The Role of Policies in Cancer Pain, Health Disparities, and Substance Use

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CHAPTER 1: Introduction

The majority of adults in the United States consume some type of recreational substances. In 2020 among people aged 12 and older, 50% reported consuming alcohol in the past month, 21% reported cigarette use in the past month, and 18% reported marijuana use in the past month.[1–3] While the health problems associated with substance use (e.g., chronic disease, injury) become more prevalent with increasing use, even moderate substance use (e.g., consuming one alcoholic drink or one cigarette daily) can increase one's risk of adverse health outcomes.[4–6]

Policies are an effective approach to reducing substance use and substance use-related adverse health outcomes,[7–9] offering population-level interventions that can target social and environmental determinants of health.[10,11] Additionally, policies – when targeting structural impediments to health by increasing access to healthcare or reducing access to harmful substances through taxation – can help narrow disparities in health for more vulnerable populations.[11,12] However, care must be given that policies do not exacerbate health disparities or have unintentional consequences that could undermine any health benefits. As such, policy outcomes must be evaluated rigorously, thoroughly, and ideally on an ongoing basis. Statistical modeling approaches for policy evaluation can vary in their strengths and limitations, which models are best suited for certain types of data, and how whether the estimates from these models allow for policy-relevant inference.[13]

In this dissertation, I developed and present three empirical studies that focus on substance use outcomes. I examined factors that influence substance use (i.e., cancer pain, policy adoption). The dissertation heavily focused on policies as interventions to reduce substance use and related health problems, but also as a potential tool to address health disparities in substance use among racial and ethnic minority groups. I did so by addressing the following aims:

First Manuscript: Cancer Pain and Substance Use Self-Medication

Prior research has found a correlation between experiencing chronic pain and using substances,[14,15] but no studies have examined this relationship for cancer survivors who experience chronic cancer pain.

Specific Aim 1: Determine the association between cancer pain and alcohol use among adult cancer survivors.

Hypothesis 1: Cancer survivors who report cancer pain will use alcohol in greater amounts compared to cancer survivors who do not report cancer pain.

Specific Aim 2: Among adult cancer survivors with cancer pain, determine the association between cancer pain management and alcohol use among adult cancer survivors.

Hypothesis 2: Among adult cancer survivors who report cancer pain, survivors who do not have their cancer pain under control (even with medication or treatment) will consume alcohol in greater amounts compared to survivors whose cancer pain is under control.

Second Manuscript: Models for Policy Evaluation

This chapter builds on the prior study by exploring statistical modeling approaches for policy evaluations and applying them to substance use outcomes. Often policies affect health outcomes, and an entire body of literature examines how various local, state, and federal policies are associated with substance use and substance use-related health outcomes. While there are many options for modeling policies, which approach is best can depend on several factors. This study describes several of the most common approaches to modeling policy outcomes, discusses strengths and weaknesses, and compares them to one another using a worked example in the field of substance use.

Specific Aim 1: Review assumptions, strengths, and limitations of statistical modeling approaches for policy outcome evaluations (fixed effects, random effects, generalized estimating equations, autoregressive integrated moving average, and synthetic control approach).

Specific Aim 2: Compare common statistical modeling approaches for policy outcome evaluations (fixed effects, random effects, generalized estimating equations, autoregressive integrated moving average, and synthetic control approach) in estimating the relationship between recreational cannabis legalization and purchasing of alcohol and cigarettes.

Third Manuscript: Medicaid Expansion and Substance Use

This paper applies the concepts from Chapter 2 to a policy that has direct implications for substance use and pain. In this study I examined how Medicaid expansion is

associated with the purchasing of recreational substances. I also assessed how this relationship differed by race and ethnicity. Policies may have differential impacts on subgroups due to differences in risk exposure experienced by those groups. When evaluating policies, including those related to substance use, it is important to consider the possibility of heterogeneous effects that may narrow or widen health disparities.

Specific Aim 1: Determine the association between state Medicaid expansion and substance purchasing (i.e., alcohol, cigarette products and e-cigarettes) at the household level.

Hypothesis 1a: Medicaid expansion will be associated with a decrease in the average amount of alcohol a household purchases.

Hypothesis 1b: Medicaid expansion will be associated with a decrease in the average number of combustible cigarettes a household purchases.

Hypothesis 1c: Medicaid expansion will be associated with an increase in the average number of smoking cessation products a household purchases.

Hypothesis 1d: Medicaid expansion will be associated with a decrease in the average number of e-cigarettes a household purchases.

Specific Aim 2: Determine how association between state Medicaid expansion and product purchasing at the household level varies by race/ethnicity.

Hypothesis 2a: Medicaid expansion will be associated with a greater decrease in the average amount of alcohol a household purchases among non-Hispanic Black, non-Hispanic Asian, and Hispanic households compared to non-Hispanic white households.

Hypothesis 2b: Medicaid expansion will be associated with a greater decrease in the average number of combustible cigarettes a household purchases among non-Hispanic Black, non-Hispanic Asian, and Hispanic households compared to non-Hispanic white households.

Hypothesis 2c: Medicaid expansion will be associated with a greater increase in the average number of smoking cessation products a household purchases among non-Hispanic Black, non-Hispanic Asian, and Hispanic households compared to non-Hispanic white households.

Hypothesis 2d: Medicaid expansion will be associated with a greater decrease in the average number of e-cigarettes a household purchases among non-Hispanic Black, non-Hispanic Asian, and Hispanic households compared to non-Hispanic white households.

CHAPTER 2: Background and Rationale

Substance use and health

Substance use is a major cause of public health problems and disease burden globally.[5] Substance abuse disorders for alcohol and other drugs can develop among people who use these substances regularly over a period of time, and are characterized by a craving or strong desire to use a given substance, inability to stop using or manage use, interference with daily life, and several other criteria described in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5).[16] Often, substance use disorders can lead to additional health consequences. Compared to the general population, mortality risk is 15 times higher for people with opioid use disorders, six times higher for people with amphetamine (e.g., Adderall) use disorder, and five times higher for people with alcohol use disorders.[17] Substance use disorders are common in the United States, with over 16 million adults reporting alcohol use disorder, nearly 4 million reporting marijuana use disorder, and nearly 2 million reporting prescription pain reliver use disorder.[18] In addition, an estimated 24% of adults age 15 to 54 exhibited nicotine dependence over their lifetime.[19]

Substance use carries additional health risks beyond substance use disorders. Alcohol use increases the risk of both intentional and unintentional injuries,[20] chronic diseases like cancer and hypertensive heart disease,[21] and infectious diseases like tuberculosis and pneumonia.[22] While the adverse health effects of marijuana are not as well understood as alcohol, current research shows a relationship between marijuana use

and several long-term cognitive problems (e.g., impaired memory).[23] In addition, marijuana consumed via smoking (e.g., hand-rolled cigarettes, bongs, blunts) can cause damage to lung tissues and small blood vessels.[24] The risk for health problems due to substance use and substance use disorder varies by age group. For example, adolescents have greater risk of motor vehicle crashes compared to adults[25] and young adults (ages 21 to 29) are more likely to drive drunk than other age groups.[26] There is a need for efforts to reduce substance use, which ultimately can impact the myriad of substance use-related health problems.

While all three of my empirical papers (Chapters 3, 4 and 5) focus on substance use as an outcome, Chapter 3 examines determinants for alcohol use. Specifically, Chapter 3 examines the relationship between cancer pain and alcohol use among cancer survivors (defined in this study to be individuals who have completed treatment for their cancer). Many of the adverse substance use-related health outcomes described earlier are more prevalent among cancer survivors, including second and recurrent cancers.[27–32] Chapters 4 and 5 also examine substance use as an outcome, but with an eye to interventions – specifically, policy interventions.

Policies as a public health strategy

Policies are one approach to reducing substance use and substance use-related health problems. However, researchers, health professionals, and advocates must have a clear understanding of policy effectiveness, as well as any unintended consequences a policy may have. In this chapter, I discuss the rationale for policies as population health

interventions using social epidemiologic lens, the effectiveness of policies in promoting good health, and how policy outcomes are evaluated. I conclude by discussing the potential benefits of health policies as well as their unintended consequences for racial/ethnic health disparities.

Social epidemiology and policies

Social epidemiology is the study of social determinants of health.[33] Social determinants are the social and environmental conditions that are related to physical and mental health outcomes. These determinants include social interventions, such as policies, where experimental manipulation of conditions is not feasible but are nonetheless viable for study through natural experiments.[34] Social epidemiology also draws heavily from Rose's population perspective of health: that individuals, embedded within social groups, societies, and environments, have a shared disease risk with the population in which they belong.[10] Given prominence that population-level health and social interventions hold in social epidemiology, policies are seen as a powerful tool for improving health by shifting the population distribution of a disease in a favorable direction. This is in contrast to targeted, individual-level interventions that often cannot affect population-level change.[35] Figure 2.1 illustrates a framework developed by the World Health Organization for understanding how policies can affect more downstream determinants of health, including behaviors and psychosocial factors, and ultimately impact health outcomes.

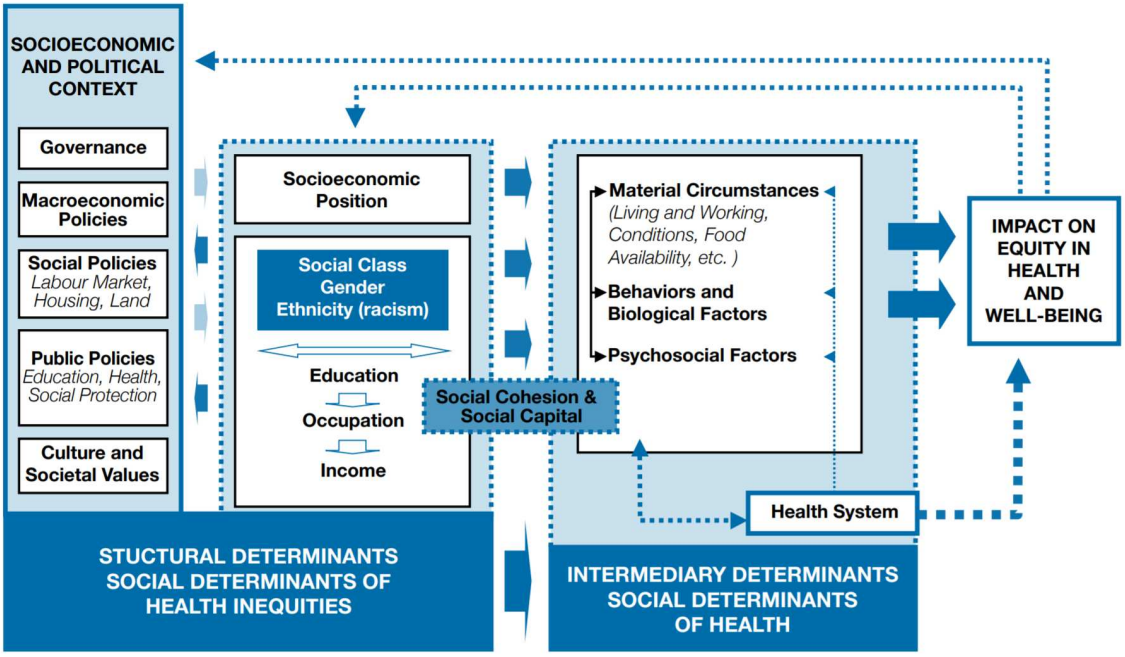

Figure 2.1. Framework for Social Determinants of Health. Developed by the Committee on Social Determinants of Health, of the World Health Organization (WHO).[36]

Policies and substance use

Policies have a long history in public health, and policies to address substance use and substance use-related problems are no exception.[7] Policies may be passed at the federal, state, local, or organizational levels.[37] Previous evaluation studies of policies regulating the alcohol retail environment have shown promising results. In a systematic review of research examining the effectiveness and cost-effectiveness of alcohol policies, there was a consensus that regulations increasing the price of alcohol and decreasing its availability (e.g., zoning restrictions to reduce alcohol outlet density) are associated with reduced alcohol-related disease.[8] Tobacco policies have shown a similar effectiveness in reducing tobacco use and tobacco use-related health problems and there is a consensus that these policies are effective public health tools. For instance, a

working group of 25 international experts convened by the International Agency for Research on Cancer (IARC) concluded that increasing tobacco excise taxes and product prices is an effective way of reducing tobacco use, preventing tobacco uptake, and promoting tobacco cessation among current users.[9]

