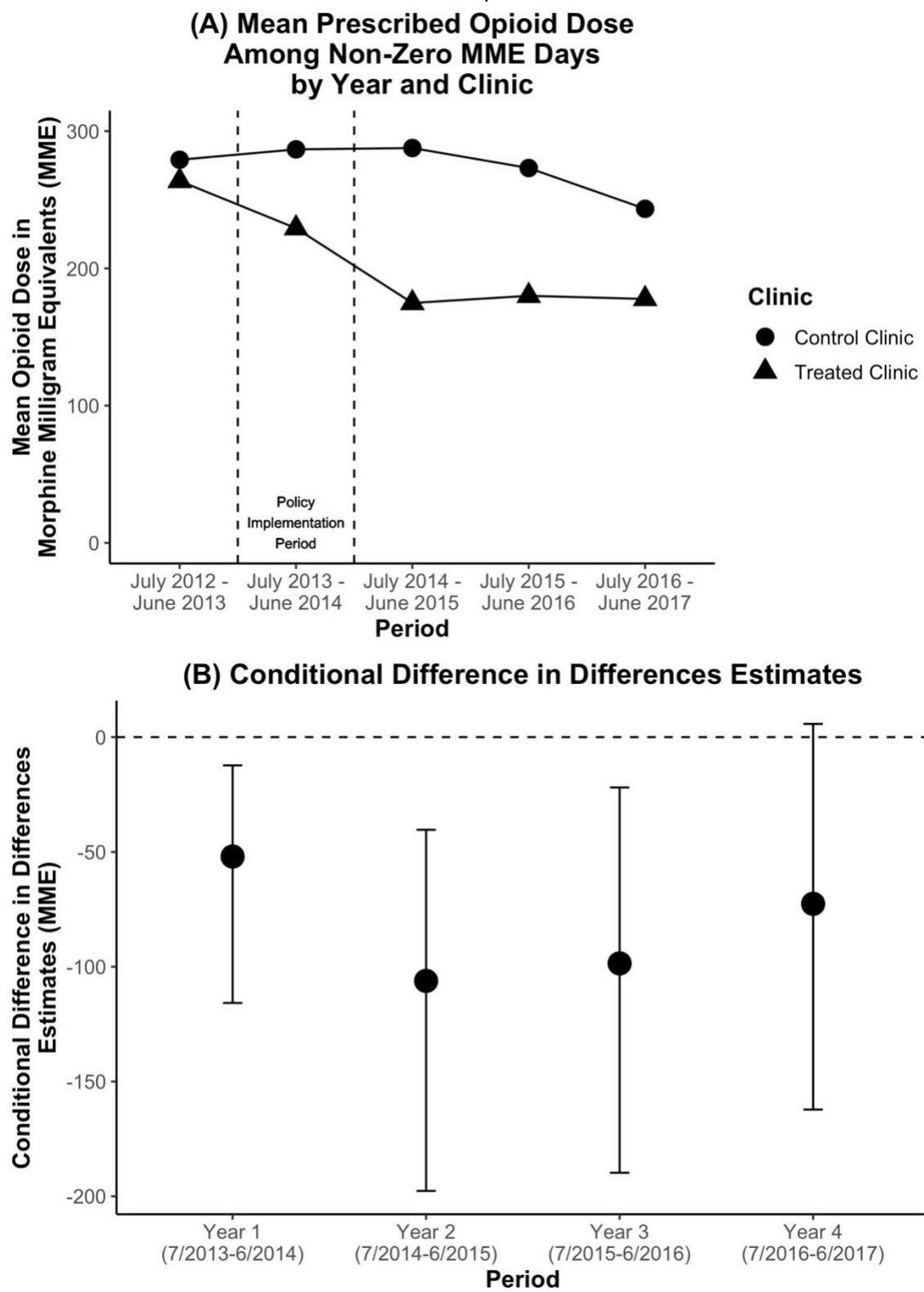


Figure 4: (A) Outcome trends by clinic and (B) conditional difference in differences estimates for the any heroin use outcome

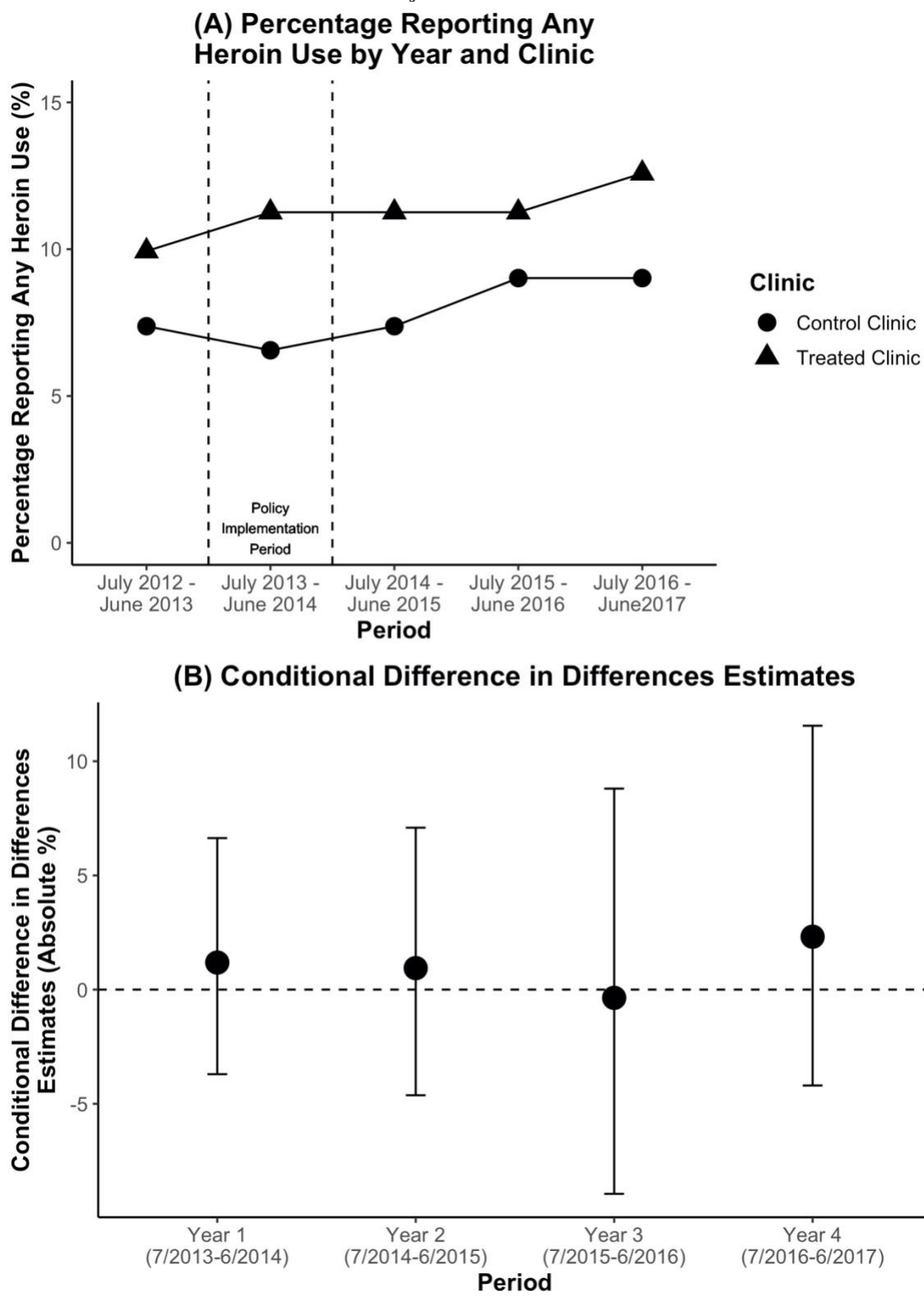


Figure 5: (A) Outcome trends by clinic and (B) conditional difference in differences estimates for heroin use frequency outcome

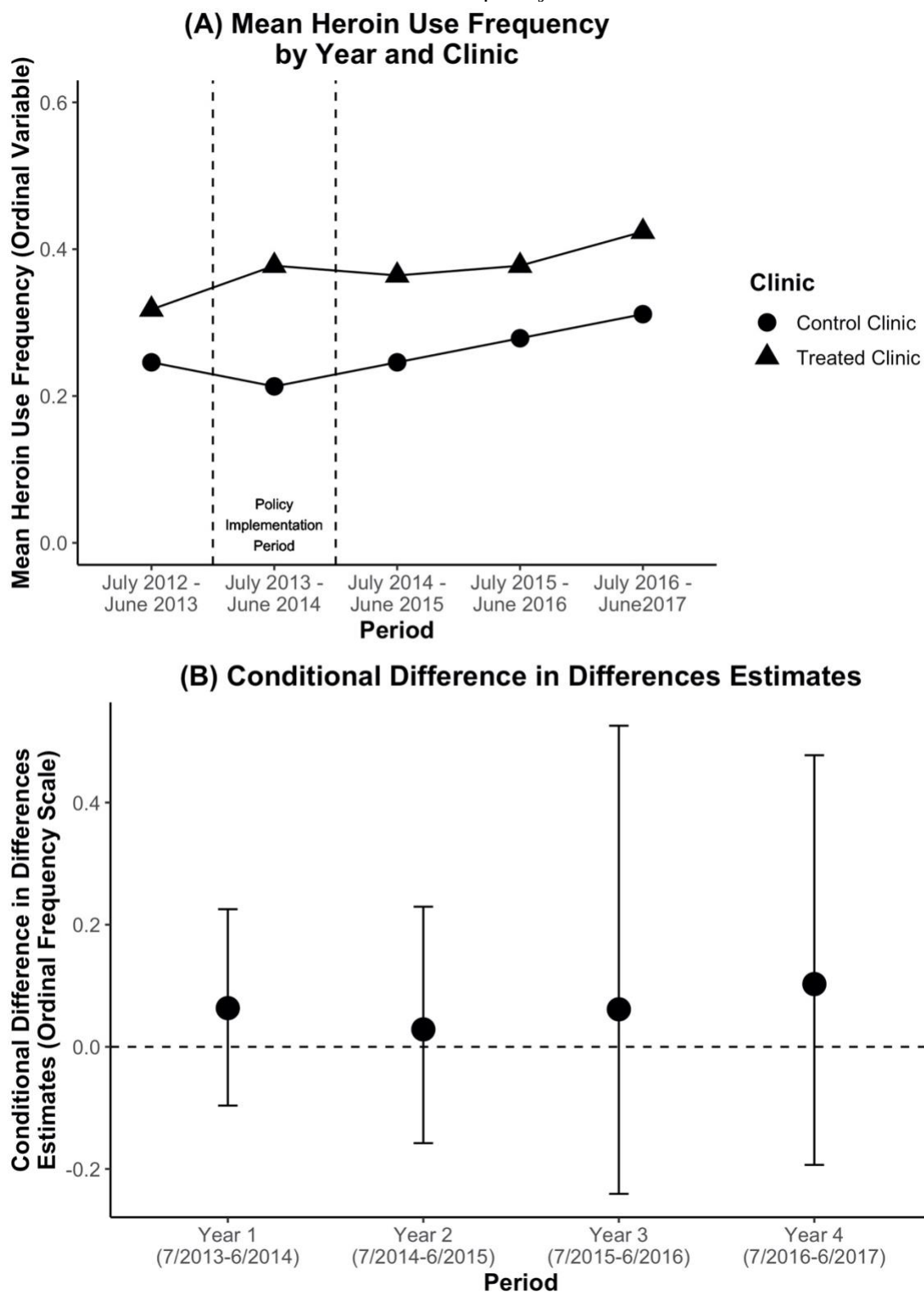


Figure 6: (A) Outcome trends by clinic and (B) conditional difference in differences estimates for the any non-prescribed opioid analgesic use outcome

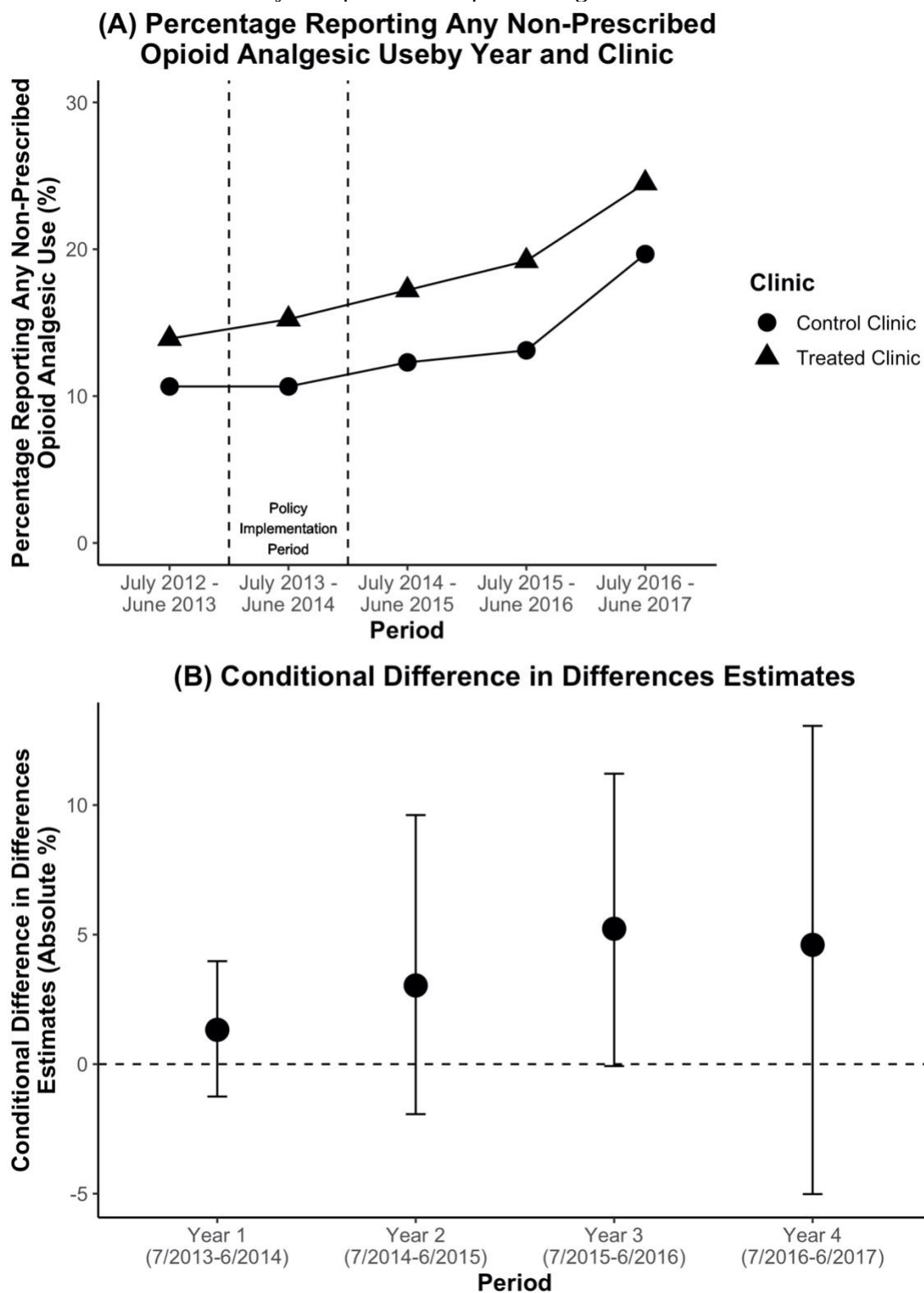


Figure 7: (A) Outcome trends by clinic and (B) conditional difference in differences estimates for the non-prescribed opioid analgesic use frequency outcome

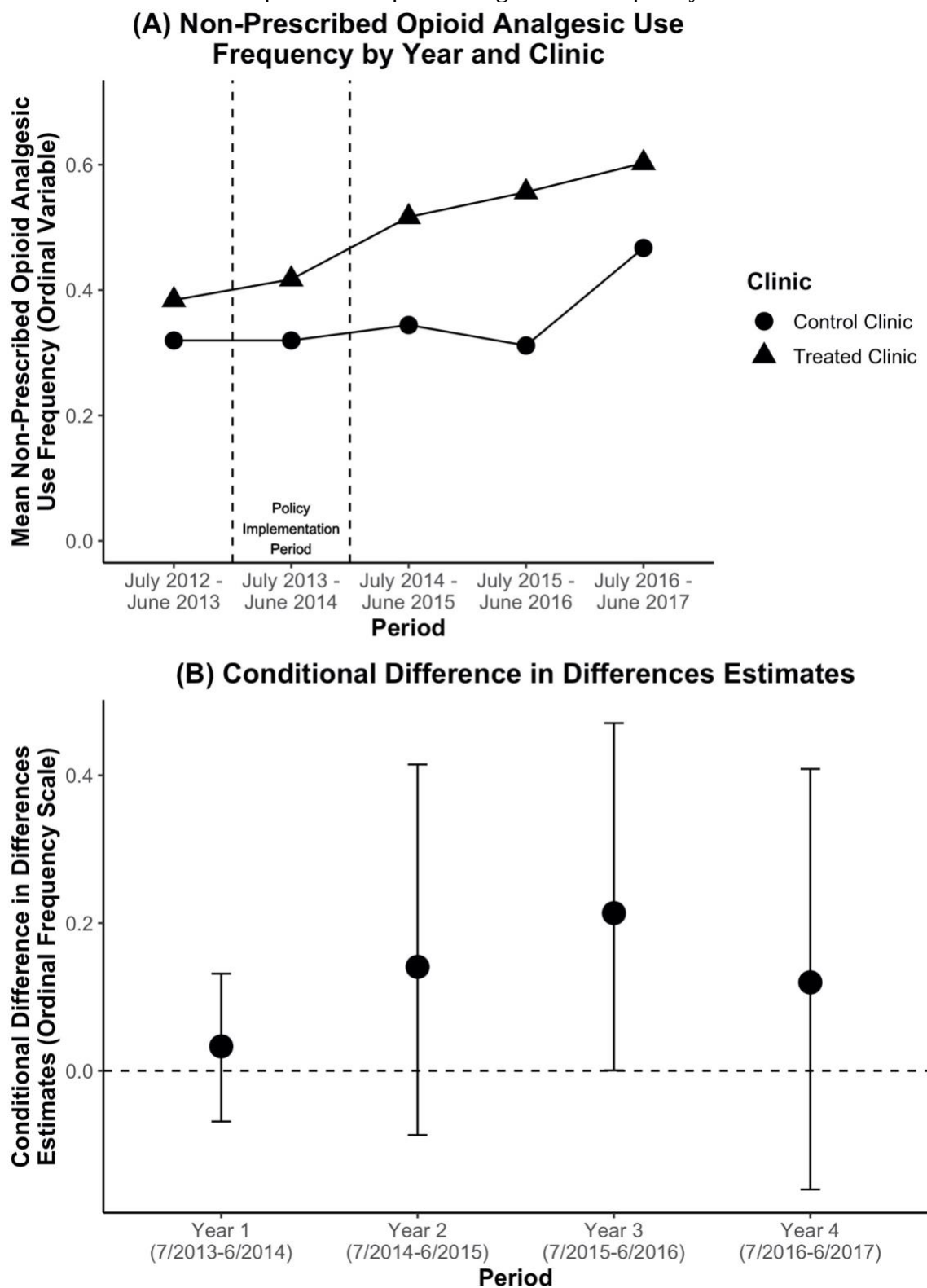


Table 1: Patient characteristics by clinic

	Entire Sample (n=273)		Treated Clinic (n=151)		Control Clinic (n=122)	
Patient Characteristics	n	(%)	n	(%)	n	(%)
Age, mean (SD)	51.4	(8.5)	52.5	(8.0)	49.9	(8.9)
Gender						
Male	175	(64.1)	86	(57.0)	89	(73.0)
Female	77	(28.2)	51	(33.8)	26	(21.3)
Transgender or other	21	(7.7)	14	(9.3)	7	(5.7)
Race						
Non-Hispanic white	95	(34.8)	58	(38.4)	37	(30.3)
Non-Hispanic black	99	(36.3)	56	(37.1)	43	(35.2)
Hispanic	38	(13.9)	13	(8.6)	25	(20.5)
Non-Hispanic other/mixed race	41	(15.0)	24	(15.9)	17	(13.9)
Education						
Less than high school	63	(23.1)	35	(23.2)	28	(23.0)
High school graduate	87	(31.9)	52	(34.4)	35	(28.7)
Some college, associate's degree, or vocational training	94	(34.4)	49	(32.5)	45	(36.9)
Bachelor's degree or higher	29	(10.6)	15	(9.9)	14	(11.5)
HIV positive	141	(51.6)	24	(15.9)	117	(95.9)
Mean pre-policy opioid dose (MME), mean (SD)	269.9	(549.0)	264.8	(490.9)	276	(615.5)
Any pre-policy heroin use	29	(10.6)	18	(11.9)	11	(9.0)
Any pre-policy non-prescribed opioid analgesic use	40	(14.7)	25	(16.6)	15	(12.3)
Any pre-policy alcohol use	155	(56.8)	83	(55.0)	72	(59.0)
Any pre-policy cocaine use	73	(26.7)	38	(25.2)	35	(28.7)
Any pre-policy methamphetamine use	47	(17.2)	29	(19.2)	18	(14.8)
Any pre-policy emergency department visits	103	(37.7)	60	(39.7)	43	(35.2)
Any pre-policy opioid-related emergency department visits	34	(12.5)	17	(11.3)	17	(13.9)
Any pre-policy pain agreements	40	(14.7)	30	(19.9)	10	(8.2)
Any pre-policy yellow flag behaviors	80	(29.3)	49	(32.5)	31	(25.4)
Any pre-policy CSMP checks	10	(3.7)	9	(6.0)	1	(0.8)

Table 2: Conditional difference in difference estimates for the association between opioid prescribing interventions and patient outcomes

Patient Outcome	Year 1		Year 2		Year 3		Year 4	
	Est.	(95% CI)	Est.	(95% CI)	Est.	(95% CI)	Est.	(95% CI)
Opioid prescription (absolute %)	3.5	(-8.4, 22.5)	0.7	(-11.7, 22.0)	6.6	(-6.3, 27.2)	2	(-12.3, 24.5)
Mean opioid dose (MME)	-52.0	(-109.9, -10.6)	-106.2	(-195.0, -34.6)	-98.6	(-198.7, -23.9)	-72.6	(-160.4, 3.6)
Heroin use								
Any use (absolute %)	1.2	(-3.7, 6.6)	0.9	(-4.6, 7.1)	-0.4	(-8.9, 8.8)	2.3	(-4.2, 11.6)
Frequency of use (ordinal use scale)	0.06	(-0.10, 0.23)	0.03	(-0.16, 0.23)	0.06	(-0.24, 0.53)	0.1	(-0.19, 0.48)
Non-prescribed opioid analgesic use								
Any use (Absolute %)	1.3	(-1.3, 4.0)	3.0	(-1.9, 9.6)	5.2	(-0.1, 11.2)	4.6	(-5.0, 13.1)
Frequency of use (ordinal use scale)	0.03	(-0.07, 0.13)	0.14	(-0.09, 0.41)	0.21	(0.00, 0.47)	0.12	(-0.16, 0.41)

Est. = Estimate

Table 3: Conditional difference in difference estimates for the association between opioid prescribing interventions and patient outcomes (pre-period outcome levels excluded from propensity score estimation)

Patient Outcome	Year 1		Year 2		Year 3		Year 4	
	Est.	(95% CI)	Est.	(95% CI)	Est.	(95% CI)	Est.	(95% CI)
Opioid prescription (absolute %)	2.4	(-8.9, 20.0)	-0.5	(-12.3, 19.6)	5.3	(-7.0, 24.0)	1.3	(-12.5, 22.5)
Mean opioid dose (MME)	-48.8	(-109.0, -5.0)	-102.3	(-191.6, -28.7)	-90.0	(-189.0, -5.6)	-58.7	(-156.7, 38.6)
Heroin use								
Any use (absolute %)	0.7	(-4.5, 5.0)	0.4	(-5.3, 5.7)	-1.5	(-10.0, 6.1)	1.4	(-4.9, 8.1)
Frequency of use (ordinal use scale)	0.05	(-0.12, 0.20)	0.01	(-0.18, 0.20)	0.01	(-0.27, 0.31)	0.06	(-0.24, 0.34)
Non-prescribed opioid analgesic use								
Any use (Absolute %)	1.3	(-1.3, 4.0)	2.8	(-2.1, 8.5)	5	(-0.4, 10.8)	4.4	(-5.1, 12.8)
Frequency of use (ordinal use scale)	0.03	(-0.07, 0.13)	0.13	(-0.10, 0.37)	0.2	(-0.01, 0.45)	0.11	(-0.16, 0.39)

Est. = Estimate

Chapter 4: Examining prisoner mortality following California's historic Public Safety Realignment Act

4.1 INTRODUCTION

The United States (US) has both the largest prison population, with over two million current prisoners, and the highest incarceration rate in the world.¹ Although the country has recently started shifting away from more punitive and towards more rehabilitative forms of criminal justice and recent legislation has successfully decreased incarceration rates,^{2,3} a substantial population remains incarcerated in prisons and jails in the US.

California has the nation's second largest prison population. Following substantial population growth in the 1980's and 1990's, California's prisons were characterized by extreme overcrowding during the 2000's. Although California's prisons were not unique in this regard, the circumstances surrounding its efforts to resolve the problem of overcrowding were. Two class action lawsuits filed on behalf of California state prisoners alleged that inadequate mental (*Coleman v. Brown*, filed 1990) and physical (*Brown v. Plata*, filed 2001) healthcare stemming from overcrowded conditions violated prisoners' constitutional rights. In connection with *Brown v. Plata*, federal courts established a receivership with full authority over the state's prison healthcare system in 2006. Components of both lawsuits were ultimately consolidated before a single three-judge court, which in 2009 declared overcrowding to be the primary reason for healthcare deficiencies and mandated the state to reduce its prison population by nearly 50,000 individuals, corresponding to approximately a 30% reduction. This order was upheld by the U.S. Supreme Court in 2011 and California was required to meet the mandated reduction target within three years of the ruling.⁴ To comply with the court's decision, California passed the Public Safety Realignment Act (Assembly Bill [AB] 109) in October 2011.

AB109 sought to decrease the prison population by prospectively shifting the custodial responsibility of non-violent, non-serious, and non-sexual offenders from state prisons to county jails and probation departments, which was motivated by the idea that local agencies could do a better job of rehabilitating offenders.^{5,6} In addition, by limiting the funds provided to counties for these additional inmates, the policy incentivized more cost-effective alternatives to incarceration, such as the use of day reporting centers, shorter post-release community supervision, intensive probation, and home detention with GPS monitoring, with the aim of lowering the overall rate of incarceration across both prisons and jails.^{5,6}

Empirical studies and policy analyses have examined the effects of AB109 on a variety of outcomes, including state prison and county jail populations,⁷⁻¹⁰ recidivism,^{7,11-16} corrections spending,⁷ and crime.^{7,8,17-19} Research suggests that AB109 significantly reduced the state prison population and extent of overcrowding, though not enough to reach the court-mandated target, while increasing the county jail population.^{7-9,11} The increase in the county jail population was

smaller than the decrease in the state prison population, resulting in a lower rate of incarceration overall. However, one study found that AB109 may have exacerbated racial, ethnic, and gender disparities in incarceration in California's prison system.¹⁰ AB109 appears to have led to modest increases in recidivism statewide, but increases were smaller for counties that prioritized reentry programs.^{7,11–15} As of 2015, the policy appears to have had no effect on rates of violent crime, but may have increased rates of property crime, particularly auto theft.^{7,8,17–19}

Despite the fact that AB109 was precipitated by inadequate healthcare in California prisons, no independent studies have examined its effect on the health of prisoners. However, monthly reports tracking a wide variety of healthcare performance indicators did document improvements following the implementation of AB109.^{20,21} Indeed, in 2013, Governor Jerry Brown of California declared that prison overcrowding no longer inhibited the delivery of timely and effective healthcare to prisoners.

AB109 was implemented amidst an evolving prison healthcare system in California, including documented improvements under the federal receivership and the opening of a new medical complex that was constructed in 2013 in response to decisions in both the *Plata* and *Coleman* cases.²⁰ As such, it is not possible to isolate the effects of AB109 from those due to other concurrent changes prompted by these lawsuits. However, given that overcrowding was identified as the primary reason for California's inadequate prison healthcare,⁴ it is plausible that any changes in health outcomes over this period are at least partially attributable to the de-crowding effects of AB109. Furthermore, the changes initiated by AB109 were unprecedented in state-level criminal justice reform, representing the largest ever court-ordered reduction of a prison population in the U.S. Indeed, AB109 has been characterized as “the biggest criminal justice experiment ever conducted in America”.²² At the end of 2018, 25 states exceeded at least one measure of prisoner capacity.²³ As these states continue to grapple with overcrowded prisons and look to California's experience with AB109, it is critical that we understand how the policy may have impacted all relevant outcomes, including prisoner health.

Leveraging several complementary data sources, we aimed to evaluate the effects of AB109 on California state prisoner mortality. By shifting the custodial responsibility of low-level offenders to county jails, AB109 impacted both the number and composition of prisoners in California state prisons. Because of these dynamics, we also sought to assess the extent to which effects of AB109 on prisoner mortality might be attributable to contemporaneous changes in the age distribution of prisoners.

4.2 METHODS

Overview

To evaluate the effects of AB109 on California state prisoner mortality and assess the extent to which changes in the age distribution may have contributed to these effects, we conducted four complementary analyses. First, we evaluated the effects of AB109 on crude mortality (i.e., not accounting for temporal changes in age distribution) using the synthetic control method. Second, we examined how the age distribution of California state prisoners changed following AB109 and compared these changes to those occurring in other states over the same timeframe. Third, we compared trends in crude and age-standardized mortality among California state prisoners before and after AB109. Lastly, we compared pre- to post-AB109 changes in mortality among California

state prisoners to those occurring in other states while accounting for differential changes in prisoner age distributions between states.

Data Sources

To comprehensively answer our research question, we would ideally leverage data on the universe of state prisoners in the US, including their ages and dates of incarceration, as well as if and when they died in prison. However, such comprehensive data were not obtainable. Instead, we leveraged three complementary data sources that were either publicly available or practically obtainable in order to conduct the four analyses outlined above.

First, we obtained the annual counts of deaths and crude mortality rates among state prisoners for all 50 states for years 2001-2015 from publicly available reports published by the Bureau of Justice Statistics (BJS).^{24,25}

Next, we obtained individual-level state prison inmate term records for California and several other states for years 2000-2015, including month and year of birth and prison term dates, from the National Corrections Reporting Program (NCRP).²⁶ Annually, the NCRP collects offender-level administrative data on prison admissions and releases and year-end custody populations from participating jurisdictions. The number of states submitting data to NCRP has varied over time, with at least 38 states providing some amount of data since 2000. These data were available from the Inter-university Consortium for Political and Social Research under restricted conditions.

Lastly, we obtained de-identified individual-level data for all deaths among California state prisoners, including age of the decedent and date of death, from the California Deaths in Custody (DIC) reporting program.²⁷ The DIC Data includes all deaths that occur in law enforcement custody. To capture deaths among California state prisoners, we retained only deaths for which the California Department of Corrections and Rehabilitation had custody of the subject immediately preceding death. We excluded decedents held in out-of-state correctional facilities, those who died by execution, and those released on medical parole. These data were publicly available through California Department of Justice's Open Justice program.²⁸

Collectively, these data sources provide or allow us to calculate crude annual mortality rates for California and control states (BJS Data), annual total mortality counts for California and control states (BJS Data), annual age-specific prisoner person-time for California and control states (NCRP Data), and annual age-specific mortality counts for California only (DIC Data). Table 1 provides an overview as to which components of these data sources were used in each of our four analyses.

Crude Mortality

To evaluate the effect of AB109 on crude mortality, we used the synthetic control method with the annual crude mortality rates from the BJS as the outcome variable.^{29,30} Specifically, we considered California as the single treated unit, and included other states in the donor pool from which to construct the synthetic control. The synthetic control approach uses pre-policy covariates and outcome data to identify a weighted combination of control units whose weighted pre-policy covariates and outcomes best fit those of the treated unit. For our analysis, the pre-policy period included years 2001-2010 and the post-policy period included years 2012-2014. The year 2011

was excluded because AB109 was implemented in October 2011. Years after 2014 were excluded because California implemented Proposition 47, another major criminal justice law that reduced penalties for many low-level crimes, in November 2014. The effect of AB109 on prisoner mortality is estimated by comparing the observed California state prisoner mortality rate to that of the synthetic control unit in the post-policy period.