Policies that target one specific health problems may have unintended or spillover effects for other health problems or social issues. State parity laws that allow for insurance plans to cover substance use disorder treatment are associated with decreases in rates of fatal motor vehicle crashes, likely by reducing rates of impaired driving.[38] While the Clean Air Act of 1963 was aimed at reducing air pollution across the U.S., people exposed to these air pollution reductions early in life had higher incomes later in life compared to people not exposed to Clean Air Act pollution reductions.[39] The Head Start Program, intended to improve educational outcomes (e.g., decrease absenteeism, improve readiness to transition into kindergarten) for three- to four-year old children, has also increased positive parenting practices and self-esteem among adults who participated.[40] At times, substance use policies may also unintentionally affect the use of other harmful substances. One study found an increase in marijuana use following increases in the legal minimum drinking age.[41]

While Chapter 3 of my dissertation does not directly evaluate the effects of policies, there are implications for how policies may affect cancer, cancer pain, and self-medication. In a review of primary and secondary cancer prevention research, the authors note that policy changes involving the built environment (e.g., land use,

housing, transportation, urban design) can influence cancer outcomes through several pathways, one of which includes changes in substance use.[42] Additionally, policies can influence pain self-medication behaviors in several ways. For example, a repeal of the Affordable Care Act (ACA) would have drastic health ramifications, including a possible increase in alcohol use disorder to self-medicate for chronic pain when patients lose access to insured pain treatments.[43]

Policy outcome evaluation

Evaluating the health outcomes of policies is key to ensuring governmental resources are allocated where they are most effective and promoting passage of future evidence-based health policies. A primary focus of my dissertation is policy evaluation – specifically Chapters 4 and Chapter 5. Chapter 4 is a methodologically-focused study of statistical approaches to modeling policy effects using secondary, aggregated data. This chapter also includes a worked example to illustrate these different approaches, by examining the association between state-level legalization of recreational marijuana and purchasing of alcoholic products. While prior studies have compared some of the modeling approaches I used (fixed effects, random effects, generalized estimating equations, autoregressive integrated moving average, and the synthetic control approach),[13,44–49] none to my knowledge have compared simultaneously across all of these approaches.

Quasi-experiments for policy evaluation

Policy evaluation is a key step in understanding and promoting public health. While the gold standard method for evaluating the effectiveness of public health interventions is through a randomized controlled trial (RCT), there are several practical and ethical barriers that prevent the random allocation of policies across cities, counties, states, or countries.[47] Thus, to evaluate the effects of new policies a quasi-experimental design can be used whereby people exposed to a policy of interest are compared to people unexposed to the policy. Quasi-experiments are favored given they rely on fewer or weaker assumptions than observational designs while offering a stronger justification for causal interpretations.[50] In quasi-experiments the comparison group is often selected to match the exposed group as closely as possible to mimic the exposed group's counterfactual (i.e., what the exposed group would have looked like had all else been held equal except its exposure status).[51]

From the perspective of causal inference, evaluating a policy change has the benefit of examining a change in exposure status among participants that is made at a level upstream from the individual.[52] This illustrates one key characteristic that differentiates quasi-experiments from other observational studies: the supposed "exogeneity" of exposure (i.e., people do not self-select into an exposure status, but are assigned it by exogenous entities like government).[53] I use the term "supposed" because while people do not have the same level of agency in their policy exposure status as individual-level exposures (e.g., exercising, eating healthy foods), there is still likely some degree of exposure self-selection when it comes to policy exposure (e.g., moving to states with

preferred laws and regulations, influencing policy-making decisions of your representatives).

When researching policy evaluations, one may encounter the term "natural experiment." Often natural experiment and quasi-experiment are both used interchangeably to describe study designs for policy evaluation, yet there are important nuances between them. While both share an assumed exogeneity of exposure (i.e., policy assignment), a natural experiment is termed as such because often the exposure of interest is a naturally occurring event (e.g., a hurricane, an earthquake).[51] At other times, the exposure may be natural in the sense that it was not planned or intended to influence the outcome of interest.[54] As such, natural experiments have an assumed random allocation of exposure status. This assumption allows for certain analytic techniques that depend on an assumption of random treatment assignment, such as instrumental variables (IV) analyses.[52] In contrast, quasi-experimental designs evaluate a planned or intentional exposure that resembles an RCT but lacks random assignment and is thus unlikely to meet the exchangeability assumption for an instrumental variable.[54]

Ultimately, the goal of policy evaluation is to allow for valid policy-relevant inference (i.e., causal inference about the effect of a policy compared to its counterfactual) minimizing sources of bias that can produce misleading conclusions.[13] Researchers must carefully consider the kind of data available to determine what approaches might be best for evaluation. Here, I will discuss three commonly used approaches to evaluating

quasi-experimental designs: difference-in-differences, interrupted time series, and controlled interrupted time series.[55]

Difference-in-differences

A difference-in-difference (DiD) approach, also called the untreated control group design with pretest and posttest or nonequivalent control group pretest design, uses observations before and after an intervention and incorporates both an exposed and unexposed group.[51,56–58] This approach compares the change (or difference) over time in the outcome of interest in an exposed group versus the change over time in an unexposed or control group.[57] The unexposed (or control) group is considered a representation of the exposed group's counterfactual had that group not been exposed.[59] In the most basic form, a DiD approach uses two outcome observations per group: one before the intervention, and one after.[55,57] In the basic DiD design, trends in the outcome pre-intervention are assumed to be parallel but cannot be verified given the lack of pre-intervention timepoints.[55] The structural form of this basic DiD can be written as:

$$Y_{ij} = \beta_0 + \beta_1 * Exposed_j + \beta_2 * Post_t + \beta_3 Exposed_j * Post_t + \varepsilon_{ij}$$

where Y_{ij} represents the outcome for subject *i* in group *j*; $Exposed_j$ is an indicator for the exposed group (e.g., who will get the policy); *Post* is an indicator for observations occurring after the policy change; and ε_{ij} is the error term. The coefficient β_3 for the interaction term between *Exposed* and *Post* represents the difference in pre-post change in *Y* between the exposed group and the unexposed group. Typically, models

that use a DiD approach also incorporate fixed effects that represent the subject (e.g., individuals, states). A more in-depth discussion of statistical modeling using a DiD approach can be found in Chapter 4.

In DiD models, selection of appropriate unexposed groups that can serve as the exposed group's counterfactual is challenging. Typically, researchers may match unexposed and exposed groups based on selected characteristics (e.g., demographics, state population). When multiple pre-intervention observations are available, researchers may also choose to match based on trends in the outcome of interest prior to the intervention. The latter approach, however, may induce bias in DiD estimates through regression to the mean if exposed and unexposed groups are drawn from different distributions.[60]

Interrupted time series

Interrupted time series designs are suited for longitudinal data, where measurements on an outcome of interest in a population are taken over multiple timepoints.[56,61] These intervals are commonly monthly,[62] but could also be weekly, quarterly, annually, or any other reasonable interval depending on available data. In addition, there must be a clearly-defined period of implementation for the intervention so that pre- and post-intervention observations can be delineated.[61] In a simple ITS design, there is no control group to serve as a counterfactual; rather, the pre-intervention trend in the exposed group serves as its counterfactual.[56,61] Thus, comparing the post-intervention trend to the pre-intervention trend provides an estimate of the intervention effect. Because of the need to establish a pre-intervention trend in order to determine the counterfactual,

a long time series of the outcome is required (usually at least 50 observations,[56] ideally evenly split pre- and post-intervention).[61] However, a long series is a potential double-edged sword; having more observations risks including substantial changes (or "shocks") in the series trend due to historical events that affect the outcome trend prior to or following the intervention of interest.[61] Figure 2.2 shows a representation of the simple ITS design, where O_i represents an observation on a subject at time *i*.

O_1	O_2	O_3	O_4	O_5	X	O_6	O_7	O_8	O_9	O_{10}

Figure 2.2. An interrupted time series design. Each O represents an observed outcome value in the time series, and X represents the "interruption" when the policy took effect. Figure adapted from Cook and Campbell.[56]

Contrary to conventional calculations for power, for an ITS power is primarily a function of the number of timepoints within a series. Increasing the number of timepoints increases power for hypothesis testing, and studies with few timepoints or with small expected effect sizes risk being underpowered.[63] Power for an ITS also depends on several other factors, including distribution of data pre- and post-intervention, variance in the outcome, effect magnitude, and confounding effects like seasonality.[61]

The effects estimates by an ITS design usually fall into two types: changes in intercept and changes in slope.[56] A change in the intercept may also be characterized as the immediate impact of an intervention, where the level of a series rises or drops following intervention. A change in slope can also considered a change in drift or trend. Other less

common effects may occur as well: persistent effects, decaying or ramping up effects, and delayed effects.[56,64] These effects, however, suffer from several threats to internal validity.[65] A major threat, called history bias, occurs when factors other than the intervention of interest occur around the same time as the intervention and impact the outcome.[56,65,66] In the case of policy evaluations, where regulations and environmental changes are occurring frequently, there is a strong possibility that changes seen in an outcome may be due to these co-occurring factors while making it appear that the policy of interest is responsible. There are several approaches to remedy this, such as incorporating non-equivalent or matched controls into analyses.[56,66]

Controlled interrupted time series

Both Chapter 4 and Chapter 5 of my dissertation employed a controlled interrupted time series (CITS) design. CITS is an extension of both ITS and DiD, combining the benefits of both by making use of multiple timepoints before and after an intervention (ITS) and incorporating a comparison group that mimics the treated group's counterfactual (DiD).[55,61] A key advantage of the CITS design is that exposed and unexposed groups can be examined for comparability pre-intervention by incorporating multiple pre-intervention observations in a long time series.[55] In addition, a CITS can account for the history bias inherent in the simple ITS designs while also accounting for issues that studies with a single pre- and post-intervention observation (e.g., maturation bias).[56,66] Figure 2.3 illustrates a standard CITS design:

O_1	O_2	O_3	O_4	O_5	X	O_6	O_7	O_8	O_9	O_{10}
O_1	O_2	O_3	O_4	O_5		O_6	O_7	O_8	O_9	O_{10}

Figure 2.3. A controlled interrupted time series design. Each O represents an observed outcome value in the time series, and X represents the "interruption" when the intervention of interest took effect. The top series is considered the exposed (or treated) series while the bottom series is the unexposed (or no-treatment control) series. Figure adapted from Cook and Campbell.[56]

Much like with the DiD design, selection of appropriate unexposed groups is important. Lopez Bernal et al. describes several options for selecting appropriate unexposed groups.[66] The recommend that choice depend on the geographic scale of the intervention (e.g., cities, counties, states), potential confounders, availability of appropriate unexposed groups (i.e., sometimes there may not be any well-suited unexposed groups), and the nature of the intervention (e.g., whether it is sustained or if it is active only temporarily).[66] In addition, it is recommended to include multiple controls of different types where several possible co-occurring and confounding events exist.[66]

While the CITS design strengthens both the DiD and ITS designs, it is still prone to several threats to validity. Many of these are found in either the DiD or ITS designs, including serial correlation, seasonality, non-linearity, and overdispersion (for Poisson models).[56,66] Design choices, such as limiting the time series, can help address non-linearity by excluding external shocks. Statistical methods are also available to address serial correlation, non-linearity, and overdispersion. Chapter 4 of this dissertation provides a more in-depth discussion of statistical modeling choices for CITS designs.

Policies and racial/ethnic health disparities

While policies are effective tools for enacting population-level health changes,[35] the benefits and consequences of policies may not be distributed equally among all subgroups of a population. Building off Rose's insights into targeted and population health approaches, Frohlich and Potvin point to how population-level interventions can exacerbate public health disparities among vulnerable populations (i.e., a subgroup who is at greater risk of risk factors because of shared social characteristics).[67] For example, people from racial and ethnic minority groups, while hailing from a wide variety of backgrounds, may all share increased risk for several adverse health outcomes (e.g., COVID-19, chronic inflammation) due to racial discrimination.[68,69] Vulnerable populations may benefit less from a population-level intervention than populations with greater privilege, resources, or power. Frohlich and Potvin illustrate this by adapting Rose's graphic of shifting the population risk distribution for a given disease (Figure 2.4). In this illustration, the effect an intervention has depends on the different distributions of risk exposure across a population. People with greater risk exposure may be considered a more vulnerable sub-population who, because of underlying mechanisms shared within their social strata, have greater risk exposure and see little benefit from an intervention. In contrast, people with less risk exposure may see greater benefit from the intervention. If an intervention does not target these underlying differences in risk exposure, the result is the risk curve for a given disease widening rather than shifting (and the benefits of an intervention being concentrated among those who are less vulnerable to begin with). This is further explained by Link and Phalen's Theory of

Fundamental Causes, which argues that benefits from our interventions to control diseases and improve health are distributed based on knowledge, wealth, power, prestige and social capital.[70]

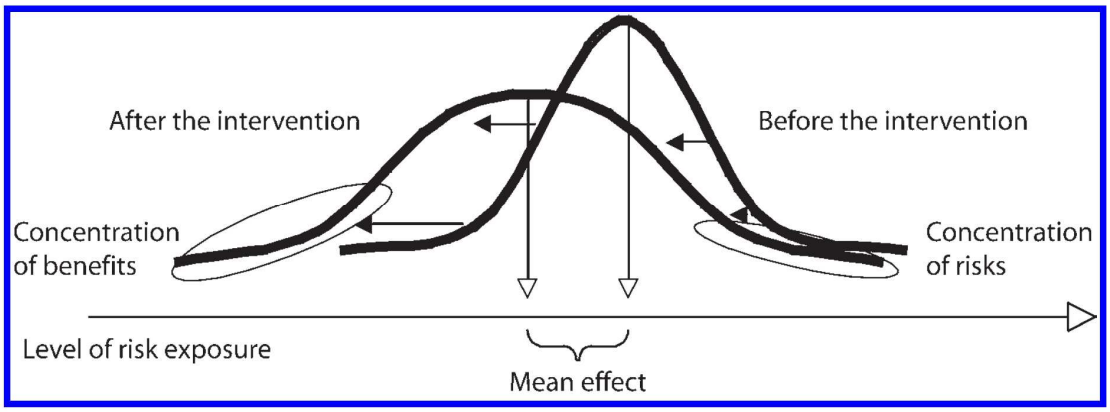

Figure 2.4. Population distribution of risk for a given disease before and after an intervention. Rather than the curve being shifted to the left (and thus reducing risk equally across the entire population) a uniform distance for everyone, the risk curve widens such that subgroups with less exposure benefit more while groups with greater exposure (i.e., vulnerable populations) benefit little. Copied from Frohlich and Potvin[67] and adapted from Rose.[10,35]

Additional work has been done to expand how population-level interventions interact with health disparities. McLaren et al. argue that interventions are less likely to exacerbate (and may sometimes help reduce) health inequalities if they target structural impediments to healthy behaviors rather than targeting the behaviors themselves.[12] The authors provide clean indoor air laws as an example of a structural population-level intervention that shows less evidence of worsening health disparities by socioeconomic status (SES). Benach et al. present classifications for how policies impact both the movement and shape of Rose's population risk curve, and gives examples of when

policies may differentially harm or benefit certain subgroups.[11] Benach et al. provide the example of smoking prevention policies in the United Kingdom (e.g., restrictions on smoking in workplaces), which have caused a decline in smoking prevalence but also widened the disparity in smoking prevalence between high and low socioeconomic groups.

People of color are another subpopulation that, because of the effects of protracted structural racism, tend to have fewer resources and privileges to benefit from health interventions. There is extensive research on racial and ethnic disparities in substance use and related adverse health problems, but relatively little work examining the differential impact of policies on these outcomes across racial/ethnic groups.[71] Some studies have shown unintended consequences from policies that disproportionately affect racial/ethnic minority groups. For example, young adults from racial and ethnic minority groups may experience increased criminalization (e.g., arrests) due to policies regulating drinking age and youth access to tobacco.[72] There may also be differential benefits from policies, whereby certain groups see greater improvements than others. In a review of state-level alcohol taxes and alcohol availability restrictions (e.g., outlet density), Subbaraman et al. found higher beer taxes were associated with reductions in odds of alcohol-related health consequences, with increased cost leading to more difficulty in affording alcoholic beverages. Reductions in alcohol-related health consequences were most pronounced among Black women, and alcohol use reductions were most pronounced among Hispanic people.[73] In Chapter 5 of my dissertation, I explored how Medicaid expansion – a population-level health intervention addressing

structural impediments to wellbeing – may differentially affect the use of harmful substances across different racial/ethnic minority groups.

Conclusion

Substance use, cancer, pain and policies are all intertwined. While substance use is a population-level public health issue, certain subgroups are particularly vulnerable to substance use-related adverse effects. Policies are one possible avenue to address structural impediments to wellbeing, but interventions must be evaluated carefully or risk providing false and misleading conclusions for policymakers, activists, and health professionals. Researchers need to carefully select the appropriate modeling approach to quantifying a policy effect on health outcomes, and interpret findings in light of each approach's limitations. Yet even when policies are properly evaluated and show promising results at a population level, the impact they have may differ across subpopulations. Additional consideration must be given to how policy effects may vary across subgroups, particularly groups that are more vulnerable or disproportionately experience hardships and barriers to better health and wellbeing.

CHAPTER 3: Cancer Pain and Substance Use Self-Medication

Abstract

Background: Cancer survivors are at increased risk of pain due to their either cancer and/or treatments. Substances like alcohol may be used to self-medicate cancer pain, however these substances pose their own health risks that may be more pronounced for cancer survivors.

Methods: We used cross-sectional data from the Behavioral Risk Factor Surveillance System (BRFSS) 2012-2019 to quantify the association between cancer pain and alcohol use. We used negative binomial regression, with interaction terms added to examine variations across age, sex, and race. We also examined whether alcohol use relates to cancer pain control status.

Results: Cancer survivors with cancer pain were more likely to be younger, female, Black, and to have been diagnosed with breast cancer. Cancer pain was associated with lower alcohol consumption (incidence rate ratio [IRR]: 0.88, confidence interval [CI]: 0.77, 0.99). This association was primarily among people 65 and older, women, and white and Hispanic people. Cancer pain control status was not related to alcohol use.

Conclusions: Lower alcohol use among cancer survivors with pain has many possible explanations, including several alternative pain management strategies or a decrease in social engagement. Our findings of racial and gender disparities in cancer pain are consistent with the broader evidence on disparities in pain.

Implications for cancer survivors: Pain management for marginalized groups of cancer survivors should be improved. Healthcare providers should screen cancer survivors for both pain and substance use, to prevent unhealthy self-medication behaviors.

Introduction

Cancer survivors (people who have a current or past diagnosis of cancer) are a growing population. In 2019, cancer survivors made up 5% (16.9 million) of the United States population, [74] and it is projected to grow to 7% of the population (26.1 million) by 2040.[75] Some of this increase can be attributed to improvements in cancer treatments that extend survival times across different cancers.[76,77] In 2011, 69% of cancer survivors lived beyond five years after their diagnosis compared to less than 50% of survivors in 1975.[78] In addition, the U.S. population of cancer survivors is expected to continue to grow as the median age of the population becomes older [79] given that cancer incidence increases with age.[80]

Compared to the general population, cancer survivors are at greater risk for several health problems, including kidney disease,[81] heart disease,[82] and diabetes mellitus.[83] Cancer survivors also have elevated risk of developing a new cancer (i.e., second primary cancer) compared to the general population.[27–32] and thus are of particular public health interest.[30,31] One possible driving force behind this increased risk of further incident cancer is consumption of alcohol (a Group 1 carcinogen linked to several types of cancer).[84] In a meta-analysis of alcohol consumption and second primary cancer risk, Druesne-Pecollo et al. compiled data on cancer patients with upper aerodigestive tract (UADT) cancers from eight cohort and eleven case-control studies.[85] Contrasting the highest category of alcohol consumption to the lowest across studies, the authors found that higher alcohol consumption was associated with a greater risk of second primary cancers across all sites (risk ratio: 1.60, CI: 1.22, 2.10). Dose-response meta-analyses

showed that for every 10-gram increase in alcohol intake per day, risk of a UADT second primary cancer increased (RR: 1.09, CI: 1.04, 1.14). Another meta-analysis, this time examining primary cancer recurrence, showed an increased risk of cancer recurrence among those with the highest level of alcohol consumption compared to those with the lowest (RR: 1.17; CI: 1.05, 1.31).[86] A systematic review examining second primary breast cancer and breast cancer recurrence found that six of the eleven studies included showed a positive association between alcohol and breast cancer recurrence, and two of five studies showed a positive association between alcohol and second primary breast cancer.[87]

Cancer survivors are also at high risk for experiencing pain due to their cancer or cancer treatment (termed "cancer pain"),[88,89] with nearly 35% of survivors reporting chronic pain.[90] Additionally they regularly report insufficient control of their cancer pain.[91] The prevalence of cancer pain varies by the phase of cancer survivorship. A meta-analysis of 122 studies on cancer pain found that 39% of survivors experienced cancer pain after cancer treatment, 55% during cancer treatment, and 66% if they had advanced, metastatic, or terminal cancer (irrespective of cancer treatment status).[92] Often cancer survivors are provided inadequate information, guidance, or resources to address their cancer pain,[89] which can have a debilitative impact on daily life including being unable to work. Cancer pain is also associated with mental health issues (e.g., depression, anxiety) and physical disability, which can also lead to being unable to work.[93–95]

While guidelines have been established for healthcare providers regarding cancer pain management for cancer survivors,[96,97] there are still barriers to effective cancer pain management, such as limited access to pain or palliative care specialists, poor pain assessment, and lack of knowledge regarding pain treatment.[98] Cancer pain can persist or arise after cancer treatment, meaning some cancer survivors are left without the active support of a cancer care team while dealing with their pain.[89] As a result, cancer survivors may seek to self-medicate to alleviate the pain they are experiencing.

Pain is a significant risk factor for substance use and abuse.[99] Lazarus and Folkman's stress, appraisal and coping theory[100] suggests that individuals may self-medicate using substances (e.g., alcohol, drugs) to cope with stressors like chronic pain. Pain is conceptualized as an important stressor that interferes with everyday life and can lead to associated stressors (e.g., depression).[101,102] Coping, in turn, is defined by Lazarus and Folkman as behavior made in response to a stressor.[100] Substance use (i.e., alcohol consumption) can be one such coping mechanism to temporarily alleviate stressors like pain. The current study draws on stress, appraisal, and coping theory to explain why cancer pain may lead to self-medication using these substances.

Several studies have shown that people who suffer from pain are at an elevated risk of consuming harmful substances as a form of self-medication to ameliorate their pain.[14,15] For cancer survivors, pain caused by their cancer or cancer treatment may also be a risk factor for substance use self-medication but few studies have examined the role of cancer pain in substance use among cancer survivors. In a study of childhood cancer

survivors, the presence of cancer pain was associated with a 1.2 times greater odds of heavy alcohol drinking compared to survivors without cancer pain (though this estimate was not statistically significant).[103] Zeltzer and colleagues found that, while cancer survivors were less likely to be current or heavy drinkers compared to siblings without a cancer history, survivors diagnosed with somatic distress disorder (i.e., an extreme focus of physical symptoms like pain or fatigue that results in problems functioning in daily life) had higher odds of heavy drinking (OR, 1.7; CI: 1.2, 2.2) compared to survivors without somatic distress.[104] The relationship between pain and substance use may also vary across different social groups. Previous research has shown differences in behavioral strategies for pain-related coping across age,[105] sex,[106] and race/ethnicity.[107]

There is an important need for research that examines patterns of substance use among people suffering from chronic cancer-related pain given that substance use may be increasing risk of second and recurrent cancers. In light of gaps in research on cancer pain and substance use, this study will examine the relationship between cancer pain and substance use (i.e., alcohol use) among cancer survivors who have completed their cancer treatment.