In our implementation, we included all annual values of the pre-policy prison mortality rates and no other covariates in the construction of the synthetic control unit. We considered several covariates but obtained a substantially improved pre-policy fit in terms of mean squared prediction error (MSPE) when including only pre-policy outcomes. Specifically, we considered the following state-level covariates: age-adjusted all-cause mortality rate among the general population, incarceration rate, proportion of male prisoners, proportion of prisoners over 55, and prison population as a percentage of the lowest reported measure of prison facility capacity. General population mortality rates were obtained from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database;³¹ incarceration rates, proportions of male prisoners, and capacity measures were obtained from annual BJS Prisoners Series reports;³² and the proportions of prisoners over 55 were obtained from NCRP data that was processed and published by the Prison Policy Initiative.³³ Each prison-related measure referred to the prison population at year end. We attribute the better fit of the outcome-only model to the limited predictive power (with regard to the outcome) of the small number of covariates that were available.

The synthetic control approach precludes traditional approaches to statistical inference; however, it is standard to conduct inference using a permutation test to compare the estimated treatment effect for the state that implemented the policy under study to estimates for states where the policy was not implemented.^{29,30} Specifically, we applied the synthetic control estimator to every state in the control donor pool for the same time period assessed for the main analysis and compared the estimated treatment effect to these placebo effects in two ways: (1) comparing the post-policy MSPE (i.e., the sum of squared differences between the observed and synthetic mortality rates over the post-policy years) for California's synthetic control to those of each of the control states, while restricting to subsets of states with good pre-policy fits (i.e., within 5x and 2x of the pre-policy MSPE for California's synthetic control); and (2) comparing the ratio of the post- to pre-policy MSPE for California's synthetic control to those of each of the control states. This latter measure precludes choosing an arbitrary cutoff for excluding control states with poor pre-policy fits by standardizing post-policy effect sizes by the quality of the pre-policy fit. The permutation test provides a distribution of placebo effects for each of these measures to which we can compare the values for California. We generated plots to visualize the results and calculated the proportion of control states that had post-policy MSPEs and ratios of post- to pre-policy MSPEs that were less extreme than those of California. Each of these inferential approaches have been described in greater detail elsewhere.^{29,30}

We also conducted two separate robustness checks. First, we conducted an "in-time" placebo test, in which we applied the synthetic control method to California but considered 2001-2006 as the pre-policy period, 2007 as the excluded implementation year, and 2008-2010 as the post-policy period and also conducted a permutation test as described above. These years were selected because they allowed for the greatest number of pre-policy years while maintaining three post-

policy years that occurred prior to the actual implementation of AB109. Because AB109 was not implemented until 2011, we should expect the mortality rates of the synthetic control unit to mirror those observed in California from 2008-2010. Second, for each control state that contributed to the synthetic control unit in the main analysis, we constructed a new synthetic control for California while excluding that state from the donor pool. We then compare the outcome trajectories of these leave-one-out synthetic control units to those of the original synthetic control unit that included the entire donor pool. These comparisons assess the robustness of our main estimates to the exclusion of any single state.

Changes in prisoner age distributions

In order to investigate the extent to which the effects of AB109 on crude mortality may be attributable to changes in California's prisoner age distribution, we first sought to assess how the age distribution of California state prisoners changed following AB109 relative to other states over the same timeframe. If California experienced a change in age-distribution following AB109 that was extreme relative to concurrent changes in other states, this would support the plausibility that effects of AB109 on mortality could be attributable to a shift in the California's prisoner age-distribution. To do this, we calculated the proportion of prisoner person-time corresponding to specific age groups (under 26, 26-35, 36-45, 46-55, 56-65, 66-75, over 75) for 2010 and each year 2012-2014 for California and each control state. Prisoner person-time was derived from the NCRP individual-level term records. Specifically, for each state and year, this involved summing up the incarcerated person-time among prisoners falling within each age group and dividing by the total incarcerated person-time to obtain proportions. We then calculated the relative change in each age group proportion from 2010 to each of the three post-policy years for each state.

Comparing crude and age-standardized mortality among California state prisoners

Next, we sought to investigate differences between the trend in crude California state prisoner mortality and the trend in California state prisoner mortality that accounts for changes in the age-distribution of prisoners over time and, particularly, following AB109. To do so, we compared the annual crude mortality rates among California state prisoners from 2008-2014 to annual age-standardized mortality rates over the same period, both calculated with death counts from the DIC data and person-time measures from the individual-level NCRP data. To calculate the annual age-standardized mortality rates, California's annual age-specific mortality rates for each year from 2008-2014 were applied to the California state prisoner age-distribution from 2008, which preceded the implementation of AB109. This procedure is known as direct standardization. The age-standardized mortality rates for each year were thus calculated as:

$$\lambda_{CA,j}^{AS} = \frac{\sum_{k=1}^K \lambda_{CA,j,k} pt_{CA,2008,k}}{\sum_{k=1}^K pt_{CA,2008,k}} \text{ for years } j = 2008, 2009, \dots, 2014$$

Where $\lambda_{CA,j}^{AS}$ is the California age-standardized rate for year j ; $\lambda_{CA,j,k}$ is the California mortality rate for year j and age group k ; and $pt_{CA,2008,k}$ is the California incarcerated person-time for 2008 and age group k . The age-standardized mortality trend illustrates how crude mortality would have changed if the California state prisoner age-distribution were static from 2008 to 2014. We were only able to standardize California's age-specific prisoner mortality rates in this way because we had access to annual age-specific mortality rates for California but not for any control states.

Comparing age-standardized mortality between California and other states

Lastly, we sought to evaluate the effects of AB109 on mortality net of any effect due to resultant changes in the age distribution of California state prisoners and any secular trends approximated by the experience of other states. To do so, we compared California's change in state prisoner mortality from pre- to post-policy years to that experienced by other states, while controlling for differential changes in age distribution between California and other states over the same period. Standard approaches to adjust for differential changes in age distribution between California and other states would require that annual age specific mortality rates among California and other states be compared directly or standardized to and summed over the same age distribution, such as California's age distribution in a given year (i.e., direct standardization). However, as previously noted, the data available for this analysis precluded the ability to calculate age-specific rates for any state but California. We did, however, have access to the annual age-specific person-time from the NCRP data and the total number of deaths from the BJS data for control states.

To compare mortality trends between California and other states while accounting for differential changes in age distribution, this combination of data is amenable to an extension of the method of indirect age standardization, in which a set of "standard" age-specific mortality rates are standardized to and summed over a target age distribution to obtain the total number or rate of deaths expected in the target population had it experienced the "standard" age-specific mortality rates. We calculated a single measure for each control state and post-policy year that captured the excess (or deficit) change in mortality that would have occurred in the control state had it experienced California's age-group specific mortality rates in the pre- and relevant post-policy year. Specifically, we used California's annual age-specific mortality rates as the "standard" set of rates, which we standardized to and summed over the age distribution of each control state for each corresponding year. Thus, for each control state, we obtained four quantities that corresponded to the crude mortality rate expected in each control state had it experienced California's age-group specific mortality rates in 2010 and each year 2012-2014. Then, for each control state and post-policy year, we calculated the difference between the change in the expected crude mortality rate from 2010 to a post-policy year and the change in the control state's observed crude mortality rate over the same period. Thus, the age-adjusted excess mortality was calculated as:

$$EM_{i,j} = \left(\frac{\sum_{k=1}^K \lambda_{CA,j,k} pt_{i,j,k}}{\sum_{k=1}^K pt_{i,j,k}} - \frac{\sum_{k=1}^K \lambda_{CA,2010,k} pt_{i,2010,k}}{\sum_{k=1}^K pt_{i,2010,k}} \right) - (CR_{i,j} - CR_{i,2010})$$

for comparison states $i = 1, \dots, n$ and years $j = 2012, 2013, 2014$

Where $EM_{i,j}$ is the age-adjusted excess mortality for control state i and post-policy year j ; $\lambda_{CA,j,k}$ is the mortality rate for California in post-policy year j for age group k ; $pt_{i,j,k}$ is the incarcerated person-time for control state i , post-policy year j , and age group k ; and $CR_{i,j}$ is the crude mortality rate for control state i and post-policy year j . A positive value for this quantity suggests that the change in the crude mortality rate associated with California's pre- and post-policy age-specific mortality rates was greater than the change associated with the control state's pre- and post-policy age-specific mortality rates, a negative value suggests the opposite, and a value of zero suggests that there was no difference between the two. This quantity can also be framed as a difference-in-differences estimate, for which California's age-specific mortality rates applied to a control state's

age distribution represent the treated unit and the control states observed mortality rates represent the control unit.

For each post-policy year, we present the age-adjusted excess mortality rate estimates for each control state, the median value, and exact confidence intervals. Exact confidence intervals were obtained for the closest confidence levels above and below the 95% level via inversion of the one-sample sign test. The sign test is a non-parametric statistical test that makes no distributional assumptions about the underlying data distribution other than that data are drawn independently from a continuous distribution.

We also conducted a placebo test using 2008 as the pre-policy year and 2010 as the post-policy year and present the median and exact confidence intervals as described above. These years were selected so as to skip a single “implementation” year as in the main analysis and because 2010 is the last year prior to the actual implementation of AB109.

Control States

For both the crude and age adjusted mortality analyses, we excluded several control states. Specifically, we excluded states that had 10 or fewer deaths during any year under study. The BJS considers 10 or fewer deaths an insufficient number to provide a reliable rate.^{24,25} Florida was excluded because the state privatized its prison healthcare system in 2011, which an independent audit found to correspond with decreased quality of care.³⁴ Alaska, Connecticut, Delaware, Hawaii, Rhode Island, and Vermont were excluded because prisons and jails form one integrated system in these states and mortality data were only available among the combined prison and jail populations.^{24,25}

For the age-adjusted analysis, we excluded additional states for which the person time measures calculated using the NCRP data were determined not to be sufficiently accurate. Through the National Prisoner Statistics (NPS) Program, the BJS collects and reports the year-end custody population for each state prison system (i.e., the number of prisoners in physical custody on December 31 of each year).^{35,36} We used the individual-level term records from the NCRP to calculate the year-end custody population for each state and year for 2007-2014. We excluded states for which the year-end custody population calculated using NCRP data differed by more than 10% from the number reported by BJS during any year. A 10% accuracy threshold between NCRP and NPS data has been used in prior analyses using NCRP data.^{37,38}

The inclusion status and reasons for exclusion for all 50 states for both the crude and age-adjusted mortality analyses are presented in Table 2.

Because we do not have access to age-specific mortality rates for any control states, we cannot examine whether there were systematic differences in these rates between the states that were included and excluded from the age-adjusted analysis. However, we investigated whether the changes in crude mortality rates from 2010 to each post policy year from the BJS data are different by inclusion status for the age-adjusted analysis. Specifically, we assess whether the changes in each group (included vs. excluded) are likely to arise from the same underlying distribution using Kolmogorov-Smirnov tests for each post policy year. For this assessment, we only consider states that were included in the crude mortality analysis.

Sensitivity Analysis for Differences in Mortality Reporting

As previously described, our comparison of changes in age-adjusted mortality rates between California and other states leveraged multiple complementary datasets. There were small differences between the annual number of deaths among California state prisoners in the DIC and BJS data, with DIC data consistently reporting fewer deaths than the BJS data (Table 3). For the main age-adjusted analysis, we used the deaths present in the DIC data. To account for the possibility that DIC data are not comprehensive and that the BJS data represent the truth, we conducted a sensitivity analysis in which we added deaths to the DIC data such that the annual number of deaths matched the number in the BJS data for 2010 and each post-policy year 2012-2014. Over 1000 iterations, we randomly assigned the added deaths to different age groups (with equal probability), calculated the age-adjusted excess mortality rate estimates for each state and post-policy year, and calculated the median value for each post policy year. We then present the 2.5% and 97.5% quantiles of the distributions of the median values for each post-policy year.

Bias Analyses for Concurrent Policy Changes

Two sources of potential bias in estimating the effects of AB109 on California state prisoner mortality are the nearly concurrent introduction of the medical parole program and the subsequent introduction of the elderly parole program in the California state prison system. The medical parole program began in January 2011, granted its first parole in June 2011, and was expanded in July 2014. This program initiated a parole hearing process that allowed grantees who are permanently medically incapacitated and who require 24-hour care to be placed in a licensed healthcare facility in the community. The elderly parole program began in October 2014 and initiated a parole hearing process by which prisoners over 60 years old who have served at least 25 years of continuous incarceration could be assessed for parole. An elderly parole hearing differs from a standard parole hearing in that the panel gives special attention to the prisoner's age, physical condition, and long-term confinement when determining a prisoner's suitability for parole.

These two programs may have implications for our analysis because they were introduced after the end of the pre-policy period and could have impacted the mortality rate among California state prisoners if those granted parole through the programs were at systematically higher or lower risk of death than those who remained incarcerated. If this were the case, any changes in mortality in the post-policy period could be at least partially due to the initiation of these parole programs.

We sought to assess the impact of these parole programs on the results of our comparison of age-adjusted mortality rates between California and other states. It seems reasonable to assume that medical parolees would be at greater risk of death than other age-comparable prisoners, and thus their release from custody may have resulted in a reduction in age-specific prisoner mortality rates. However, two points are worth noting. First, medical parole differs from compassionate release, which involves a recall of sentence for California state prisoners who are terminally ill and are estimated to have less than six months to live. Although medical parolees are permanently medically incapacitated, they are not necessarily terminally ill. Second, there were never more than seven medical parole deaths during any post-policy year (Table 4), which represent a small fraction of the annual number of deaths among California state prisoners. Regarding the elderly parole program, we have no specific reason to expect elderly parolees to be more or less at risk of death than age-comparable prisoners who remained incarcerated.

To assess the sensitivity of our age-standardized analysis results to the introduction of the medical parole program, we calculated age-standardized excess mortality rates as described above but included deaths among California medical parolees and person time attributed among these deceased medical parolees in the calculation of the age-specific annual California mortality rates. Deaths among medical parolees were present in the DIC data and were excluded from our main analysis. In addition, we re-ran the sensitivity analysis described above to correct for differences in death counts between DIC and BJS data, but for each iteration we added medical parolee deaths after updating the annual DIC death counts to match those reported by BJS.

Because the medical parole program began after the end of the pre-policy period, including deaths among California medical parolees had no effect on the synthetic control fit for our crude mortality analysis. Their inclusion increased California's observed mortality rate by <2% for each post-policy year and thus we do not present this sensitivity analysis for crude mortality.

To explore the potential impact of the elderly parole program on the California prison mortality rate, we compared the trend in the mortality rate among California state prisoners aged 60 and older before and after the start of the elderly parole program to the trend in rate among prisoners younger than 60. Specifically, we calculated mortality rates separately among prisoners above and below age 60 for each calendar quarter in 2013 and 2014. Because the variance of quarterly mortality rates among prisoners aged 60 and older were substantially larger than those among prisoners under 60 (60 and older variance = 100,463; under 60 variance = 530), we calculated the change in quarterly mortality rate since the rate in the first quarter (Q1) of 2013 standardized by the standard deviation of quarterly rates in 2013-2014 for each group. If the beginning of the elderly parole program led to a meaningful change in the mortality rate among prisoners aged 60 and older, we might expect to observe a standardized change in the mortality rate among this group in Q4 2014 that is not evident among prisoners under 60.

4.3 RESULTS

Crude Mortality

The composition of the synthetic California is presented in Table 5, the crude mortality rates for California and the synthetic California are presented in Figure 1, and the difference between the rates are presented in Figure 2. Mortality among California state prisoners increased after the implementation of AB109 relative to those of the synthetic California, but the two rates converged by 2014. These estimates suggest that, without accounting for age distribution changes, the mortality rate among California state prisoners was higher in 2012 and 2013 than would have been expected in the absence of AB109.

Permutation test plots of the differences between each control state's mortality rate and that of their corresponding synthetic control are presented for all control states (Figure 3) and those within 5x (Figure 4) and 2x (Figure 5) of California's pre-policy MSPE. Nine (31.0%) of all 29 control states, five (26.3%) of 19 states within 5x of California's pre-policy MSPE, and zero (0.0%) of 7 states within 2x of California's pre-policy MSPE had a post-policy MSPE greater than that of California. The plot of the ratios of post- to pre- policy MSPE for California and all control states is presented in Figure 6. Three (10.3%) of 29 control states had ratios of post- to pre-policy MSPE greater than that of California.

A sizeable proportion of control states had greater post-policy MSPE values than California, yet few of these states had particularly good pre-policy fits. When restricting to seven states with good pre-policy fits, California's estimated effect was more extreme than those of all placebo states. Similarly, California's ratio of post- to pre-policy MSPE, which standardizes effect size by the quality of the pre-policy fit, exceeded those of 90% of placebo states. Thus, when accounting for pre-policy fit, the estimated effect of AB109 on mortality is relatively large compared to the distribution of placebo effects. These results provide modest, but not conclusive, evidence that the estimated effect in Figure 1 is due to AB109.