Methods

Study Design and Data

This study uses data from the Behavioral Risk Factor Surveillance System (BRFSS) to determine the association between cancer pain and substance use. The BRFSS is an annual telephone survey conducted by the U.S. Centers for Disease Control and

Prevention since 1984.[108] Currently the BRFSS collects data on the health conditions and behaviors of adults across all 50 states, with over 400,000 surveys completed each year. This study combines eight cross-sectional waves of BRFSS data (specifically, data collected from 2012-2019).

Beginning in 2009, the BRFSS included an optional state module on cancer survivorship, which includes questions about cancer history (e.g., prior cancer diagnoses, age of first diagnosis, cancer type) and survivorship care (e.g., cancer pain, health insurance coverage for cancer treatment). Because this is an optional module, not all 50 states are represented and the states that are included can vary from year to year (the states and territories included are: Alabama, Alaska, Delaware, Georgia, Hawaii, Idaho, Indiana, Iowa, Louisiana, Michigan, Mississippi, Missouri, Nebraska, New Jersey, Oklahoma, South Dakota, Vermont, Wisconsin, Wyoming, and the Virgin Islands). In the present study, data from this optional module were analyzed beginning in 2012 due to changes in the BRFSS survey methodology.

Sample

The study sample was restricted to cancer survivors who completed their cancer treatment. In the BRFSS, participants are only asked about cancer pain if they report having completed treatment for their cancer (from here on called “post-treatment cancer survivors”). There was no information to discern whether or not post-treatment cancer survivors were free of cancer. The final sample size was 25,054 participants.

Exposure Variable: Cancer Pain

The BRFSS optional cancer survivorship module includes the question “Do you currently have physical pain caused by your cancer or cancer treatment?” that can be answered with “Yes,” “No,” or “Don’t know/Not sure.” Only 1% of the sample answered, “Don’t know/Not sure” and these participants were excluded from the analyses. Thus, cancer pain was measured with a Yes/No binary variable.

We also included a measure of cancer pain treatment status (medication, non-medication; and whether or not the pain is under control) and substance use. In the BRFSS, the question “Is your pain currently under control?” was asked as a follow-up for participants who said they currently have cancer pain. Answer options were: “Yes, with medication (or treatment),” “Yes, without medication (or treatment),” “No, with medication (or treatment),” “No, without medication (or treatment),” and “Don’t know/Not Sure.” Analyses used a four-level categorical variable matching the categories of the original BRFSS measure but excluding the “Don’t know” category (because “Don’t know” answers account for only 2% of responses and do not have a sufficient sample size for inference).

Outcome Variables: Alcohol Use

The outcome was alcohol consumption over a 30-day period. For alcohol, the BRFSS survey questions ask how many days a given person drank alcohol (“During the past 30 days, how many days per week or per month did you have at least one drink of any alcoholic beverage such as beer, wine, a malt beverage or liquor?”), the average number of drinks they have on those days (“During the past 30 days, on the days when you

drank, about how many drinks did you drink on the average?", and how many days they binge drank ("Considering all types of alcoholic beverages, how many times during the past 30 days did you have 5 or more drinks for men or 4 or more drinks for women on an occasion?"). A drink is defined as "equivalent to a 12-ounce beer, a 5-ounce glass of wine, or a drink with one shot of liquor." We calculated a continuous quantity-frequency variable for the amount of alcohol consumed in 30 days by multiplying the number of drinking days by the average number of drinks per day. Because self-report measures of alcohol consumption tend to underestimate average alcohol consumption by omitting binge drinking, we used indexing[109,110] to incorporate information on binge drinking into the quantity-frequency calculation.

Covariates

Regression models included several sociodemographic and economic variables that are associated with both substance use and cancer pain. Prior studies have shown that substance use for alcohol varies by sex,[111] stress related to structural/institutional/interpersonal racism,[112,113] age,[114] and access to healthcare.[115,116] These factors are also related to risk of experiencing cancer pain.[117,118] Thus, key covariates were sex, race/ethnicity (a proxy for racism), categories of age (based on categories used in prior studies of cancer survivors),[79,119] educational attainment, healthcare coverage (a proxy for healthcare access), and most recent cancer type to be diagnosed with (categorized based on previous studies examining cancer

pain).[89,92,120] Because of regional variation in both alcohol use and alcohol-related policies, we included dummy variables for state.

Analysis

To examine the relationship between alcohol use and cancer pain, we used negative binomial regression. Alcohol was fit as a count outcome, and the negative binomial model was most appropriate due to overdispersion (i.e., the variance exceeded the mean). To examine whether the relationship between cancer pain and substance use varied across key demographic characteristics (i.e., age, sex, and race/ethnicity), we fit the same negative binomial model three times – one for each demographic characteristic interacted with the binary indicator for cancer pain. We also estimated the marginal mean number of drinks for those with cancer pain and for those without cancer pain across the entire sample of 25,054 post-treatment cancer survivors and stratified by the three key demographic characteristics. This was done using the *mimrgns* community-contributed program for Stata.[121]

A negative binomial model was also used to measure the relationship between alcohol use and cancer pain treatment. Covariates used in the previously described models were used in this model as well, except for state dummy variables due to nonconvergence with multiple imputation models. To account for missing values in the outcome and model covariates, we used multivariate imputation with 100 iterations to reduce bias in regression estimates and standard errors. Specifically, we used multiple imputation by chained equations (MICE) in which separate imputation models are

specified for each variable with missing data, and an appropriate distribution for each variable is chosen. We assumed data were missing at random (MAR) after including model covariates and key auxiliary variables. Among the sample of 25,054 post-treatment cancer survivors, less than 1% were missing values for cancer pain, 2% had missing values for alcohol use, less than 1% for education, and less than 5% for cancer type. Among the 1,794 post-treatment cancer survivors who reported cancer pain, 2% were missing values for cancer pain treatment status.

Results

Descriptive

The demographic characteristics, alcohol consumption, and cancer types among the sample of post-treatment cancer survivors (n=25,054) are shown in Table 3.1. The sample was primarily female (61%), white, (91%), had some form of health insurance coverage (97%), had an income of at least $35,000 (52%), and had undergone some education beyond high school (64%). Among the six named cancer types included, breast cancer was the most common (17%) followed by urogenital (13%). The majority of post-treatment cancer survivors reported having no pain due to cancer (92%; n=23,167). On average, respondents who reported cancer pain had fewer alcoholic drinks over a 30-day period compared to respondents who reported no cancer pain (7.13 drinks vs. 9.56).

A disproportionately higher percentage of post-treatment cancer survivors with cancer pain were younger than 65 (57% among survivors with cancer pain versus 32% among

survivors without cancer pain), female (72% versus 60%), Black (7% versus 3%), and had breast cancer (31% versus 16%), and had less than a college degree (36% versus 29%). Cancer survivors with a head/neck cancer diagnosis were most likely to report cancer pain, followed by lung/bronchus, then breast, gastrointestinal, gynecological, and urogenital (not shown in tables).

Multivariable

The multivariable model examining alcohol use is shown at the top of Table 3.2. Compared to post-treatment cancer survivors without cancer pain, survivors with pain reported having fewer alcoholic drinks over a 30-day period (adjusted incidence rate ratio [IRR]: 0.88; confidence interval [CI]: 0.77, 0.99). Based on these regression estimates, the marginal mean number of alcoholic drinks consumed over 30 days for post-treatment survivors with cancer pain was 6.75 (CI: 6.97, 7.63) while the average number for survivors without pain was 7.71 (7.46, 7.97) drinks.

Table 3.2 also shows estimates from the three multivariable models examining whether the association between cancer pain and alcohol use varied across age, sex, and race/ethnicity. Among those aged 18-44 there was no relationship between cancer pain and alcohol use, while those 45-64 showed a non-significant 13% decrease (IRR: 0.87; CI: 0.72, 1.04) and those 65 and over showed a statistically significant 19% decrease (IRR: 0.81; CI: 0.68, 0.98) in alcohol consumed over a 30-day period. We were unable to conclude that there was a difference in this association between the 18-44 and the 65+ age groups (p=0.17). The association between cancer pain and alcohol use also did not

differ statistically significantly between participants identifying as male and as female. However, when stratifying by sex we found that women showed a 15% decrease in alcohol consumption (IRR: 0.85; CI: 0.73, 0.99) while men showed no statistically significant change. Across race and ethnicity, reductions in alcohol use associated with cancer pain were primarily found among white (IRR: 0.84; CI: 0.73, 0.96) and Hispanic (IRR: 0.36; CI: 0.15; 0.90) cancer survivors.

When restricting the sample to post-treatment cancer survivors who reported having cancer pain (n=1,794), we found no statistically significant association between cancer pain treatment status and the amount of alcohol consumed over 30 days (Table 3.3).

Discussion

We hypothesized, based on theories of stress, appraisal, and coping, that post-treatment cancer survivors with cancer pain would consume more alcohol compared to survivors without pain, as a way to self-medicate for their cancer pain. Instead, cancer pain was associated with fewer alcoholic drinks on average. While a statistically significant difference, the actual difference (approximately one fewer drink over a 30-day period) may not be clinically significant in its impact on health.

We found evidence of disparities in cancer pain among post-treatment cancer survivors, with greater prevalence of pain among those who were younger than 65, Black, female, had less than a college education, and had breast cancer. The inverse relationship between cancer pain and age is consistent with some previous studies showing both a higher prevalence of both cancer pain and more frequent pain flares among younger

cancer survivors.[89,117] However, the literature on the relationship between age and cancer pain is mixed and reasons for any differences are not well understood.[92] Black cancer survivors tend to have higher cancer pain severity,[122] and are more likely to receive inadequate pain treatment compared to white cancer survivors even when experiencing similar painful conditions.[123] The higher percentage of breast cancer diagnoses among people with cancer pain may be partly explained by the higher percentage of women in this group. While there is some evidence of disparities in cancer pain prevalence and treatment across gender (with women more likely to experience inadequate pain management than men), studies are few and more research in this area is needed.[124,125]

The majority of the sample reported having no pain due to cancer. However this statistic should not be compared to studies that attempt to estimate cancer pain prevalence. Because the purpose of this study was to quantify the association between cancer pain and substance use (not to estimate a true prevalence of cancer pain), and due to the small number of respondents across certain demographic categories (e.g., Asian respondents, respondents with head or neck cancer) and presence of singleton primary sampling units within our subsample of post-treatment cancer survivors, we did not incorporate survey weights into descriptive statics or regression models. In addition, the BRFSS optional module on cancer survivorship (which asks the question about cancer pain) was not asked in all 50 states; state health departments choose whether or not to ask questions in optional modules, meaning our sample of post-treatment cancer survivors is not a true random sample.

Counter to our hypotheses, post-treatment cancer survivors with cancer pain drank less alcohol on average compared to survivors without pain. Moreover, among post-treatment cancer survivors with cancer pain, neither pain treatments nor whether pain was under control predicted alcohol use. There are several potential reasons for the inverse relationship between cancer pain and alcohol use, which runs counter to findings from both Lown et al.[103] and Zeltzer et al.[104] In the former study, there was no significant difference in the likelihood of heavy drinking between childhood cancer survivors with cancer pain and those without cancer pain. The authors measured heavy drinking as five or more drinks in a day for women and six or more drinks for men. In contrast, we measured alcohol consumption over a 30-day period, and incorporate episodes of binge drinking into this measure rather than examining it as a separate binary variable. It is possible that while cancer survivors have a similar likelihood of heavy drinking compared to the general population, they may consume fewer alcoholic beverages on average over a 30-day period. Zeltzer and colleagues examined somatic distress, which is a broader measurement than cancer pain (somatic distress includes distress due to cancer or non-cancer pain, weakness, shortness of breath, or other physical health problems). Thus, respondents with high somatic distress not only may have physical health issues, but also may be experiencing a psychological disorder. Psychological distress, either through prior history or because of a cancer diagnosis, may be positively associated with heavy alcohol consumption among cancer survivors. To support cancer survivors who may use or misuse alcohol, future studies should examine the role of psychological distress and/or presence of psychopathology in substance use

and differentiate distress attributed to pain from distress attributed to other sources such as prognosis or treatments.

Another possibility is that post-treatment cancer survivors with cancer pain may be using other methods of pain control, such as prescribed opioid therapy, and limiting alcohol consumption to avoid harmful interactions between alcoholic beverages and medications based on physician advice. While co-use of alcohol and opioids may be relatively common,[126] few studies have examined pain-related co-use and opportunity remains for research on the interaction of different substances for self-medication. A study of over 5,000 individuals from the 2005 Danish health survey found that people reporting chronic pain were less likely to binge drink than people without pain (OR: 0.87; CI: 0.74, 1.02), and the likelihood was further reduced for people with chronic pain who were undergoing opioid treatment (OR: 0.36; CI: 0.22, 0.57).[127] While opioid prescribing has decreased since 2010, opioid overdoses from opioid misuse have increased and the amount of opioids prescribed in 2015 was three times higher than the amount in 1999.[128,129] There is a possibility that opioids may be substituted for alcohol to self-medicate cancer pain, but research is needed to determine the nature of the relationship between alcohol and opioid use. In addition, the present study is restricted to cancer survivors who have completed their cancer treatment. Because of the variability in both the prevalence and intensity of cancer pain depending on the phase of cancer survivorship (e.g., prior to or during treatment, immediately following treatment),[92] the relationship between cancer pain and substance use may differ across these phases.

When examining the relationship between cancer pain and alcohol use across demographic characteristics, we found that survivors 65 and older, women, and white and Hispanic people saw decreases in alcohol use while other groups did not. There are several possible explanations for these differences. First, different social groups may tend to use different coping strategies for pain. In a mixed-methods study comparing how younger (18-59 years old) and older (60+ years old) adults with cancer-related pain adapt to their pain, older adults were more likely to modify their daily activities to accommodate their pain and forego unhelpful pain control behaviors. Our finding that pain is associated with a reduction in alcohol consumption among white cancer survivors may be explained by disparities in access to healthcare and analgesics;[130] white cancer survivors, with better access to pain treatments like opioid therapy, may be less likely to consume alcohol to avoid harmful interactions with medications. However, this would not account for the reduced alcohol use among Hispanic cancer survivors with pain given that Hispanic cancer survivors have been shown to receive inadequate treatment with analgesics compared to white survivors. We are unsure of what mechanisms may explain this association and more research is needed to investigate this, as well as mechanisms behind variability in the relationship between cancer pain and alcohol use across other social groups. Finally, differences may be partially explained by differences in sample size and power to detect these effects: survivors aged 65 and over, women, and white participants were the most prevalent across age, sex, and race respectively.

Among post-treatment cancer survivors who were experiencing cancer pain, both pain medication/treatment use and the status of their pain (controlled or uncontrolled) did not predict alcohol consumption. Compared to survivors whose pain was under control due to medications or other treatments, only survivors whose pain was not under control (even with medications or treatments) differed notably (though still not statically significantly) by drinking less alcohol on average. One possible reason for this is that respondents who report their pain is not under control may be experiencing more frequent or intense pain, and thus may withdraw from social activities that could involve alcohol consumption.

Limitations

The findings from this study should be viewed in light of several limitations. The optional BRFSS modules for both cancer survivorship was offered in a limited number of states, limiting generalizability to the wider U.S. While we were interested in examining the association between cancer pain and other substances (e.g., marijuana), the available sample size for examining marijuana use among cancer survivors was small due to limited use of the optional BRFSS marijuana use module across states. Future research exploring this question should ensure adequate sampling to power models of marijuana use and cancer pain. Our sample of cancer survivors who reported cancer pain (7%) was much lower than prevalence estimates in other studies that analyze samples from cancer care settings or other community samples. While this unexpected low prevalence does not hamper the internal validity of our analyses, researchers who wish to estimate

cancer pain prevalence from BRFSS must take into account the limitations of these data compared to other sources. Black cancer survivors, who experienced a disproportionately higher prevalence of cancer pain compared to other racial and ethnic groups, were underrepresented in our sample (3% of all cancer survivors). Systemic factors, such as underdiagnosis of pain for Black patients compared to white patients and long-held distrust of research, may contribute to less representation from Black cancer survivors and hinder our understanding of disparities in cancer survivorship. Because no identifiers were included in the dataset, data were treated as cross-sectional which prevents causal statements about the relationship between cancer pain and substance use. Cross-sectional data also prevents us from exploring other substantive questions around the relationship of alcohol use and cancer, such as the role of alcohol misuse prior to cancer diagnosis. Individuals with a history of alcohol misuse may differ in whether alcohol is used as a coping strategy, and consumption levels following cancer treatment. More research using longitudinal data is warranted to determine whether alcohol misuse history is an important screening factor for cancer survivors. Residual confounding may remain, such as the type of cancer treatment a survivor received, whether cancer remained after treatment, LGBTQ status, and the level of social support available to deal with pain and substance use.

Implications and Conclusions

Our findings contribute to a body of literature on cancer pain management, but there remains a paucity of studies examining how cancer pain relates to substance use.

Because a high proportion of cancer survivors with pain report inadequate pain management, it is important to understand how survivors cope with their pain and whether they do so in ways that are harmful. Given the disparities in cancer pain across race/ethnicity, gender, and age seen here, there is a particular need to improve cancer pain management for marginalized groups.

Table 3.1. Alcohol use and demographic characteristics and of study sample by cancer pain status

	All survivors (n=25,054)	Cancer pain (n=1,794)	No cancer pain (n=23,167)
	Mean (SD)	Mean (SD)	Mean (SD)
Alcoholic drinks consumed (30 days)[1]	9.39 (0.16)[2]	7.13 (0.48)[2]	9.56 (0.16)[2]
	% (n)	% (n)	% (n)
Age			
18-44	5% (1,163)	10% (185)	4% (966)
45-64	30% (7,458)	47% (846)	28% (6,591)
65 and over	65% (16,241)	42% (749)	67% (15,433)
Sex			
Male	39% (9,780)	28% (508)	40% (9,236)
Female	61% (15,274)	72% (1,286)	60% (13,931)
Race/Ethnicity			
White	91% (22,759)	83% (1,482)	92% (21,201)
Black	3% (866)	7% (131)	3% (730)
American Indian/Alaskan Native	1% (362)	3% (51)	1% (309)
Asian	<1% (38)	<1% (4)	<1% (34)
Native Hawaiian/Pacific Islander	<1% (56)	1% (9)	<1% (47)
Hispanic	1% (250)	2% (39)	1% (209)
Reported “other”/multiracial	2% (448)	3% (52)	2% (392)
Has healthcare coverage	97% (24,345)	95% (1,698)	97% (22,560)
Income			
<$10,000	3% (747)	6% (102)	3% (641)
$10,000-$14,999	5% (1,192)	8% (141)	5% (1,044)
$15,000-$19,999	6% (1,622)	9% (159)	6% (1,453)
$20,000-$24,999	9% (2,150)	10% (172)	8% (1,967)
$25,000-$34,999	11% (2,692)	11% (198)	11% (2,487)
$35,000-$49,999	15% (3,685)	14% (246)	15% (3,429)
$50,000-$74,999	14% (3,540)	12% (209)	14% (3,317)
$75,000+	23% (5,729)	18% (316)	23% (5,400)
Don’t know/Not sure	6% (1,547)	7% (119)	6% (1,416)
Refused	9% (2,150)	7% (132)	9% (2,013)
Education			
No high school graduation	6% (1,534)	9% (165)	6% (1,362)
High school grad/GED	30% (7,437)	30% (537)	30% (6,861)
Some college	28% (7,044)	31% (562)	28% (6,458)
College degree	36% (9,000)	29% (522)	37% (8,455)
Cancer type			
Head/neck	<1% (66)	1% (17)	<1% (49)
Gynecological	8% (1,976)	9% (154)	8% (1,805)
Gastrointestinal	5% (1,304)	10% (177)	5% (1,122)
Lung/bronchus	2% (444)	5% (91)	2% (351)

Breast	17% (3,995)	31% (551)	16% (3,432)
Urogenital	13% (3,013)	10% (171)	13% (2,831)
All other types	55% (13,092)	34% (594)	57% (12,454)

[1]The study sample examining alcohol use consisted of 25,054 participants. The BRFSS included questions on alcohol use for all 50 states and across all years included in the study (2012 to 2019).

[2]Use is self-reported based on recall over the course of a 30-day period. Values are mean and standard deviation for alcoholic drinks consumed. All other values are column percentages and raw numbers.

Table 3.2. Interaction between age categories and cancer pain on alcohol consumption (n=25,054)

Cancer pain status	Incidence rate ratio (95% CI)	P-value for main effect
Has cancer pain	0.88 (0.77, 0.99)[1]	0.04
No cancer pain	Reference group	
Variables interacted with cancer pain	**Incidence rate ratio (95% CI)**	**P-value for interaction**
Age		
18-44	1.11 (0.74, 1.66)	Reference group
45-64	0.90 (0.75, 1.09)	0.36
65+	0.81 (0.68, 0.98)	0.17
Don't know/missing/refused	0.48 (0.07, 3.03)	0.38
Sex		
Male	0.95 (0.76, 1.19)	Reference group
Female	0.85 (0.73, 0.99)	0.42
Race		
White	0.84 (0.73, 0.96)	Reference group
Black	1.30 (0.82, 2.07)	0.07
American Indian/Alaskan Native	0.78 (0.31, 1.99)	0.90
Asian	1.30 (0.10, 16.78)	0.74
Native Hawaiian/Pacific Islander	0.22 (0.03, 1.39)	0.16
Multiracial	1.91 (0.94, 3.89)	0.03
Hispanic	0.36 (0.15, 0.90)	0.08
Don't know/Refused	1.06 (0.40, 2.85)	0.63

The regression models are adjusted for age, race, sex, health coverage status, income level, education level, state, and cancer type from most recent cancer diagnosis.

[1]Estimate is the incidence rate ratio (or prevalence ratio, in this case) for the association between cancer pain and amount of alcoholic drinks over a 30-day period. Example interpretation for alcohol use: Among cancer survivors, people who report cancer pain had 13% fewer drinks on average than people who did not report cancer pain.

Table 3.3. Alcohol use among cancer survivors with cancer pain by pain treatment status (n=1,794)

Treatment for cancer pain	Ratio of mean drink count (95% CI)[1]
Pain under control – with medication or treatment	Reference group
Pain under control – without medication or treatment	1.02 (0.75, 1.38)
Pain not under control – with medication or treatment	0.68 (0.40, 1.15)
Pain not under control – without medication or treatment	1.02 (0.64, 1.62)

The regression models are adjusted for age, race, sex, health coverage status, income level, education level, and cancer type from most recent cancer diagnosis.

CHAPTER 4: Models for Policy Evaluation

Introduction

Evaluation of health policy outcomes is a core part of epidemiologic research and public health promotion.[131] Yet despite the popularity of policy evaluations in public health research, there is little consensus about how to formally model the health effects of a policy change. Choice of statistical model is crucial, as studies with identical data sources that use different modeling approaches can yield disparate or conflicting conclusions.[132,133] In part, the model chosen for analyses may be determined by the type of data and study design being used. For example, autoregressive integrated moving average (ARIMA) models are specific to time series data.[56] Academic fields also may have their own preferred models, as in the case of fixed effects for economics (employed for policy evaluations because they adjust for both measured and unmeasured time-invariant confounders) and random effects for social epidemiology (favored for their statistical efficiency and ability to generalize results).[52,134] Ultimately, the goal in model choice in policy evaluation is to allow for policy-relevant inference (i.e., causal inference about the effect of a policy compared to its counterfactual) without sufficient enough bias to produce misleading conclusions.[13] Thus, choice of model is an important decision point when conducting policy evaluations and must be considered carefully.