For the "in-time" placebo test treating 2007 as the policy implementation year, the crude mortality rates for California and the synthetic control and the difference between California's annual mortality rate and those for the synthetic California are presented in Figures 7-8. Mortality rates were very similar between California and the synthetic California from 2008 to 2010.

The corresponding plots of the gaps between each control state's mortality rate and that of their corresponding synthetic control are presented for all control states (Figure 9) and those within 5x (Figure 10) and 2x (Figure 11) of California's pre-policy MSPE. Twenty-two (78.6%) of 28 control states (a solution did not converge for one state), 16 (76.2%) of 21 states within 5x of California's pre-policy MSPE, and 10 (76.9%) of 13 states within 2x of California's pre-policy MSPE had a post-policy MSPE greater than that of California. The plot of the ratios of post- to pre-policy MSPE for California and all control states is presented in Figure 12. Nineteen (67.9%) of 28 control states had ratios of post- to pre-policy MSPE greater than that of California.

The effect size and corresponding permutation test when treating the implementation year as 2007 provide no evidence for an effect on California state prisoner mortality during this placebo period. These results demonstrate that the synthetic control method applied to these data was able to accurately reconstruct California's observed mortality rates in the absence of a major intervention, increasing confidence in our estimates of the effects of AB109.

The leave-one-out estimates obtained when excluding single control states from the donor pool are presented in the Figure 13. Exclusion of any of the states that contributed to the synthetic control unit in the main analysis had little impact on the estimates of AB109's effect on mortality.

It is worth noting that the 2012 crude mortality rate for California reported by the BJS is and used in this analysis likely to over-estimate the true mortality rate (in deaths per person-time). The BJS uses the year-end custody population as the denominator for calculating annual rates, and AB109 led to a large and rapid reduction in the prison population that did not stabilize until the end of 2012. Specifically, the year-end custody populations reported by BJS for 2011 and 2012 were 147,051 and 132,624, respectively. As a result of this reduction from year-end 2011 to year-end 2012, the year-end population will underestimate the true incarcerated person-time more in 2012 than in other years.

Changes in prisoner age distributions

After the implementation of AB109, the proportion of California state prisoners in older age groups increased and those in lower age groups decreased (Figures 14-16). From 2010 to 2012, California

had relative increases in the proportion of prisoners in older age groups that exceeded those of most control states with reliable person-time data (62% of control states for prisoners aged 45-55 and 100% of control states for prisoners aged 56-65, 65-75, and over 75). Similarly, California had relative decreases in the proportion of prisoners for some younger age groups that exceeded those of most control states (77% of control states for prisoners aged 36-45; 100% of control states for prisoners aged 26-35; 38% of control states for prisoners aged 18-25). Similar patterns were sustained through 2013 and 2014.

Comparing crude and age-standardized mortality among California state prisoners

Both the crude and age-standardized mortality rates among California state prisoners from the period 2008-2014 are presented in Figure 17. The increase that was observed for crude mortality rates following the implementation of AB109 is absent from the age-standardized mortality rates. Whereas the crude mortality rate increased from 247.7 deaths per 100,000 person-years in 2010 to 260.5 in 2012 and 266.0 in 2013, the age-standardized mortality rate decreased from 223.4 in 2010 to 205.2 in 2012 and 202.5 in 2013. We also present the age-specific mortality rates among California state prisoners for each year from 2008 to 2014 in Table 6. Age-specific mortality rates declined for all but one age group (46-55 year-olds) from 2010 to 2012 and declined for all age groups from 2010 to 2013 and 2014.

Comparing age-standardized mortality between California and other states

The age-standardized excess mortality rate estimates for each state and post-policy year are presented in Figure 18 and Table 7. Among the 13 control states included in the analysis, the median excess mortality rates were 5.6 (97.8% exact confidence interval: -71.7, 34.5; 90.8% exact confidence interval: -37.1, 34.4) in 2012, -18.6 (-78.4, 42.6; -68.5, 13.1) in 2013, and -48.6 (-100.6, -27.2; -48.7, -30.0) in 2014. These results suggest that if each control state's prison population had experienced California's age-specific mortality rates from 2010 to 2014, they would have tended to have greater decreases in mortality relative to what they actually experienced. By 2014, the median state would have experienced nearly 50 fewer deaths per 100,000 prisoners, representing a nearly 20% reduction from the median mortality rate of 259 per 100,000 among the 13 control states in that year.

When applied to the pre-policy period (2008 to 2010), the median excess mortality rate was 37.0 (-3.6, 110.3; 19.8, 85.7). This result suggests that if each control state's prison population had experienced California's age-specific mortality rates from 2008 to 2010, they would have tended to have greater increases in mortality relative to what they actually experienced.

There was no evidence that the changes in crude mortality among states included in the analysis arise from a different distribution than excluded states from 2010 to 2012 ($p=0.402$), 2013 ($p=0.806$), or 2014 ($p=0.943$), as assessed using Kolmogorov-Smirnov tests.

Sensitivity Analysis for Differences in Mortality Reporting

The results of our sensitivity analysis in which we randomly corrected for differences between the annual numbers of California state prisoner deaths included in the DIC data and those reported by BJS were consistent with our main age-standardized analysis results comparing changes in California to those in other states and are presented in Table 8.

Bias Analyses for Concurrent Policy Changes

The results of our sensitivity analysis that incorporated medical parole deaths were also similar to our main age-standardized analysis results comparing changes in California to those in other states (Table 9). As with our main analysis, randomly correcting for differences between DIC and BJS data had little effect on these estimates (Table 10).

In regards to the elderly parole program, the standardized changes over time in quarterly mortality rates among prisoners above and below 60 years of age were very similar throughout 2013 and 2014, with the exception of a spike in deaths among prisoners 60 and older in Q1 2014 (Figure 19). Under the assumption that the relationship between the mortality trends among those above and below 60 years of age would have continued through Q4 2014 in the absence of the elderly parole program, there is no indication that the elderly parole program impacted mortality rates among prisoners aged 60 and over.

4.4 DISCUSSION

Following the implementation of AB109, California prisons experienced an increase in crude mortality that attenuated by 2014 and appears to be attributable to a concurrent shift in the age distribution of California state prisoners. When accounting for this change in the age distribution, California's change in mortality rate appeared consistent with those of other states in the first two post-policy years but exhibited a greater reduction relative to other states in the third year after implementation. This is the first study evaluating California state prisoner mortality following the implementation of California's historic criminal justice initiative, and our analysis suggests improved mortality outcomes three years after implementation.

The results of our synthetic control analysis suggest that the crude mortality among California state prisoners increased relative to what would have occurred in the absence of AB109, with the largest increase occurring in 2012. This finding is supported by our permutation test when restricting to control states with good pre-policy fits and our robustness checks. However, as previously noted, the crude mortality among California state prisoners that is reported by BJS and used in this analysis over-estimates the true mortality rate in 2012, thus the magnitude of the effect in this year is likely exaggerated. Importantly, our age-focused analyses suggest that this increase is attributable to a substantial shift in the age distribution of California state prisoners as opposed to other mechanisms elevating prisoners' mortality risk. We explored this possibility in three ways.

First, we found that California experienced a shift in age distribution among prisoners that was more extreme than most control states, particularly in regard to increasing proportions of older prisoners, following the implementation of AB109. AB109 provisions were implemented prospectively such that that new low-level offenders would be incarcerated in county jails instead of state prisons but existing state prisoners would not be transferred to county jails or granted early release. Although both admissions and releases declined after AB109, the reduction in California's prison population was driven by a decline in admissions that exceeded the corresponding decline in releases. The rapid change in the age distribution of California's prisoner population following AB109 aligns with the fact that that older prisoners are more likely to be serving longer sentences,³⁹ such that prisoners released in a given year are disproportionately younger than the overall prisoner population. Prior to AB109, these releases would be approximately offset by new admissions, but new admissions were reduced under AB109, a dynamic that resulted in a smaller

and older prisoner population. It is well established that mortality risk increases with age both in and out of prisons,^{24,40} thus it is plausible that the age-shift precipitated by AB109 could increase the crude mortality rates.

Second, we found that the California state prisoner age-specific mortality rates actually declined for nearly all age groups following the implementation of AB109. This is also reflected in our finding that while the crude mortality rate increased from 2010 to 2012 and subsequently declined through 2014, the age-standardized rate declined over the entire period.

Lastly, in our comparison of changes in age-standardized mortality rates between California and other states, we found no evidence that changes in California age-specific mortality rates were systematically different from those of 13 control states from 2010 to 2012 or 2013, but we did find that California's age-specific rates decreased more than those of all but one control state in 2014. Furthermore, we presented evidence that if each control state had experienced California's age-specific mortality rates before and after AB109, the median state would have experienced 50 fewer deaths per 100,000 prisoners compared to what was actually observed, or 20% relative to the median 2014 mortality rate among control states.

Taken together, our findings suggest that crude mortality increased among California state prisoners following AB109 due to an evident change in the age distribution and corresponding risk profile of California's prison population, but that mortality within age strata declined both relative to the year before implementation and relative to contemporaneous changes in other states. Understanding the overall (i.e. crude) mortality risk of the incarcerated population is critical for surveillance and healthcare planning; however, to understand how the de-population of California's state prisons under AB109 may have impacted the health of individual prisoners, it is essential to account for the concurrent change in age distribution and the corresponding mortality risk.

The discrepant findings between our crude and age-adjusted analyses highlight an important methodological consideration when studying trends or impacts of policies on population measures. Specifically, researchers must take special care when applying methods and interpreting results when the internal composition of an aggregate population being studied may change in a manner that impacts the outcome of interest. In the present scenario, a careless interpretation of the results of our synthetic control analysis might conclude that AB109 increased the mortality risk among California state prisoners, which our age-adjusted analyses suggest is not the case. Importantly, any approach effectively accounting for such dynamics requires data at a level more granular than crude population measures (e.g., individual-level data or measures stratified by relevant covariates), which might not always be available.

It is important to place our findings within the broader context of the California prison healthcare system leading up to and following the implementation of AB109. As noted in the Introduction, California's prison healthcare system has a unique and complex history dating back decades from the implementation in AB109. Most notably, from 2006 through the end of the study period, California's healthcare system was under full authority of a federal receiver specifically tasked with improving the quality of care.²⁰ From 2008 to 2010, both the crude and age-standardized mortality rates among California state prisoners increased; in fact, when calculating age-

standardized excess mortality rates for this period, California appeared to have a greater increase age-specific mortality rates than control states. Despite these increases in the early years of the receivership, a 2015 report by the receiver summarized substantial improvements to the structure, processes, and outcomes related to medical care in California prisons since 2008, though it also noted extensive variability in quality of care at the institutional level. Also, from 2006 to 2014, a comprehensive death review process documented a reduction in the rate of medically preventable deaths.⁴¹ In addition to these changes that spanned the pre- and post-AB109 periods, the state opened the California Health Care Facility (CHCF) in July 2013. The CHCF is a 54-building and nearly 3000-prisoner capacity medical complex for prisoners with long-term medical or acute mental-health needs. It is thus clear that the de-population of California prisons under AB109 occurred in tandem with dedicated and seemingly effective efforts to improve the quality of medical care provided to prisoners. Indeed, although the original court decision and subsequent Supreme Court opinion for *Coleman/Plata vs. Brown* declared overcrowding as the primary reason for healthcare deficiencies, they also made clear that resolving overcrowding alone would not be sufficient to improve the quality of care for prisoners.

The changes that spanned or occurred during the post-policy period offer potential explanations for why we only observed the reduction in age-standardized prisoner mortality in 2014, the third year after the implementation of AB109. Although the CHCF opened in July 2013, the receiver halted intake in January 2014 citing inadequate staffing and supply chain issues that precluded effective provision of healthcare at the facility.⁴² Following a series of improvements, intake at CHCF resumed in July 2014.⁴³ Thus, after a challenging first 6-12 months in operation, CHCF may have impacted system-wide mortality rates by admitting and providing care for prisoners with the most complex and severe medical needs in 2014. Indeed, CHCF's average end-of-month population was 366 across all 12 months in 2013 and 1,620 in 2014.⁴⁴ In addition, the state's death review process determined that the rate of medically preventable deaths was relatively stable from 2009 to 2013 but decreased by one-third in 2014, which aligns with our findings.⁴¹ On the other hand, the average number of identified lapses in care per prisoner death showed no meaningful trend prior to 2010 but decreased from 1.1 in 2010 to 0.8 in 2012-2013 and to 0.5 in 2014,⁴¹ which aligns with the timing of AB109 implementation. It is worth noting that death is the most severe health outcome and that improvements in medical care are likely to impact intermediate health outcomes before ultimately impacting mortality. This is particularly true in the context of chronic conditions such as diabetes or hypertension, which require ongoing care and management and are more prevalent among incarcerated populations.⁴⁵ Accordingly, it seems plausible that de-population under AB109 could facilitate improvements in the quality of prisoner care that would correspond to the observed lag between the implementation of AB109 and changes in mortality.

Our study is novel in that it evaluates the impacts of decarceration on individuals who remain incarcerated and that it focuses on a health outcome. Prior work has noted the potential for decarceration efforts to improve the health and well-being of prisoners by reducing overcrowding and decreasing prisoner-to-staff ratios;⁴⁶ indeed, AB109 was predicated on this idea.⁴ However, as illustrated by other research evaluating AB109,^{7,8,11-19} outcomes related to public safety and recidivism tend to receive more attention among efforts to understand the impacts of decarceration. Our findings that AB109 may have decreased the risk of mortality among California state prisoners provides an important complement to this other work, and allows for a more comprehensive view of the impacts of AB109 and of decarceration more broadly.

The present study has several limitations. First, our synthetic control analysis and our age-standardized excess mortality rate measures both rely on the assumption that the mortality experience of other states can be used to approximate what would have occurred in California in the absence of AB109, which is untestable. Second, we are unable to disentangle the mortality effects of de-population under AB109 and concurrent improvements in the quality of medical care in California's prisons that were prompted by the same lawsuits as AB109; however, given that these were intended as concurrent and complementary strategies for improving prisoner healthcare, we are not certain that it would be meaningful to do so. Third, only 29 and 13 control states were included in the crude and age-adjusted analyses, respectively; however, the majority of states were excluded due to small population sizes and numbers of prisoner deaths or having integrated prison and jail systems, which may limit their comparability to California, which has the nation's second largest state prison system. In addition, among states included in the crude mortality analysis, there was no difference in the distributions of crude mortality trends between those that were included and excluded from the age-adjusted analysis. Fourth, our age-adjusted analysis combines data from multiple sources, which involved population data of variable quality in NCRP data and discordant counts of annual deaths among California state prisoners in the BJS and DIC data. We sought to address the variable quality in the NCRP data by validating year-end custody counts against NPS data and only retaining states that exhibited reasonable quality over the entire study period. We sought to address the discordant death counts in our stochastic sensitivity analysis, which had trivial effects on our estimates and no impact on our conclusions. It is important to note that broader availability of reliable data on US prison populations, including health-related measures, would mitigate the majority of these limitations and improve the ability of researchers to rigorously evaluate the impacts of changes to the nation's prison systems. Indeed, a study surveyed 36 prominent publicly available health datasets and found the none could be used to assess the health of incarcerated individuals, highlighting the dearth of these data.⁴⁷

Despite these limitations, we leveraged multiple data sources to examine mortality among California state prisoners following a historic and unprecedented de-populating of a state prison system. Although the crude mortality rate increased initially, our findings suggest this was due to an expected shift in age distribution of California state prisoners. When accounting for this shift in age distribution, we found that mortality decreased more in California relative to control states three years after the implementation of AB109. As other states seek to reduce their prison populations to address overcrowding and corresponding healthcare deficiencies, any assessment of California's experience with AB109 should consider this potential benefit.

4.5 REFERENCES

1. R W. *World Prison Population List, 12th Edition*. Institute for Criminal Policy Research (ICPR) at Birkbeck, University of London; 2018.
2. Bronson J, Carson EA. *Prisoners in 2017*. Bureau of Justice Statistics, Office of Justice Programs, U.S. Department of Justice; 2019.
3. Schrantz D, DeBor S, Mauer M. *Decarceration Strategies: How 5 States Achieved Substantial Prison Population Reductions*. The Sentencing Project; 2018.
4. *Brown v. Plata*. (United States Supreme Court 2011).