When evaluating the outcome of policies, there are several common challenges that must be considered when determining which statistical models are most appropriate for

a given analysis.[135] French and Heagerty describe these challenges as: 1) identifying appropriate comparison groups (i.e., subjects that have not experienced the policy change of interest); 2) separating the effects of a policy from trends over time; 3) accounting for serial correlation due to repeated observations on the same subject (a violation of the independence assumption; not accounting for this can lead to underestimates of variance and risk a type 1 error); and 4) accounting for differences across policies. Without addressing each of these challenges, results from an analysis may not accurately represent effects of the policy on outcomes. In the following study, we focus on challenges 1 through 3 by describing and comparing different statistical models commonly used in policy evaluations. Different models have different advantages and disadvantages when it comes to addressing each of these challenges.

Several studies have compared fixed effects (regression models incorporating dummy variables for each cluster) and random effects models (where clusters are drawn from a distribution of clusters) for policy evaluations.[44,136] Random effects models tend to provide greater statistical efficiency by modeling cluster variance as a single regression parameter rather than removing cluster variance through many parameters (i.e., fixed effects).[46,52] Fixed effects models tend to have higher variance and reduced power due to the higher number of parameter estimates, and this is made worse as the number of observations within each cluster decreases.[46] In comparison, random effects models need fewer observations per cluster as long as there are at least 10-20 clusters and some of those clusters have at least two observations.[137] In addition, random effects models allow for examination of relationships between cluster-level variables and the

outcome[52] while fixed effects models are limited to within-cluster inference.[13] Because random effects use random variables (implying clusters drawn from a larger pool of clusters), this means that results may be generalized to the underlying population rather than to just the clusters included in the analysis.[138]

The weakness of random effects compared to fixed effects is greater risk of bias due to violations of the random effects assumption (e.g., the assumption that the unmeasured characteristics of a cluster do not impact its exposure status).[46,52] An example of this violation in the context of policy evaluation would be that unmeasured state characteristics are associated with whether or not a state passes the policy of interest. In practice, the Hausman specification test (a test for whether the random effects error term is correlated with any model covariates) is recommended to detect violations of the random effects assumption.[139] Including important cluster-level covariates can reduce the bias caused by violation of the random effects assumption. Clarke et al. argue that with an understanding of exposure selection (i.e., which cluster-level variables are associated with exposure) and quality data (i.e., measurement of these important cluster-level variables), the advantages of random effects models make it the preferred approach over fixed effects models.[13] In addition, so-called "hybrid models" have been proposed as an extension of random effects models that account for bias by including the means of cluster-level versions of all covariates,[44,52,136,140] such as covariates for averages of various state-level demographic characteristics.

ARIMA models are another approach used in policy evaluation research, yet few studies have compared ARIMA models with fixed effects or random effects models. Ye and Kerr examined the effect of liquor privatization on liquor sales and found consistent results between estimates from difference-in-differences (DiD) fixed effects models and ARIMA models using a monthly time series (from January 2009 to October 2014).[141] Another study by the same authors compared across ARIMA, generalized estimating equation (GEE), fixed effects, random effects, and generalized least squares models to examine the relationship between alcohol consumption and liver cirrhosis mortality.[48] All models showed a positive relationship between per capita alcohol consumption and liver cirrhosis mortality rates, however estimates diverged when comparing panel models and ARIMA models that examined specific alcoholic products (beer, liquor, wine). The authors contend that ARIMA and random effects models have the benefit of modeling cluster-specific trajectories (e.g., policy effects for each state) and between-cluster differences (e.g., comparing differences in policy effects between states), but that multiple models should be used to test the robustness of findings.[48]

Some regression models will provide consistent numeric results because they can be made mathematically equivalent. For example, estimates from GEE models may be nearly identical to random effects model estimates when the outcome variable is continuous and an exchangeable correlation structure (i.e., within-subject observations are assumed to be equally correlated) is specified for the GEE model; this is because a random intercept model assumes an exchangeable structure.[142] While GEE models have the advantage of simplicity compared to random effects models by averaging rather

than producing cluster-specific estimates, French and Heagerty point out that GEE models are more limited when trends in an outcome vary over time and the effects of a policy differ between states.[135]

To illustrate and compare the different methods for modeling a policy effect, we use data from the Nielsen Consumer Panel to examine how recreational cannabis legalization affects alcohol and cigarette purchasing. Drugs like cannabis can act as a substitute or complement to alcohol and cigarette use.[143] Two drugs are considered substitutes if the use of one increases as use of the other decreases, and are considered complements if the use of both are in tandem.[144] Interventions affecting one substance can thus affect others; for example, policies that increase or decrease availability of one substance can cause a change in the use of a different substance.

Findings on the relationship between cannabis legalization and alcohol use have been mixed.[145,146] In addition, studies examining this relationship have employed a variety of statistical models, including fixed effects and DiD,[147,148,149] ARIMA,[150] and GEE.[151] In a recent study, Veligati et al. used DiD fixed effects models to compare changes in per-capita cigarette and alcohol sales (1990-2016) between states that legalized recreational cannabis, states that legalized medical cannabis, and states prohibiting cannabis.[152] Results did not show any relationship between cannabis legalization and sales of these substances, though the authors note that their models did not meet the parallel trends assumption of the DiD approach. Looking at survey data of alcohol and cannabis use in Washington (January 2014 to October 2016), the introduction of recreational cannabis

stores saw no changes in alcohol consumption but saw decreases in "alcohol-related harms" (i.e., broad harms to work, home, health or finances due to alcohol).[153] Differences in findings across these studies may be partially explained by the differences in modeling choices. However, given the overall small number of studies examining this question, and the lack of any studies using the same panel of data over the same span of time, it is difficult to pinpoint whether mixed findings are due to differences in models, different data, or different choices in variables of interest for modeling.

While there are numerous ways to model policy effects, we focus on what we perceive as commonly-used approaches to regression modeling of quasi-experimental policy data. Specifically, we compare fixed effects, random effects, GEE, ARIMA models, which have different approaches to accounting for autocorrelation in longitudinal data. We also compare with the synthetic control method, which constructs a control group for a state that has experienced a policy intervention. We will compare estimates using data pooled from multiple states across these models to determine consistency, and discuss propriety of each approach for specific types of data and policy evaluation research questions. ARIMA and synthetic control models, which are originally designed for measuring intervention effects on a single group, will also be compared using state-specific models (i.e., measuring the effects of cannabis legalization on substance use purchasing separately for each state that legalized). We conduct both pooled and state-specific comparisons because policy evaluations can take either form, depending on the research question and available data. Our goal is to provide guidance to public health researchers interested in policy evaluations on how to select the most appropriate

model for their analysis. We include a motivating example using a longitudinal dataset or alcohol and cigarette purchases to compare these policy evaluation modeling approaches.

Review of Modeling Approaches and Methods

Data and Measures

We used household-level purchasing data of alcohol and cigarette products from the Nielsen Consumer Panel (NCP) for the years 2009 to 2019. All purchases were aggregated to the month and state-level for each product. The NCP has several strengths, including having purchases recorded daily using a scanner rather than relying on consumer recollection, several years of purchasing data, and weights to adjust for over- and under-sampling of households across several demographic characteristics.

Alcoholic product purchases. Alcohol product purchases were measured as liters of pure ethanol by summing total liters purchased in each month and multiplying this amount by the average proportion of ethanol in each alcoholic beverage type. Proportions of ethanol were based on the American Epidemiologic Data System (AEDS) methodology where the proportion is 0.045 for beer, 0.411 for liquor, and 0.129 for wine.[154] Liters of pure ethanol was measured separately for beer, liquor, and wine as well as in aggregate across all alcoholic beverages. All measures of liters of pure ethanol were log-transformed to account for right-skewing.

Cigarette product purchases. Cigarette product purchases were measured as a count of individual cigarettes. For a household that purchased two 20-packs of cigarettes in a

month, this would equate to purchasing 40 total cigarettes. In panel models this variable was treated as a count outcome, while in ARIMA models we applied a log-transformation to fulfill the normality assumption.

Recreational marijuana legalization. Recreational marijuana legalization served as the key exposure variable and was parameterized using a difference-in-differences (DiD) approach by interacting a binary time-invariant indicator for whether a state ever legalized with a time-varying indicator for when a state implemented marijuana legalization. Dates for implementation of recreational marijuana legalization were drawn from state government websites.

We included covariates for state-level year-specific poverty and unemployment rates, the proportion of people under the age of 30, and population size using data from Integrated Public Use Microdata Series (IPUMS) USA.[155] Previous research has shown that both poverty and unemployment are related to increased alcohol and cigarette use.[156–158] Previous alcohol studies have incorporated the percent of a state population under 30 as a regression covariate to account for the confounding effect of age on substance use.[159]

Study Design

The study uses a controlled interrupted time series (CITS) design. CITS is an extension of both a standard interrupted time series (ITS) and DiD, combining the benefits of both by incorporating multiple timepoints before and after an intervention (ITS) and a control group that mimics the intervention group's counterfactual (DiD).[55,61] A key advantage of

the CITS design is that the intervention and control groups can be examined for comparability pre-intervention by incorporating multiple pre-intervention observations in a long time series.[55] Figure 4.1 illustrates a standard CITS design:

O_1	O_2	O_3	O_4	O_5	X	O_6	O_7	O_8	O_9	O_{10}
O_1	O_2	O_3	O_4	O_5		O_6	O_7	O_8	O_9	O_{10}

Figure 4.1. A controlled interrupted time series design. Each O represents an observed outcome value in the time series, and X represents the "interruption" when the intervention of interest took effect. The top series is considered the exposed (or treated) series while the bottom series is the unexposed (or no-treatment control) series. Figure adapted from Cook and Campbell.[56]

There are two additional considerations when conducting an intervention evaluation using an interrupted time series design: historical changes in trend and staggered intervention timing (which is when interventions are implemented at different points in time for different groups). A historical change in trend, often caused by other interventions or events that affect the outcome, risks violating the assumption of linearity and creating an inaccurate representation of current trends.[61] To address this we limit observations to three years prior to and three years following legalization of recreational marijuana for both intervention and control states. Staggered intervention timing, if not accounted for, can induce negative weighting that biases DiD effect estimates by subtracting the effects of early-implementers from the effects seen in late-implementers.[160] This issue is specific to models that pool across all intervention states (i.e., fixed effects, random effects, and GEE). To address this, we use a stacked DiD approach for fixed effects, random effects, and GEE models that aligns intervention timing across states. This method is described in greater detail elsewhere.[161]

Panel model: fixed effects modeling

i. Model background and assumptions

Fixed effects models are commonly found in econometrics and used for policy evaluations because they adjust for both measured and unmeasured time-invariant (or "fixed") confounders. Dummy variables for each cluster are the fixed effects; in the case of policy evaluations, these may be the geographic unit (e.g., county, state) or other identifier for a cluster (e.g., household ID, subject ID). The fixed effect does not account for within-cluster correlation, so typically clustered standard errors are used to correct the variance of model estimates. The key causal assumption of fixed effects models is that all time-varying confounders between intervention and outcome are included in the model.

ii. Strengths and limitations

A strength of fixed effects models is the ability to account for both measured and unmeasured time-invariant confounding between clusters. By making comparisons within the same cluster, fixed effects models account for any correlation between intervention and cluster that may confound estimates; in essence, differences between clusters that may impact the outcome are adjusted for through the cluster-level fixed effects. However, using cluster-level fixed effects also prevents inference of any time-invariant effects on the outcome. This is because any cluster-level time-invariant characteristics would be multicollinear. In addition, fixed effects require more degrees

of freedom due to estimation of cluster-level intercepts (specifically, fixed effects will cost one fewer degree of freedom than there are clusters in the model). As a result, fixed effects models tend to have higher variance and reduced power compared to other modeling approaches.

iii. Where is it best suited

Fixed effects models tend to have less biased estimates than their random effects counterparts, specifically because they account for confounding between intervention and clusters. Thus, fixed effects models are best-suited if there is concern that cluster and intervention are confounded by unmeasured cluster-level factors. In addition, these models are appropriate when an investigator does not need to generalize their results beyond their sample (e.g., when clusters are a census of all 50 states) and are not interested in the effects of time-invariant cluster-level characteristics on the outcome. Because policy evaluation studies typically measure a change in policy, and this change occurs within clusters, the policy would be considered a time-variant measure and thus estimable using these models.

iv. Motivating example model specification

For our example estimating the effect of recreational marijuana legalization on alcohol and cigarette purchases, we specify a fixed effects model with dummy variables for each state. We also apply a cluster-robust sandwich estimator (a generalization of the Huber sandwich estimator specific to within-cluster correlation) to account for autocorrelation in our outcome variables. Because our covariates are time-varying, they can be included

in the model without being collinear with state fixed effects and can account for state-level time varying confounding. We used linear regression models for alcoholic products and negative binomial models for cigarette product purchases.