CHAPTER 4: PUBLIC SAFETY REALIGNMENT ACT

5. Mischynski D. *Corrections Realignment: One Year Later*. Public Policy Institute of California; 2012.
6. Lofstrom M, Bird M, Martin B. *California's Historic Corrections Reforms*. Public Policy Institute of California; 2016.
7. Lofstrom M, Martin B. *Public Safety Realignment: Impacts So Far*. Public Policy Institute of California; 2015.
8. Lofstrom M, Raphael S. *Realignment, Incarceration, and Crime Trends in California*. Public Policy Institute of California; 2015.
9. Lofstrom M, Raphael S. *Impact of Realignment on County Jail Populations*. Public Policy Institute of California; 2013.
10. Gottlieb A, Charles P, McLeod B, Kjellstrand J, Bonsu J. Were California's Decarceration Efforts Smart? A Quasi-Experimental Examination of Racial, Ethnic, and Gender Disparities. *Criminal Justice and Behavior*. Published online June 1, 2020:009385482092338. doi:10.1177/0093854820923384
11. Wootton A. AB 109 and its impact on prison overcrowding and recidivism: A policy analysis. *Themis: Research Journal of Justice Studies and Forensic Science*. 2016;4.
12. Bird M, Grattet R, Nguyen V. *Realignment and Recidivism in California*. Public Policy Institute of California; 2017.
13. Bird M, Grattet R. *Do Local Realignment Policies Affect Recidivism in California?* Public Policy Institute of California; 2014.
14. Lofstrom M, Raphael S, Grattet R. *Is Public Safety Realignment Reducing Recidivism in California?* Public Policy Institute of California; 2014.
15. Bird M, Grattet R. Realignment and recidivism. *The ANNALS of the American Academy of Political and Social Science*. 2016;664(1):176-195.
16. Bird M, Grattet R. Policy change and recidivism: the effects of California realignment and local implementation strategies on rearrest and reconviction. *Criminal Justice Policy Review*. 2015;28(6):601-623.
17. Lofstrom M, Raphael S. *Public Safety Realignment and Crime Rates in California*. Public Policy Institute of California; 2013.
18. Sundt J, Salisbury EJ, Harmon MG. Is downsizing prisons dangerous? The effect of California's realignment act on public safety. *Criminology and Public Policy*. 2016;15(2):315-341.

CHAPTER 4: PUBLIC SAFETY REALIGNMENT ACT

19. Lofstrom M, Raphael S. Incarceration and crime: evidence from California's public safety realignment reform. *The ANNALS of the American Academy of Political and Social Science*. 2016;664(1):196-220.
20. Kelso, J.C. *Special Report: Improvements in the Quality of California's Prison Medical Care System*.; 2015. Accessed August 31, 2020. <https://cchcs.ca.gov/wp-content/uploads/sites/60/2017/08/Kelso-Special-Report-Filed-031015.pdf>
21. California Correctional Health Care Services. Health Care Services Dashboard. Accessed August 31, 2020. <https://cchcs.ca.gov/reports/#dashboard>
22. Petersilia J. Looking back to see the future of prison downsizing in America. Keynote Address presented at the: National Institute of Justice (NIJ) Conference; June 2012. <https://www.ojp.gov/library/publications/looking-back-see-future-prison-downsizing-america-keynote-address-2012-nij>
23. Carson EA. *Prisoners in 2018*. Bureau of Justice Statistics, Office of Justice Programs, U.S. Department of Justice; 2020.
24. Carson EA, Cowhig MP. *Mortality in State and Federal Prisons, 2001-2016 - Statistical Tables*. United States Department of Justice, Office of Justice Programs, Bureau of Justice Statistics; 2020.
25. Noonan ME. *Mortality in State Prisons, 2001-2014 - Statistical Tables*. United States Department of Justice, Office of Justice Programs, Bureau of Justice Statistics; 2016.
26. United States Department Of Justice. Office Of Justice Programs. Bureau Of Justice Statistics. National Corrections Reporting Program, 2000-2015: Version 1. Published online 2017. doi:10.3886/ICPSR36746.V1
27. State of California, Department of Justice, Criminal Justice Statistics Center. Deaths in Custody Data, 2005-2018. Published online June 2019.
28. California Department of Justice. Open Justice. Published 2020. Accessed September 30, 2020. <https://openjustice.doj.ca.gov/>
29. Abadie A, Diamond A, Hainmueller J. Synthetic control methods for comparative case studies: Estimating the effect of California's tobacco control program. *Journal of the American Statistical Association*. 2010;105(490):493-505.
30. Abadie A, Diamond A, Hainmueller J. Comparative Politics and the Synthetic Control Method. *American Journal of Political Science*. 2015;59(2):495-510. doi:10.1111/ajps.12116
31. Centers for Disease Control and Prevention National Center for Health Statistics. Multiple Cause of Death 1999-2018 on CDC WONDER Online Database, released 2019. Published online March 17, 2018. <http://wonder.cdc.gov/>

CHAPTER 4: PUBLIC SAFETY REALIGNMENT ACT

32. United States Department Of Justice. Office Of Justice Programs. Bureau Of Justice Statistics. Prisoners Series. Accessed November 30, 2020. <https://www.bjs.gov/index.cfm?ty=pbse&sid=40>
33. Prison Policy Initiative. Percentage of incarcerated state prison population 55 years of age and older for each state, with comparative total prison population counts. https://www.prisonpolicy.org/data/older_prisonpopulations.xlsx
34. Carter Goble Associates, LLC. *Health Care Study: Florida Department of Corrections.*; 2019. Accessed August 18, 2020. <https://oppaga.fl.gov/Products/ReportDetail?rn=19-FDCMed>
35. Carson EA, Mulako-Wangota J. Count of custody population - sentences less than or equal to 1 year. Generated using the Corrections Statistical Analysis Tool (CSAT)-Prisoners at www.bjs.gov.
36. Carson EA, Mulako-Wangota J. Count of custody population - sentences greater than 1 year. Generated using the Corrections Statistical Analysis Tool (CSAT)-Prisoners at www.bjs.gov.
37. Neal D, Armin R. The Prison Boom and the Lack of Black Progress after Smith and Welch. *NBER Working Paper No w20283*. Published online July 2014.
38. Pfaff JF. The Myths and Realities of Correctional Severity: Evidence from the National Corrections Reporting Program on Sentencing Practices. *American Law and Economics Review*. 2011;13(2):491-531. doi:10.1093/aler/ahr010
39. Urban Institute. *A Matter of Time: The Causes and Consequences of Rising Time Served in America's Prisons.*; 2017. Accessed September 3, 2020. <https://apps.urban.org/features/long-prison-terms/intro.html>
40. Xu J, Murphy S, Kochanek K, Arias E. *Mortality in the United States, 2018*. National Center for Health Statistics; 2020.
41. Imai K. *Analysis of 2014 Inmate Death Reviews in the California Correctional Healthcare System.*; 2015. Accessed August 31, 2020. https://cchcs.ca.gov/wp-content/uploads/sites/60/2017/08/OTRES_DeathReviewAnalysisYear2014_20150730.pdf
42. California Correctional Health Care Receivership. *Achieving a Constitutional Level of Medical Care in California's Prisons: Twenty-Fifth Tri-Annual Report of the Federal Receiver's Turnaround Plan of Action For September 1 - December, 2013.*; 2014.
43. California Correctional Health Care Receivership. *Achieving a Constitutional Level of Medical Care in California's Prisons: Twenty-Seventh Tri-Annual Report of the Federal Receiver's Turnaround Plan of Action For May 1 - August 31, 2014.*; 2014.
44. California Department of Corrections and Rehabilitation. *Monthly Reports of Population, July 2013 - December 2014.*

45. Maruschak L, Berzofsky M, Unangst J. *Medical Problems of State and Federal Prisoners and Jail Inmates, 2011-2012*. U.S. Department of Justice. Office of Justice Programs. Bureau of Justice Statistics.; 2015.
46. Garland B, Hogan N, Wodahl E, Hass A, Stohr MK, Lambert E. Decarceration and its possible effects on inmates, staff, and communities. *Punishment & Society*. 2014;16(4):448-473. doi:10.1177/1462474514539535
47. Ahalt C, Binswanger IA, Steinman M, Tulskey J, Williams BA. Confined to ignorance: the absence of prisoner information from nationally representative health data sets. *J Gen Intern Med*. 2012;27(2):160-166. doi:10.1007/s11606-011-1858-7

4.6 FIGURES AND TABLES

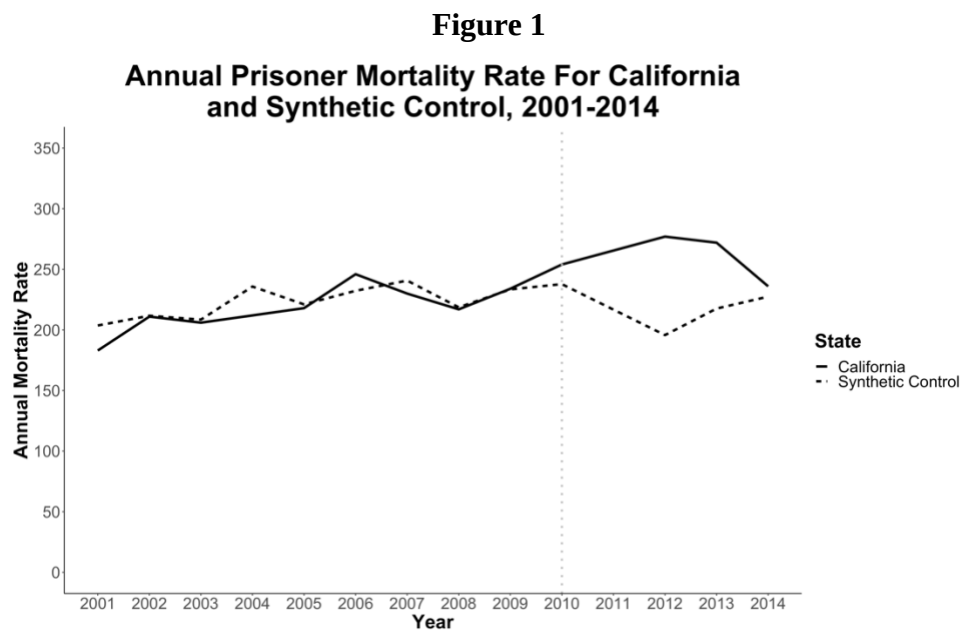


Figure 2

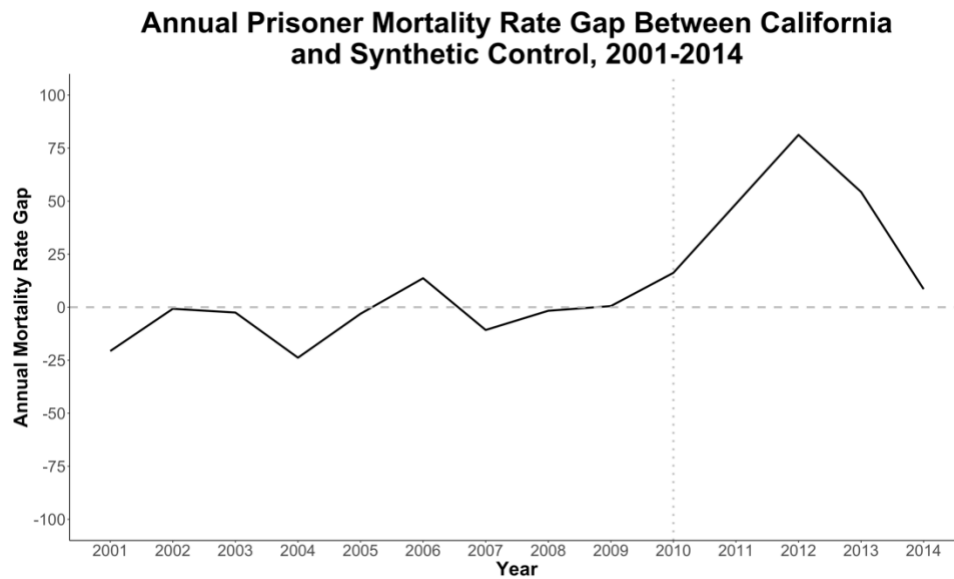


Figure 3

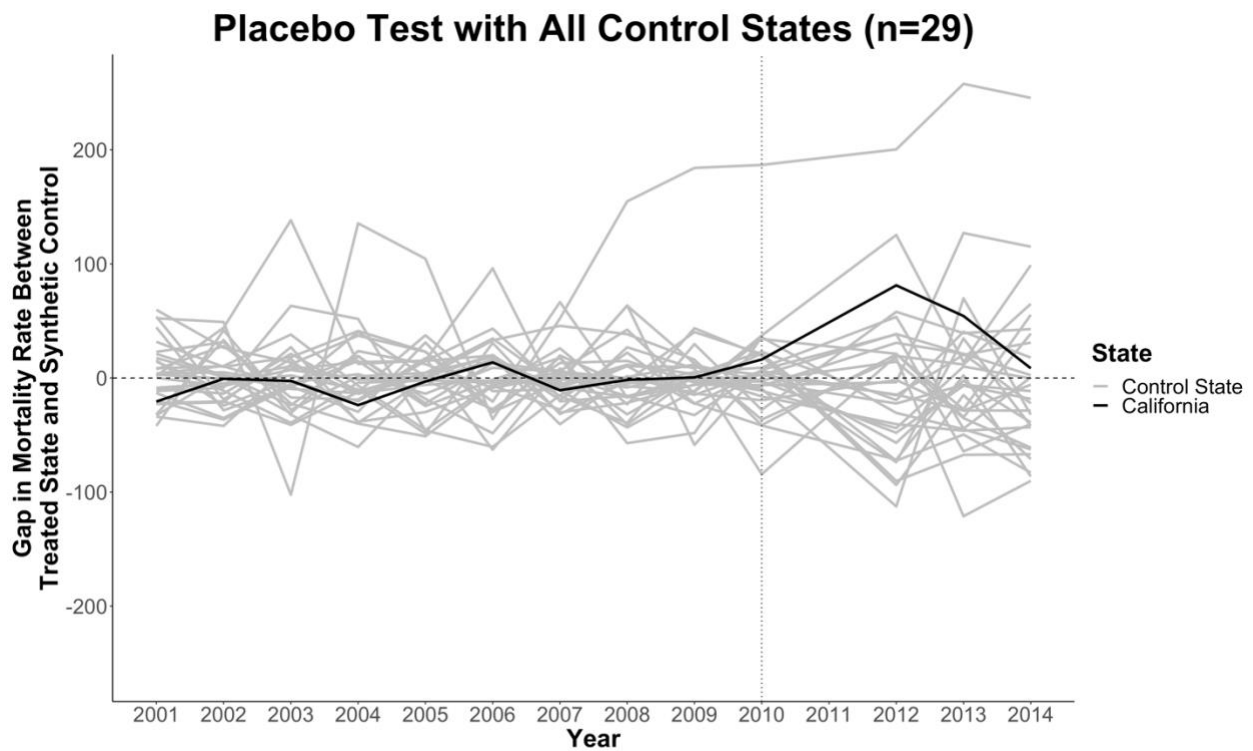


Figure 4
Placebo Test with Control States
<5x California's Pre-Policy MSPE (n=19)

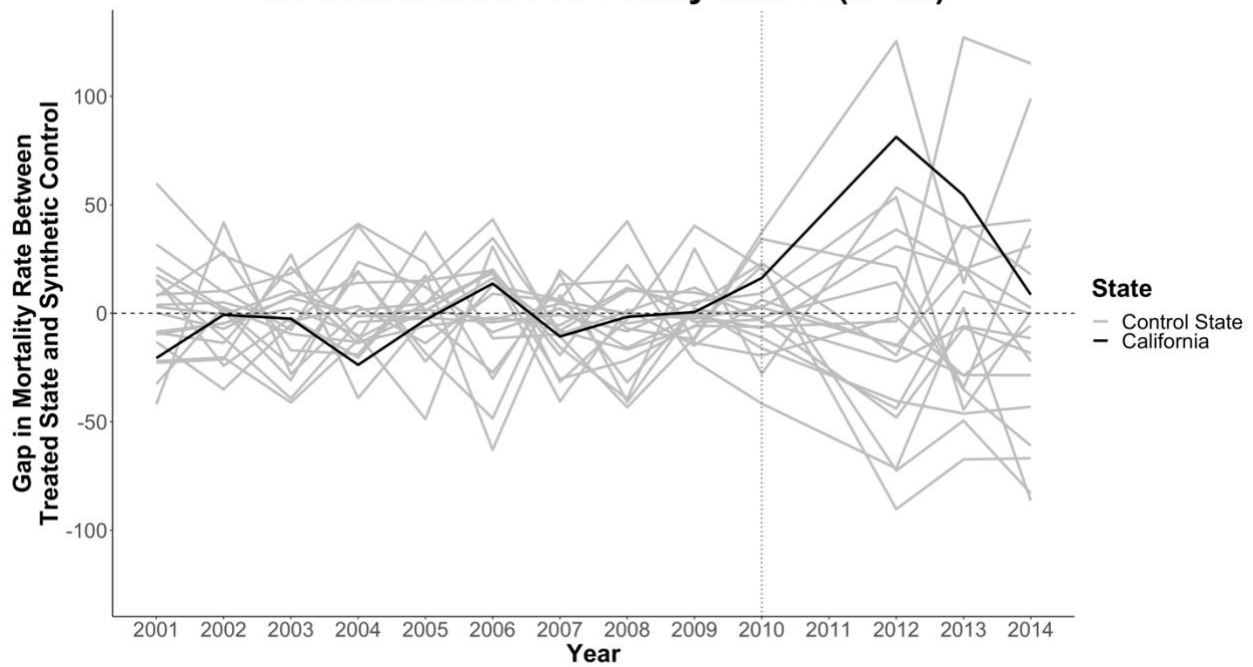


Figure 5
Placebo Test with Control States
<2x California's Pre-Policy MSPE (n=7)

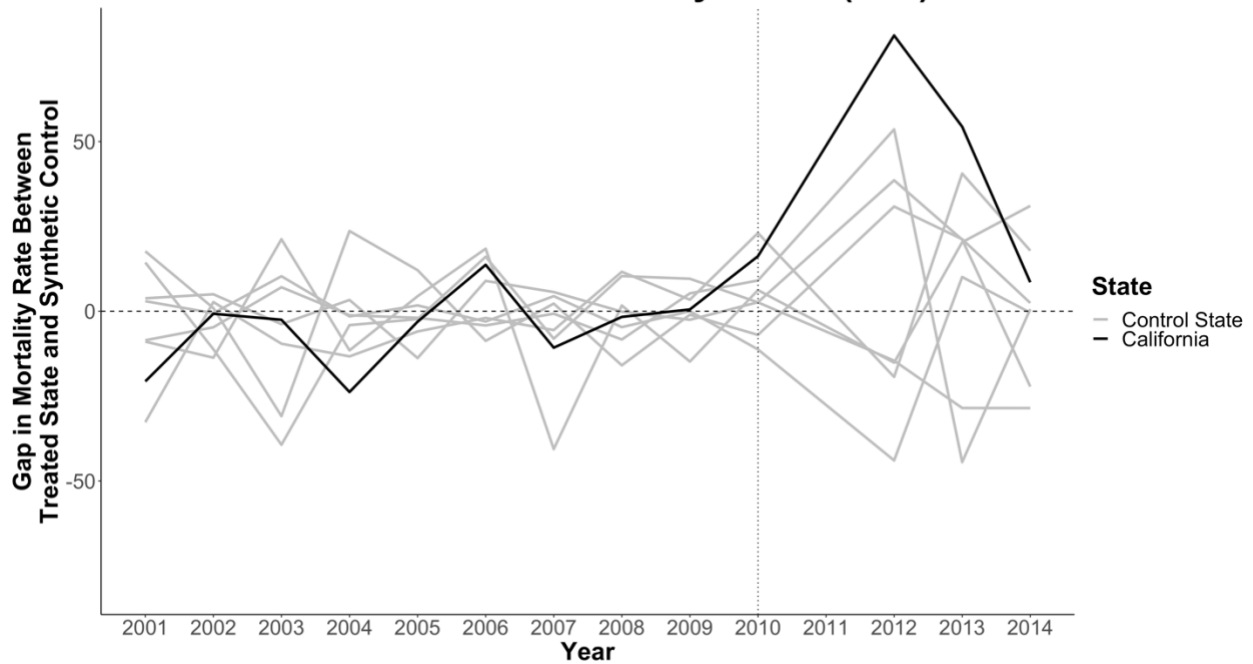


Figure 6
Ratio of Post to Pre MSPE for
Treated Unit and All Control Units

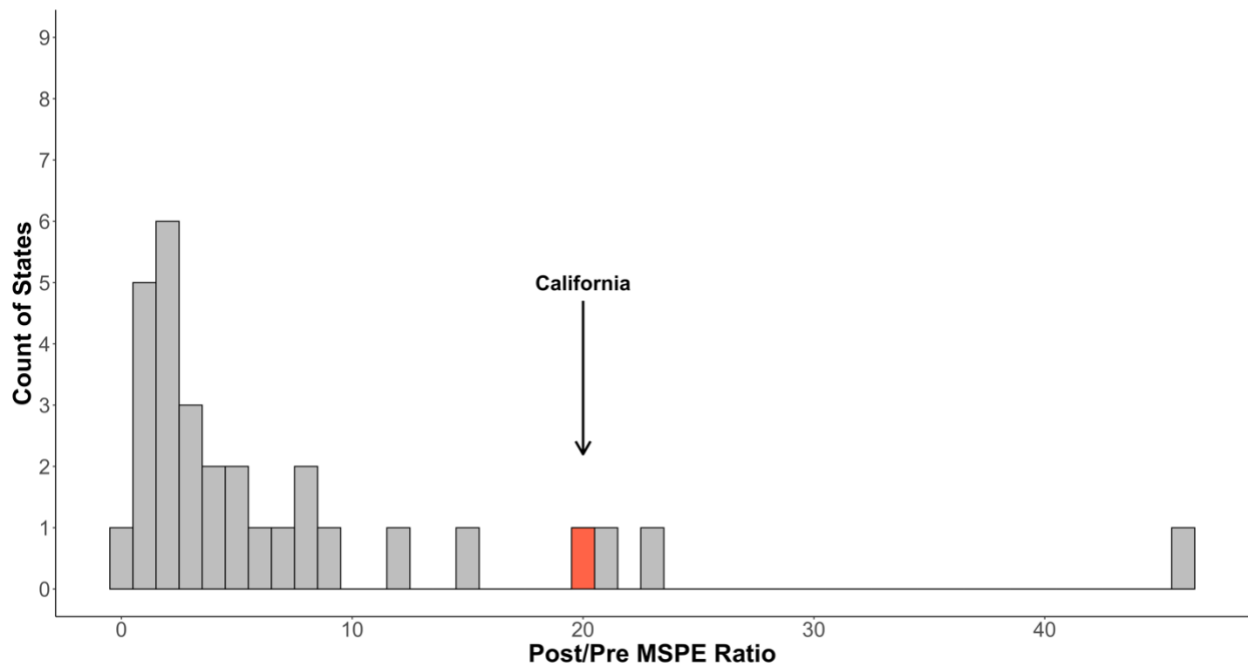


Figure 7
Annual Prisoner Mortality Rate For California
and Synthetic Control, 2001-2010 (Time Placebo)

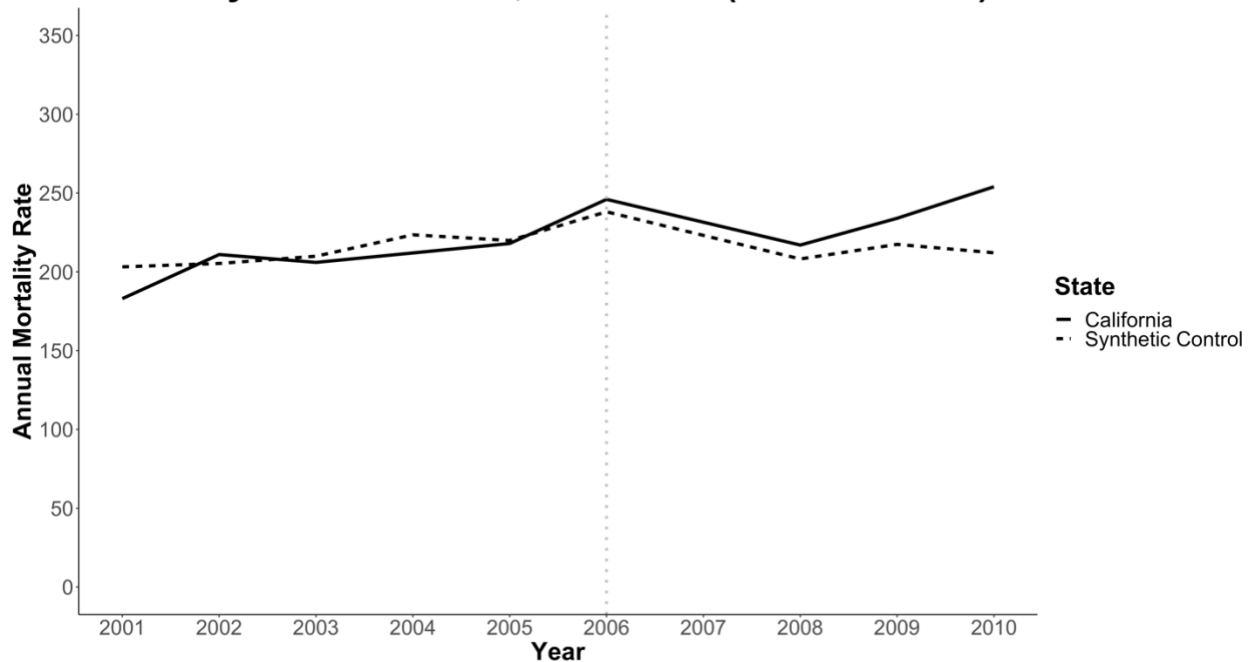


Figure 8
Annual Prisoner Mortality Rate Gap Between California and Synthetic Control, 2001-2010 (Time Placebo)

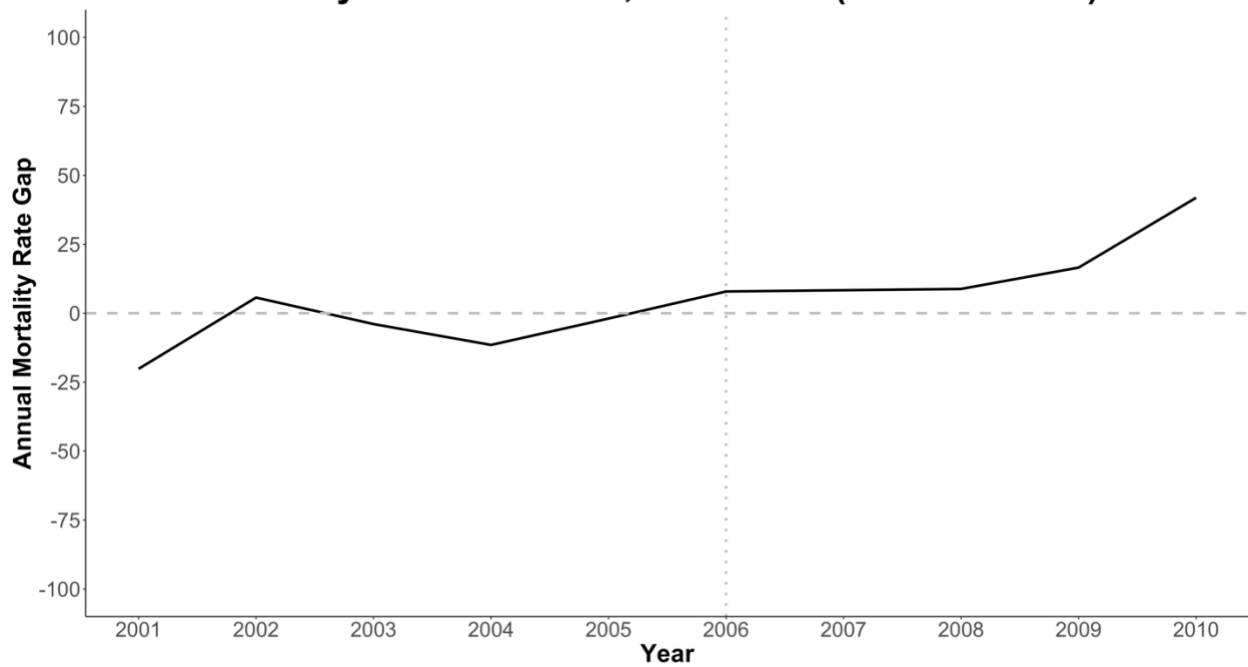


Figure 9
Time Placebo Test with All Control States (n=28)

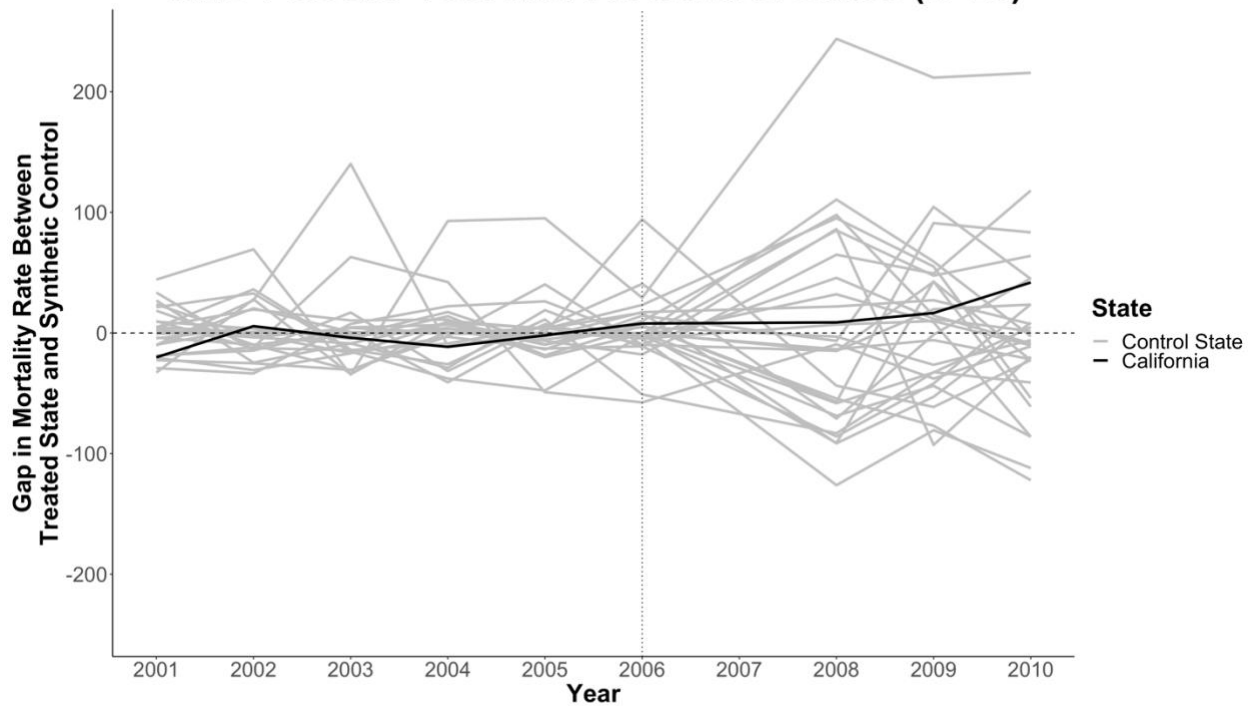


Figure 10
Time Placebo Test with Control States
<5x California's Pre-Policy MSPE (n=21)

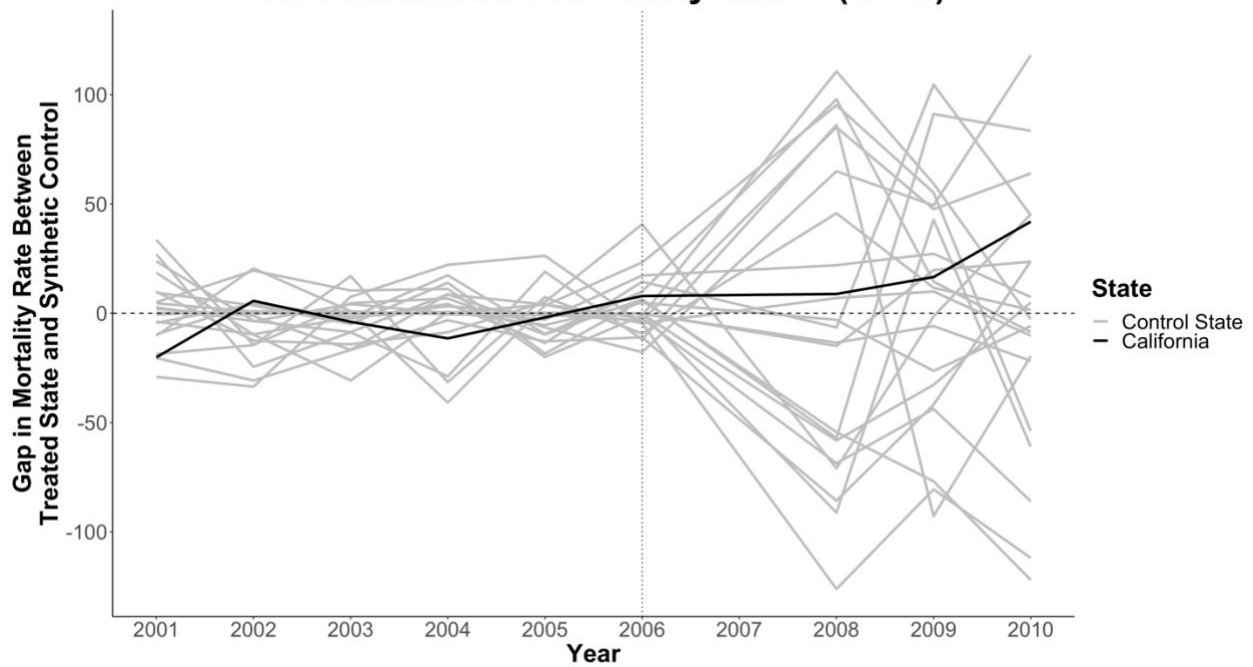


Figure 11
Time Placebo Test with Control States
<2x California's Pre-Policy MSPE (n=13)