Panel model: random effects modeling

i. Model background and assumptions

Random effects models are more commonly-used in epidemiology than fixed effects models. Rather than removing cluster-level variability entirely, random effects models partition it into two components: an individual-level variance and a cluster-level variance. The cluster-level variance is drawn from a normal distribution of cluster intercepts, which means there is only the need to estimate one parameter rather than a parameter for each cluster. Random effects models allow for the calculation of both random intercepts and random slopes that account for autocorrelation in an outcome and explore heterogeneity in outcome trends across clusters. Unique to random effects models is the causal assumption that clusters are not correlated with the intervention; this assumption is sometimes called the random effects assumption.

ii. Strengths and limitations

The tradeoff between fixed effects and random effects models is often described as one between bias in estimates versus efficiency.[162] If the random effects assumption is met, then random effects models tend to have higher efficiency (i.e., smaller variance for effect estimates) due to estimating fewer parameters. Because random effects models partition variance rather than removing it entirely (as fixed effects models do), it is

possible to estimate the effects of time-invariant cluster-level characteristics. Cluster intercepts are also drawn from a normal distribution of clusters, allowing for the results of these models to be generalized beyond the clusters included in the analysis. However, these strengths come with the caveat that if the random effects assumption is not met, effect estimates will be biased. The Hausman test can be used to evaluate the presence of bias in random effects models, though this test bears the same power requirements as other significance tests.[139] In addition, both time-invariant and time-varying confounding remain issues that need to be addressed. Without the benefit of cluster-level fixed effects, random effects models are also vulnerable to unmeasured time-invariant confounding whereas fixed effects models are not.

iii. Where is it best suited

Random effects models are best suited when a sample does not include every cluster of interest and the investigator wishes to generalize their results. In the case of a policy evaluation, this may be due to having data on only a portion of counties or countries. Random effects models are also well-suited if an investigator is interested in heterogeneity of effects across clusters or the effects of time-invariant factors, and they believe they can include crucial time-invariant cluster-level confounders in their model.

iv. Motivating example model specification

We specify a random effects model with random intercepts for each state. Because random intercepts account for autocorrelation, we do not use cluster-robust standard errors as we do for fixed effects. State fixed effects are also excluded from the model.

Otherwise, random effects models followed the same structure as the fixed effects models.

Panel model: GEE modeling

i. Model background and assumptions

While fixed effects and random effects models are grouped into a conditional (or subject-specific) approach to analyzing correlated data, GEE models offer a marginal (or population-averaged) approach that extends the standard generalized linear model (GLM) to account for autocorrelation.[142,163] In practice, this means that estimates from GEE models represent the average effect of a change in the exposure on the outcome of interest across an entire population, whereas fixed and random effects models measure the effect of a change in exposure for the same given individual within a population over time. GEE models allow for autocorrelation among within-cluster residuals and corrects variances using a researcher-specified within-cluster correlation structure. Assumptions of GEE models are similar to GLM models, with the unique addition that within-cluster correlation has some structure, and that structure must be correctly specified.

ii. Strengths and limitations

An advantage of GEE models compared to fixed and random effects models is the need for fewer assumptions and fewer parameter estimates. Specifically, GEE models are not subject to the random effects assumption as they do not attempt to parameterize autocorrelation, nor do they require degrees of freedom to estimate cluster-level intercepts.[164] GEE modeling assumptions are based on observed data whereas random

effects models use assumptions involving unobserved variables represented as random effects. Often when evaluating policy effects, investigators are interested in population-level parameters and standard errors that are corrected for autocorrelation. At the same time, GEE models are vulnerable to time-variant and time-invariant confounding. These models also rely on the investigator correctly specifying for within-cluster correlation structure, though increasing the number of clusters can provide some robustness to biasing effects from misspecification.[163] Finally, random effects models do not employ maximum-likelihood estimation and therefore do not produce likelihood-based fit indices to compare across models.

iii. Where is it best suited

GEE models offer a way to examine the effects of cluster-level time-invariant factors while avoiding bias induced from violation of the random effects assumption. As long as the within-cluster correlation structure is correctly specified, GEE models can also estimate policy effects when the number of clusters would make fixed effects models untenable.

iv. Motivating example model specification

GEE models were fit separately across three within-cluster correlation structures: independent (no correlation is assumed for within-cluster observations), exchangeable (within-subject observations are assumed to be equally correlated), and first-order autoregressive structure (AR-1; within-cluster correlations are assumed to have an exponential decreasing correlation over time). The independent correlation structure

was supplemented with cluster-robust standard errors to account for autocorrelation. As with fixed and random effects models, GEE models are fit using linear regression for alcoholic products and negative binomial regression.

ARIMA modeling

i. Model background and assumptions

ARIMA models diverge from fixed effects, random effects, and GEE models in that they are typically fit to a single time series and require more timepoints.[65] The modeling techniques first proposed by Box and Jenkins are primarily used for analyses using ARIMA models.[165] These techniques involve researcher-chosen model specifications to address serial correlation and secular trends in a time series of outcome values for one cluster (either the exposed or unexposed group). Three key assumptions of ARIMA models are: 1) a linear relationship between the outcome and time; 2) the outcome is normally distributed; and 3) autoregressive and moving average parameters (*p, d, q*) are correctly specified such that residuals are no longer correlated and any remaining variation is random (also called “white noise”).

ii. Strengths and limitations

ARIMA models offer investigators a greater degree of control over modeling autocorrelation compared to other approaches, including seasonal patterns. Like random effects models, ARIMA models can estimate cluster-specific trajectories and between-cluster differences. By correctly parameterizing autocorrelation in a time series, ARIMA models can also be used to forecast future values in a series. However

with this degree of control around specifying the autocorrelation structure comes a great deal of complexity and opportunity for error. Effect estimates and standard errors are both sensitive to changes in ARIMA parameters. Additionally, because ARIMA models are fit for single time series, covariates cannot be incorporated to adjust for differences between intervention and control groups the same way they are in other models. The process for inducing stationarity in a time series (called "differencing", whereby the outcome value at a time *t* and the value at *t-1* are subtracted from one-another) can risk removing the intervention effect if there is a stochastic trend unrelated to the intervention that occurs around the same time.

iii. Where is it best suited

When a comparison group is not available, then ARIMA models can be the best option for generating policy effect estimates. Long time series are particularly well-suited for these models, especially if they do not include any structural breaks. Finally, investigators interested in forecasting future values will find ARIMA models already tailored for this purpose.

iv. Motivating example model specification

We fit ARIMA models for each outcome and each state using the Box and Jenkins approach, described in detail elsewhere.[165] After identifying appropriate autoregressive and moving average parameters, we used the Portmanteau Q test for white noise,[166] as well as ACF and PACF plots of residuals to test for any remaining autocorrelation. We then pooled individual time series estimates using a meta-analytic approach with both

fixed effects and random effects. This method has been used previously for pooling ARIMA estimates, and is considered more appropriate than other pooling techniques for its ability to account for state-level differences in variance.[48]

Synthetic control method

i. Model background and assumptions

The synthetic control method (SCM) is a relatively new approach that builds off of DiD.[167] The clusters that did not receive the intervention (hereby referred to as the "donor pool") are used to construct a synthetic control group based off of their comparability across investigator-chosen covariates. Typically, these covariates are considered confounders to the relationship between intervention status and the outcome. Weights are then constructed using a regression-based method that incorporates the pre-intervention outcome and selected covariates. Those weights are then applied to each donor cluster such that differences in intercept and trend pre-intervention between the intervention group and the synthetic control are minimized. Key assumptions of SCM are: 1) the donor pool must be composed of subjects that are similar to the exposed group based on key confounding variables but do not have the exposure of interest (or any spillover), and 2) any events occurring after an intervention that would affect the outcome will equally affect intervention and control groups.

ii. Strengths and limitations

The primary purpose and strength of SCM is construction of a control group that mimics the intervention group's counterfactual. Assuming correct identification of relevant

confounders and no spillover effects from exposed subjects into unexposed subjects, the synthetic control represents the counterfactual trend in the outcome that can be compared to the observed trend in the exposed group. With a large number of pre-intervention timepoints, Abadie et al. asserts that SCM can also adjust for unobserved time-varying confounders[168] – a significant advantage over standard fixed effects and DiD that account for time-invariant and observed time-variant confounders alone.[47] However, SCM relies on there being an adequate donor pool to construct a synthetic control group. If there are few clusters available that have not received the intervention, and fewer still that are similar to the intervention group, then SCM may not be possible. The same holds true if the intervention group is an outlier.

iii. Where is it best suited

SCM is valuable when the parallel trends assumption of DiD cannot be met. Standard SCM is also restricted to a single intervention cluster or risk a significant loss to power, so studies examining a single intervention group (e.g., the policy effect in a specific county or state) are well-suited. In particular, new policies passed in a small number of localities may provide the best opportunity for leveraging SCM by taking advantage of a large donor pool to construct synthetic controls.

iv. Motivating example model specification

Synthetic control groups were constructed for each state that legalized recreational marijuana using the community-contributed *synth* command in Stata.[169] Donor pools

were comprised of states that had not legalized recreational marijuana within three years prior to and following when a given intervention state had legalized it.

Control group selection

Control states for the panel models (fixed effects, random effects, and GEE) and SCM were comprised of all states that did not legalize recreational marijuana three years before and three years after when a given intervention state did legalize. For ARIMA models, control states were selected for each intervention state based on similarity of pre-policy outcome trend and comparability of covariate values.

Incorporating time

Time trends, usually through secular trends or seasonal effects, can bias the policy effect estimates from regression models. To de-trend the data and remove this biasing effect, panel models and ARIMA models tend to take different approaches: the former will use regression covariates to model time trends while the latter will difference the time series to achieve stationarity. With regression covariates, investigators have the choice of using continuous time variables or time dummy variables. Continuous time variables are more parsimonious but impose a structure on the data and requires monotonicity. Time dummy variables are more flexible and can model shocks (i.e., a rapid deviation from trend) but requires many more parameters to be estimated (and costs degrees of freedom equal to the number of timepoints minus 1). In contrast, ARIMA models involve subtracting the outcome value at one point in time from the outcome value at the

following point in time. However, the primary purpose of differencing is to remove a unit root from the data (i.e., a stochastic trend).

Given the large amount of data available through the NCP, we used time fixed effects for month and year in panel models. These fixed effects account for both secular trends and seasonal patterns in purchasing. Prior studies have found that both alcohol and cigarette use follow seasonal trends, with elevated sales of alcohol in the spring[170] and of cigarettes in the summer.[171] For ARIMA models we used the Dickey-Fuller test to determine whether a unit root was present in the series, and whether the unit root had been accounted for after applying an order of differencing.[172] We used ACF and PACF plots to evaluate for seasonality and, if present, used multiplicative ARIMA models that address both seasonality and potential seasonal unit roots.