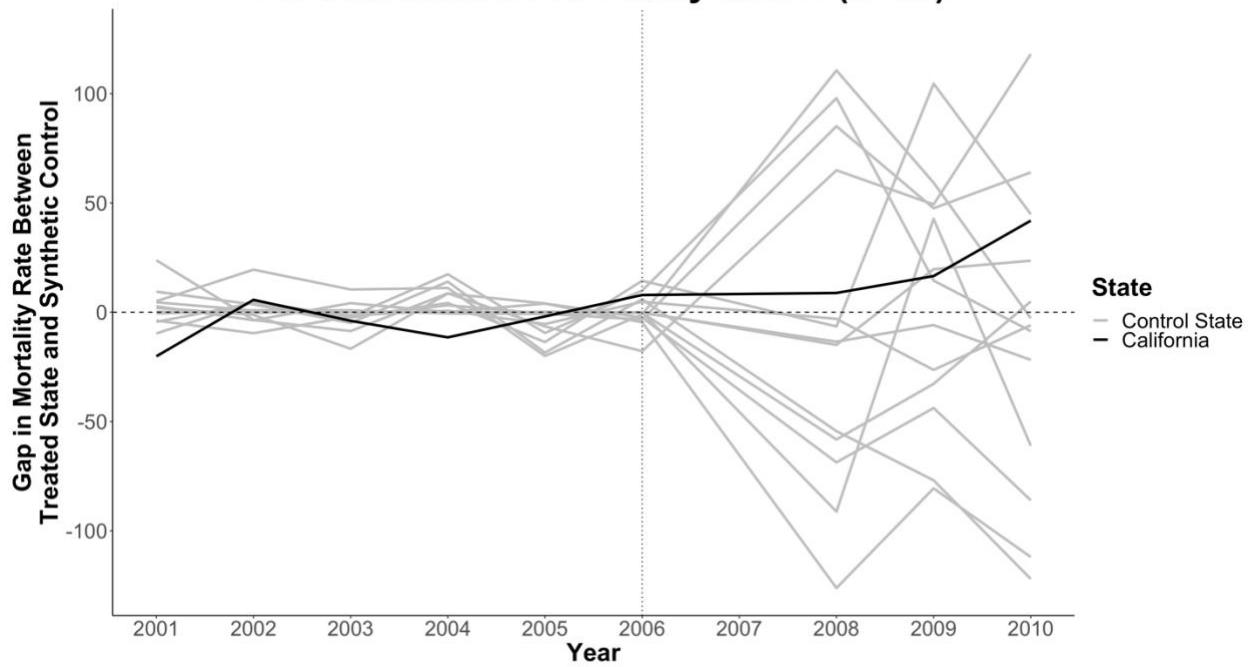


Figure 12
Ratio of Post to Pre MSPE for
Treated Unit and All Control Units

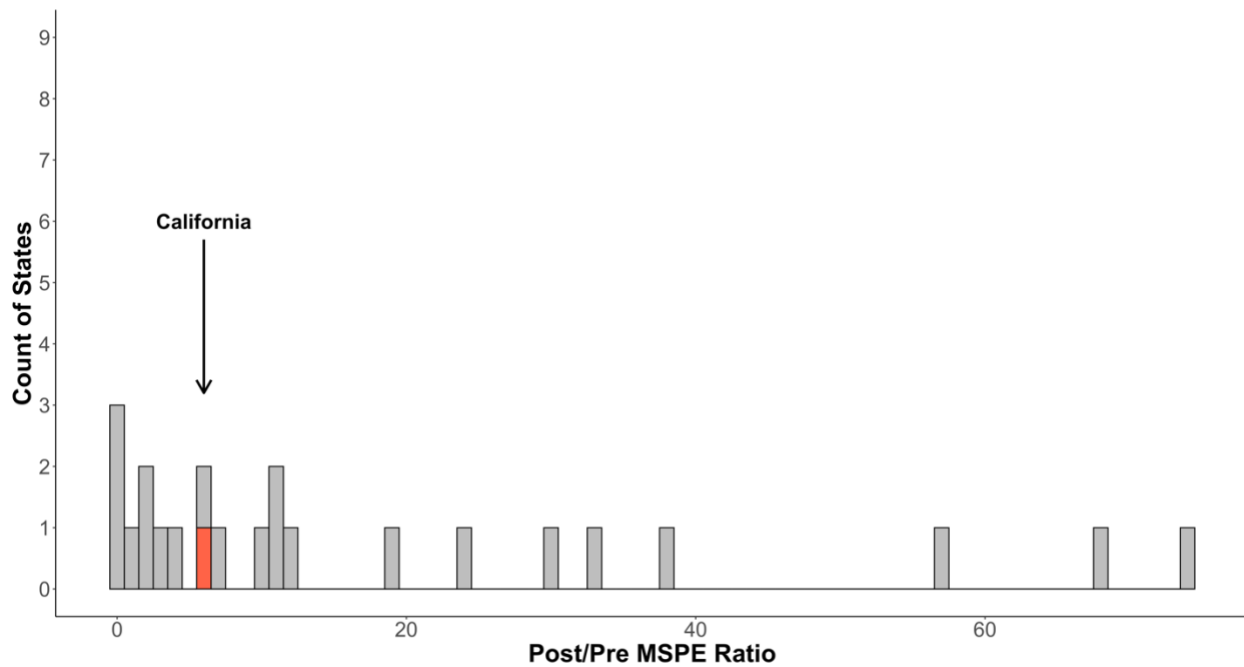


Figure 13
Annual Prisoner Mortality Rate For California
and Synthetic Controls Constructed with Single
States Excluded from Donor Pool, 2001-2014

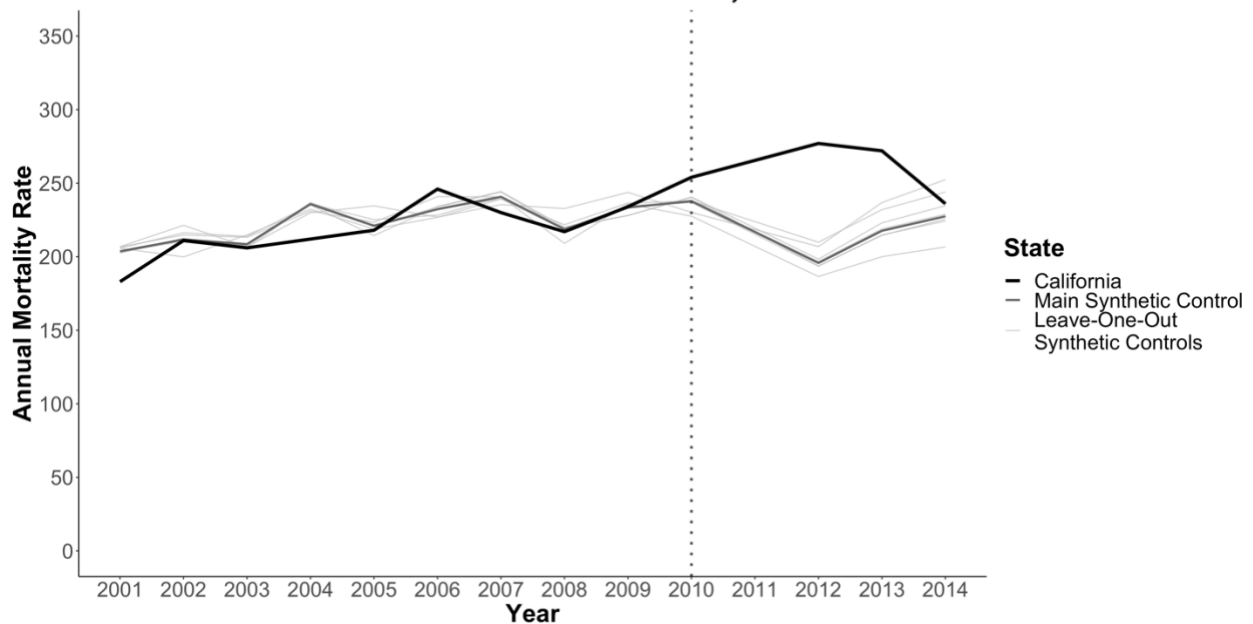


Figure 14
Relative Difference in Proportion of Person Time By Age Group
For 14 States with Reliable NCRP Data
2010 vs. 2012

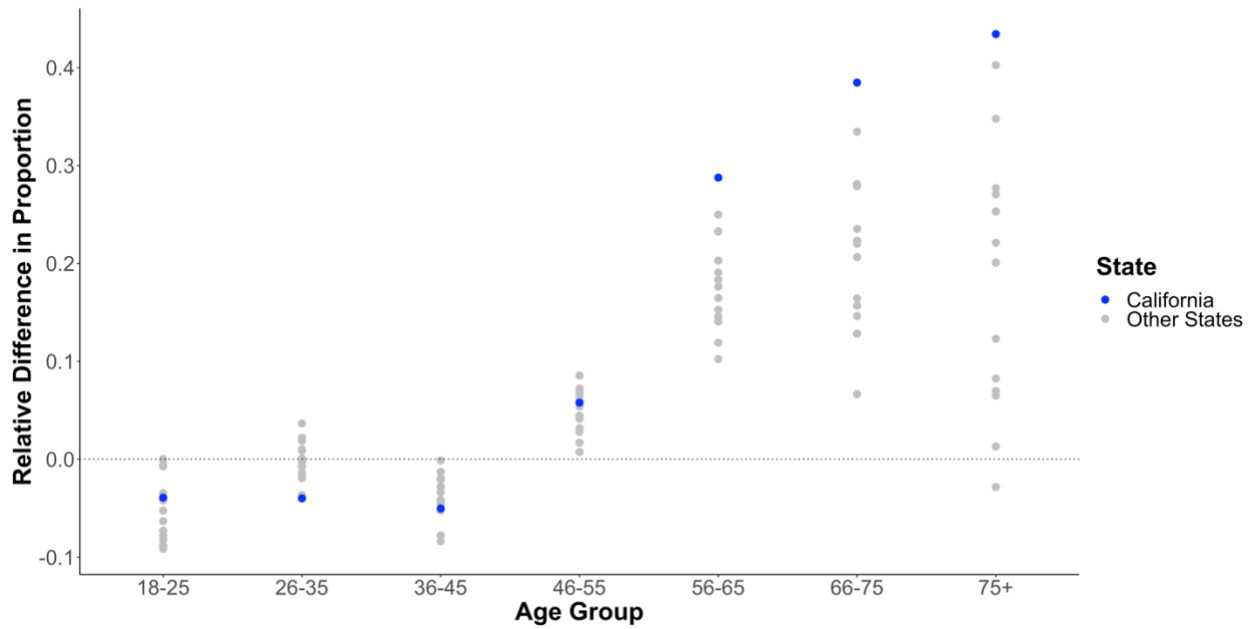


Figure 15
Relative Difference in Proportion of Person Time By Age Group
For 14 States with Reliable NCRP Data
2010 vs. 2013

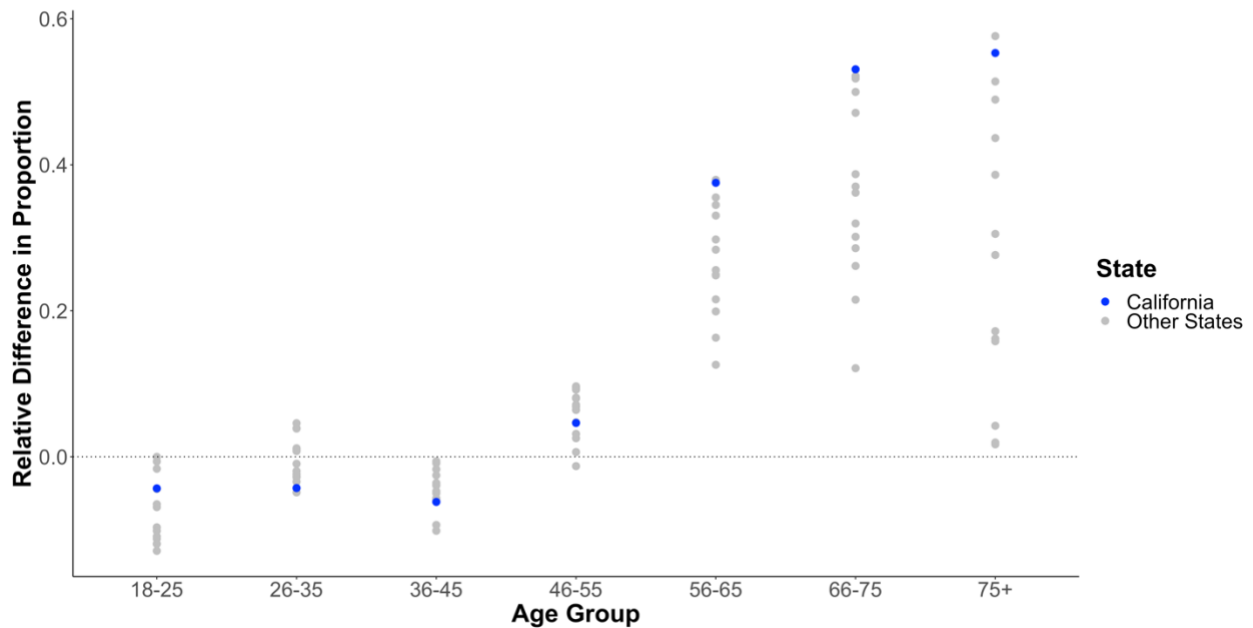


Figure 16
Relative Difference in Proportion of Person Time By Age Group
For 14 States with Reliable NCRP Data
2010 vs. 2014

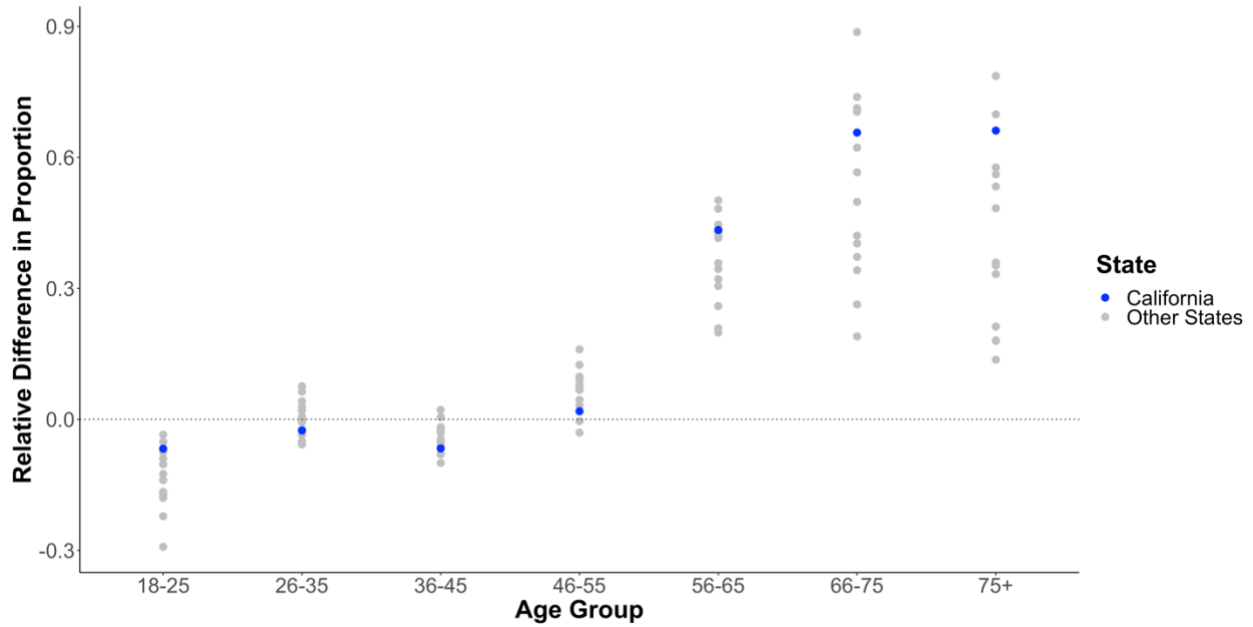
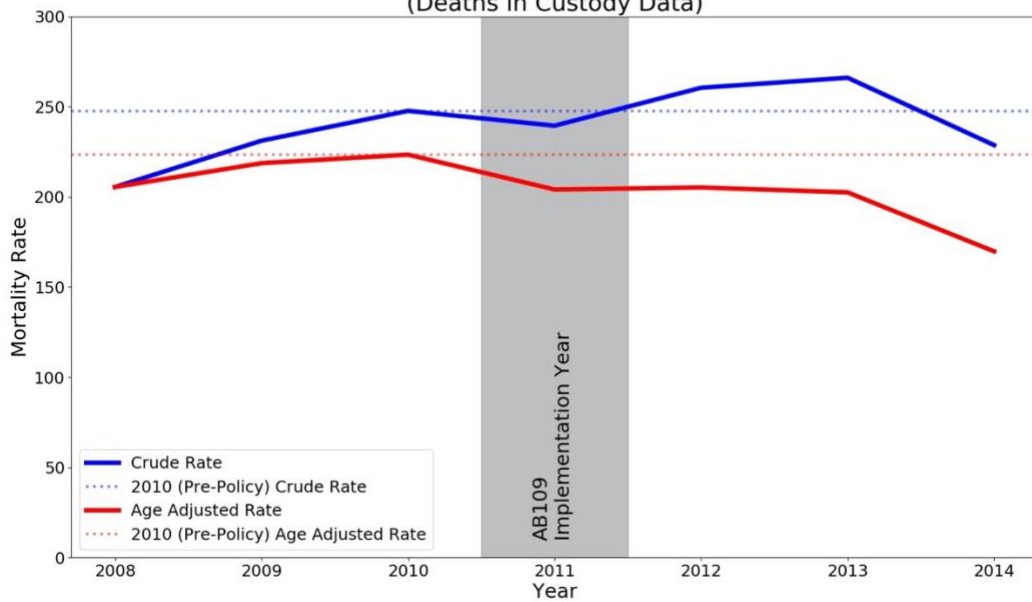


Figure 17
Crude and Age Adjusted California Prisoner
Mortality Rates, 2008-2014
(Deaths in Custody Data)



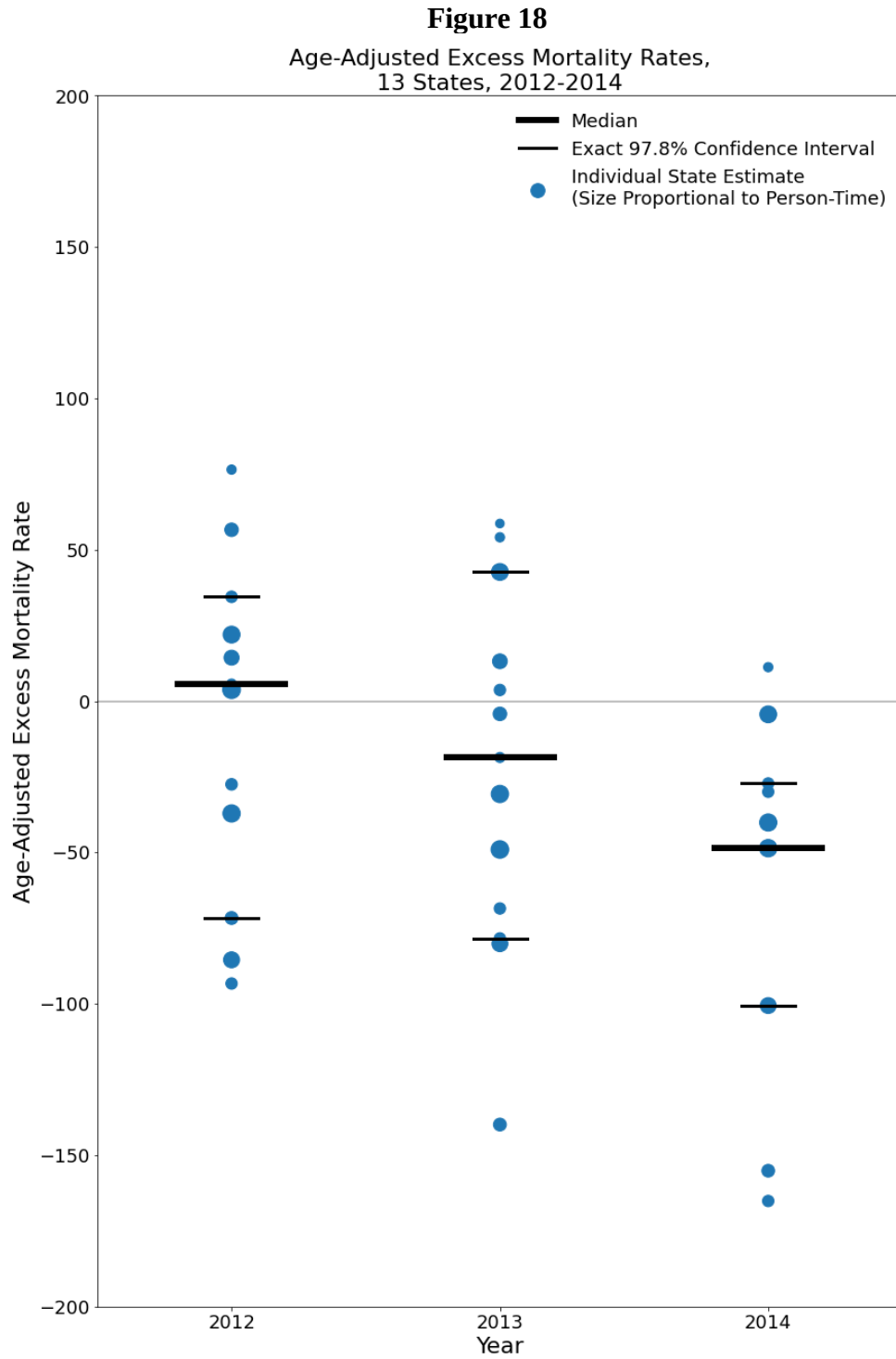
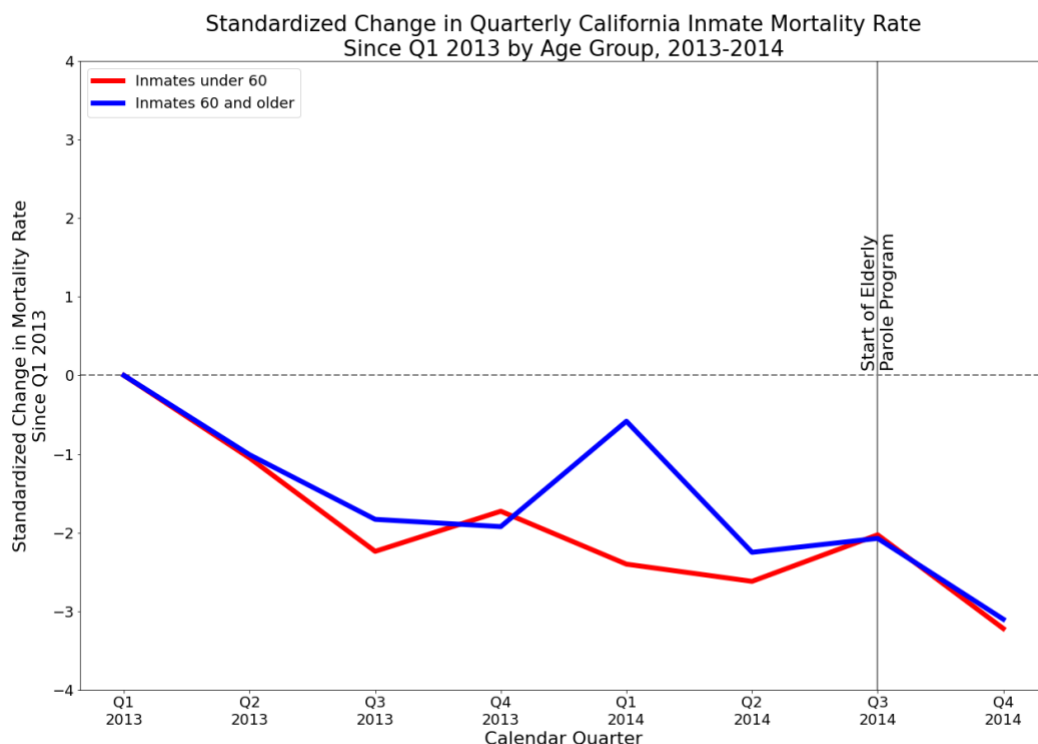


Figure 19**Table 1:** Overview of analyses and contributed data sources

Analysis	Contributing Data Sources	Data Source Components
Evaluating effects of AB109 on crude mortality using synthetic control method	BJS Data	Annual mortality rates among California and control state inmates
Comparing changes in inmate age distribution between California and control states	NCRP Data	Age-specific annual incarcerated person-time among California and control state inmates, calculated from individual-level term records
Comparing trends in crude and age-standardized mortality rates among California inmates	DIC Data	Total and age-specific annual mortality counts among California inmates
	NCRP Data	Age-specific annual incarcerated person-time among California inmates, calculated from individual-level term records
Comparing changes in age-standardized mortality rates between California and other states	BJS Data	Total annual mortality counts among control state inmates
	NCRP Data	Age-specific annual incarcerated person-time among California and control state inmates, calculated from individual-level term records
	DIC Data	Age-specific annual mortality counts among California inmates

BJS = Bureau of Justice Statistics; NCRP = National Corrections Reporting Program; DIC = Deaths in Custody Reporting Program

Table 2: States included in crude and age-adjusted mortality analyses.

State	Included in Crude Mortality Analysis	Included in Age-Adjusted Mortality Analysis
Alabama	X	X
Alaska ^{a,b,d}		
Arizona ^d	X	
Arkansas ^d	X	
California	X	X
Colorado ^d	X	
Connecticut ^{b,d}		
Delaware ^{a,b,d}		
Florida ^{c,d}		
Georgia ^d	X	
Hawaii ^{a,d}		
Idaho ^{a,d}		
Illinois	X	X
Indiana ^d	X	
Iowa ^{a,d}		
Kansas ^d	X	
Kentucky ^d	X	
Louisiana ^d	X	
Maine ^{a,d}		
Maryland	X	X
Massachusetts ^d	X	
Michigan	X	X
Minnesota ^{a,d}		
Mississippi ^d	X	
Missouri	X	X
Montana ^{a,d}		
Nebraska ^a		
Nevada	X	X
New Hampshire ^{a,d}		
New Jersey ^d	X	
New Mexico ^{a,d}		
New York	X	X
North Carolina	X	X
North Dakota ^{a,d}		
Ohio ^d	X	
Oklahoma ^d	X	
Oregon	X	X
Pennsylvania	X	X
Rhode Island ^{a,b}		
South Carolina	X	X
South Dakota ^{a,d}		
Tennessee ^d	X	
Texas ^d	X	
Utah ^{a,d}		
Vermont ^{a,b,d}		

Virginia ^d	X	
Washington	X	X
West Virginia ^{a,d}		
Wisconsin	X	X
Wyoming ^{a,d}		

^aExcluded from both crude and age-adjusted mortality analyses due to annual number of deaths < 10 during the study period.

^bExcluded from both crude and age-adjusted mortality analyses because prisons and jails form one integrated system in these states and mortality data were only available among the combined prison and jail populations.

^cExcluded from both crude and age-adjusted mortality analyses because the state privatized its prison healthcare system in 2011, which was reported to result in decreased quality of care.

^dExcluded from age-adjusted mortality analysis because year-end custody estimates calculated with NCRP data differed by more than 10% from those reported by BJS for at least one year during the period 2007-2014.

Table 3: Differences between annual number of deaths among California state prisoners included in Deaths in Custody (DIC) data and reported by the Bureau of Justice Statistics (BJS).

Year	Included in Deaths in Custody (DIC) Data	Reported by The Bureau of Justice Statistics (BJS)	Relative Difference*
2008	355	371	4.3%
2009	392	395	0.8%
2010	413	414	0.2%
2011	386	388	0.5%
2012	363	368	1.4%
2013	360	366	1.6%
2014	313	317	1.3%

*Calculated with the BJS counts as the reference.

Table 4: Annual number of deaths among California medical parolees, 2011-2014

Year	Count of Medical Parole Deaths
2011	5
2012	7
2013	7
2014	4

Table 5: Composition of Synthetic Control

Control State	Weight
Illinois	0.301
Missouri	0.229
Oregon	0.166
Washington	0.154
Indiana	0.079
Arizona	0.044
Georgia	0.027

Table 6: Age-specific mortality rates among California state prisoners, 2008-2014*

Age Group	2008	2009	2010	2011	2012	2013	2014
Under 26	20.8	28.5	36.2	53.3	31.6	37.4	33.1
26-35	52.3	53.7	70.4	43.6	59.3	68.6	54.7
36-45	115.5	102.4	133.1	114.9	121.4	135.6	98.8
46-55	407.7	423.7	373.5	376.0	393.9	324.4	306.7
56-65	948.9	1282.5	1252.0	1079.6	1023.1	1034.8	843.8
66-75	2985.8	2579.6	2788.1	2455.8	2136.5	2540.9	2088.8
Over 75	6479.6	6995.9	5762.9	6780.2	6868.2	5443.3	4628.0

*Rates calculated using death counts from Deaths in Custody (DIC) data and incarcerated person-time from National Corrections Reporting Program (NCRP) data.

Table 7: Age-adjusted excess mortality rates before and after the implementation of AB109, 13 states

State	Pre-Policy Period	Post-Policy Period		
	2010*	2012†	2013†	2014†
Alabama	70.4	-71.7	-139.9	-155.2
Illinois	-9.4	22.0	42.6	-4.4
Maryland	150.3	-27.5	-78.4	-27.2
Michigan	19.8	-85.5	-80.2	-100.6
Missouri	26.2	56.6	-4.2	-48.6
North Carolina	110.3	14.3	13.1	-48.7
Nevada	-15.2	34.5	58.6	-48.6
New York	33.3	3.8	-49.1	-48.6
Oregon	-3.6	76.5	54.1	11.2
Pennsylvania	68.8	-37.1	-30.7	-40.1
South Carolina	85.7	34.4	3.6	-30.0
Washington	37.0	5.6	-18.6	-48.1
Wisconsin	112.7	-93.3	-68.5	-165.2
MEDIAN	37.0	5.6	-18.6	-48.6

*Refers to change in mortality from 2008 to 2010.

†Refers to change in mortality from 2010 to each post-policy year.

Table 8: 2.5% and 97.5% quantiles of median age-adjusted excess mortality rates over 1000 iterations of stochastically correcting DIC death counts to match those reported by BJS, 13 states

Post-Policy Year*	2.5% Quantile	97.5% Quantile
2012	8.2	8.9
2013	-15.3	-14.4
2014	-46.6	-46
Pre-Policy Year†	2.5% Quantile	97.5% Quantile
2010	27.0	28.2

*Refers to change in mortality from 2010 to each post-policy year.

†Refers to change in mortality from 2008 to 2010.

Table 9: Median age-adjusted excess mortality rate and exact confidence intervals calculated with the inclusion of California medical parole deaths, 13 states

Post-Policy Year*	Median	(97.8% CI)
2012	10.1	(-67.6, 39.5)
2013	-13.6	(-74.8, 45.6)
2014	-45.8	(-97.7, -24.8)

*Refers to change in mortality from 2010 to each post-policy year.

Table 10: 2.5% and 97.5% quantiles of median age-adjusted excess mortality rates over 1000 iterations of stochastically correcting DIC death counts to match those reported by BJS and adding California medical parole deaths, 13 states

Post-Policy Year*	2.5% Quantile	97.5% Quantile
2012	12.7	13.3
2013	-10.1	-9.4
2014	-43.9	-43.3

*Refers to change in mortality from 2010 to each post-policy year.