Sensitivity analyses

To test the robustness of our findings to our choice of control states, we refit panel models using the same control states selected for the ARIMA models. For synthetic control models, we conducted placebo tests on states from the donor pools to test whether the difference in policy effect between policy states and control states differed. Other studies provide more detail on SCM placebo tests.[173]

Results

We first fit panel models for alcoholic products (both individual product types and aggregated across all products) and cigarettes without including state-level covariates. Results are shown in Table 4.1. These models used a difference-in-difference modeling

approach, and effect estimates represent a multiplicative change in product purchasing following recreational marijuana legalization (e.g., an estimate of 0.90 is interpreted as a 10% decrease while a 1.20 is a 20% increase). Fixed and random effects estimates were consistent across all outcomes in both direction and magnitude. Estimates from GEE models diverged from fixed and random effects models and varied depending on the chosen within-cluster correlation structure. GEE models examining alcohol outcomes and using an exchangeable correlation structure were identical to those from random effects models, as expected given random effects models assume an exchangeable correlation structure.[142]

The final models are shown in Table 4.2. Panel models include state-level covariates while ARIMA and SCM models are unconditional due to an inability to include covariates in the regression model. Pooled ARIMA model estimates are shown using both fixed effects and random effects meta-analysis. Fixed effects, random effects, and GEE models using an exchangeable correlation structure showed high consistency across effect estimates and statistical significance for all outcomes. GEE models with an independent correlation structure and cluster-robust standard errors were largely consistent except for wine purchases and, when using an AR-1 structure, showed increases for aggregated alcoholic beverages and for wine. When examining specific alcoholic beverages, ARIMA model estimates diverged from panel models with increases in purchasing across each product. Estimates from SCM models also differed from panel and ARIMA models across alcoholic beverages but were largely consistent for cigarettes.

Tables 4.3 and 4.4 display coefficients for state-specific changes in purchasing. Estimates between ARIMA and synthetic control models frequently varied in both directionality and statistical significance. Correlation coefficients (not shown in tables) between the two modeling approaches were 0.56 for all alcoholic beverages, 0.11 for beer, 0.17 for liquor, and 0.48 for wine. Synthetic control estimates for liquor and wine purchases in California could not be generated due to a lack of appropriate comparison states in the donor pools.

Sensitivity analyses

Figure 4.2 is an example of the placebo tests for SCM estimates, highlighting the policy effect in Oregon for all alcoholic beverage purchases. Oregon was chosen given it was the only state to show a statistically significant change in alcohol purchases. The solid black line depicts the trend in total liters of pure ethanol purchased in Oregon compared to its synthetic control while the lighter blue lines show ethanol purchased for each state in the control group donor pool compared to its own synthetic control. If the solid black line is within the lighter blue lines (as in the case of this figure), this signifies that the difference in ethanol purchased in the policy state does not stand out from ethanol purchased in states that did not implement recreational marijuana legalization.

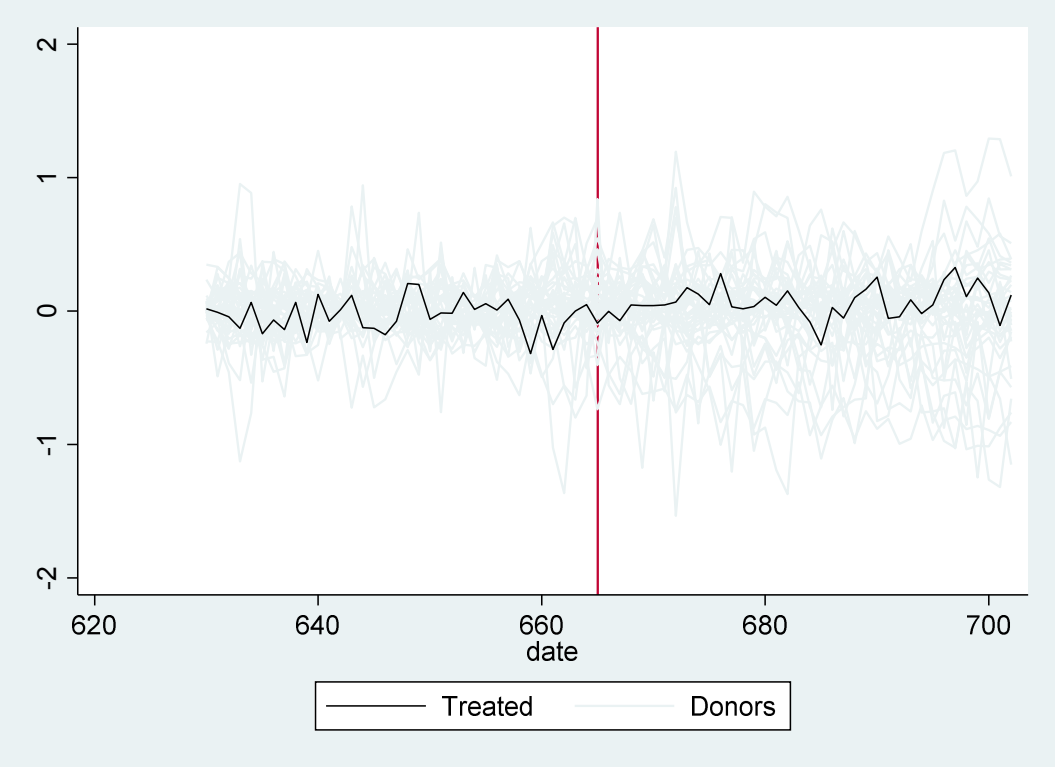

Figure 4.2. Placebo test for effect of marijuana legalization on pure ethanol purchased from all alcoholic beverages in Oregon. The black line signifies the difference in ethanol purchased (on average) among Oregon households compared to its synthetic control. Each light blue line signifies ethanol purchased in a given state (that did not legalize recreational marijuana) compared to its synthetic control.

To test whether control selection resulted in differing estimates between panel and ARIMA models, we re-fit all panel models using the same control states incorporated in the ARIMA analyses. Supplementary Table 4.1 shows estimates from crude panel models (i.e., models that did not include covariates to adjust for confounding), and Supplementary Table 4.2 shows estimates from multivariable panel models that included all covariates described earlier. Compared to the panel models using all control states, the estimates when using ARIMA control states did not differ substantially. GEE models using an AR-1 correlation structure showed more sensitivity to change when using ARIMA-specific control states than when all states were used as controls.

Discussion

Thera are many different options for modeling longitudinal data to evaluate a policy. Each modeling approach has its own assumptions, strengths, and weaknesses. In our motivating example quantifying the relationship between recreational marijuana legalization and alcohol and cigarette purchasing, choice of model influenced the results – sometimes in ways that altered conclusions about the relationship. Choice of model can also influence how staggered policy implementation timing, secular trends, and autocorrelation are addressed. The question facing researchers is which modeling approach to choose when estimating policy effects. Here we provide guidelines and recommendations for answering this question.

The nature of the research question being answered may drive choice of model. ARIMA, SCM, and random effects models are well-suited to estimating cluster-specific effects (e.g., policy effects for each state). However, if researchers are interested in the average effect of a policy on a population pooled across clusters (e.g., pooled across states), then fixed effects and GEE models may be more useful. GEE models offer flexibility in modeling autocorrelation and can accommodate estimation of time-invariant effects, whereas fixed effects models can adjust for unmeasured time-invariant confounding across clusters. If the research question involves forecasting future values, then ARIMA models are particularly well-suited with a built-in suite of forecasting options in most statistical software.

In our motivating example, we found consistency in estimates for the effect of recreational marijuana legalization on cigarette purchases but variability in estimates for alcohol purchases. Specifically, GEE models using an AR-1 correlation structure and ARIMA models tended to differ from the rest of the models. There are several possible reasons why ARIMA models may have differed from panel models. One is that ARIMA models could not incorporate covariates to adjust for differences between groups, however the estimates from crude panel models (shown in Table 4.1) still differed from ARIMA models. Another possibility is a difference in the composition of control groups between ARIMA models (which used control states selected based on similarity in intercept and trend) and panel models (which used all states that did not legalize recreational marijuana). This also does not appear likely, as panel models re-fit with the same control states as those in ARIMA models still produced different estimates (Supplementary Table 4.1). How secular trends are accounted for may also influence estimates: ARIMA models could not incorporate time as a fixed effect, but rather a continuous parameter or through an order of differencing. It is important to note that in the case of ARIMA, first-order differencing is used to remove a unit root from the time series rather than to account for a secular trend. Because a unit root can appear similar to a sustained effect from a policy or other intervention, researchers risk removing the effect of interest when differencing a series.

GEE with an AR-1 correlation structure and ARIMA models both often shared a similar or identical correlation structure specification (e.g., an autoregressive structure). This may partially explain why results from these models diverged from other panel models and

SCM when examining alcohol purchasing. Because both regression estimates and variances were sensitive to choice of correlation structure, the ability of the researcher to choose which structure will be applied can be a double-edged sword. ARIMA models have an even greater degree of flexibility and control than GEE models when setting the autocorrelation structure, which opens the way for error and inconsistency across different studies. This may partially explain why ARIMA estimates and estimates from GEE models with an AR-1 structure diverged, as the former included more complex correlation structures such as additional autoregressive terms and seasonal components to the models.

Ultimately, ARIMA models may be less suited for answering policy evaluation questions due to having more limitations and pitfalls in this particular context. While ARIMA models offer greater flexibility in modeling autocorrelation, they have less flexibility to account for time trends and are designed for continuous variables rather than binary or count outcomes. In our ARIMA models examining cigarette purchasing, we had to apply a natural log transformation. Using differencing to remove a unit root also risks removing the intervention effect, which has similar properties to the former. Fixed effects models may be the safest choice of approach given their ability to account for unmeasured time-invariant confounding at the cluster level. While fixed effects models are less efficient than random effects models, the former does not risk violating the random effects assumption. Given that policy implementation is not random, but likely influenced by several cluster-level factors (e.g., prior policies, culture, climate), the random effects assumption is likely to be violated unless all of these factors are

accounted for in the model or policy implementation is truly exogenous. Regardless of model choice, it is recommended that researchers run other models to test the robustness of their findings and investigate any differences in results.

Substantive findings

It is also worthwhile to briefly discuss the substantive findings from the motivating example. Across all models, cigarette purchasing decreased in states that legalized recreational marijuana compared to states that did not legalize (ranging from 10%-15% fewer cigarettes purchased monthly). Estimates from the SCM and pooled ARIMA using random effects meta-analysis were not statistically significant, but directionality and magnitude were consistent with other estimates. Prior evidence on the relationship between cigarettes and marijuana is mixed. Some studies have shown a similar substitution relationship as our findings, however other studies have shown no relationship[152,174] or a complementary relationship.[175] Estimates for alcohol purchases for all products combined showed no significant changes following recreational marijuana legalization, with the exception of the GEE model using an AR-1 correlation structure showing an increase in purchasing (beta: 1.07, CI: 1.01, 1.13). Estimates from panel models and SCM were consistent, but diverged significantly from ARIMA model estimates. Overall these findings suggest a decrease in cigarette purchases following recreational marijuana legalization, while the effect of legalization on alcohol purchases is unclear and warrants further investigation.

Table 4.1. Crude panel model estimates and 95% CIs

	All alcohol	Beer	Liquor	Wine	Cigarettes
Fixed effects	**0.94**	**0.90**	0.96	0.99	**0.83**
	(0.89, 0.99)	**(0.82, 0.99)**	(0.89, 1.04)	(0.90, 1.09)	**(0.74, 0.93)**
Random effects	0.96	**0.90**	0.96	0.99	**0.83**
	(0.91, 1.02)	**(0.82, 0.99)**	(0.89, 1.04)	(0.90, 1.09)	**(0.74, 0.93)**
GEE (Ind)[1]	1.09	1.05	1.05	1.17	0.88
	(0.86, 1.38)	(0.81, 1.36)	(0.83, 1.32)	(0.89, 1.54)	(0.75, 1.05)
GEE (Exch)	0.96	**0.90**	0.96	0.99	**0.79**
	(0.91, 1.01)	**(0.82, 0.99)**	(0.89, 1.04)	(0.90, 1.09)	**(0.63, 0.98)**
GEE (AR1)	0.94	0.96	1.03	**1.12**	0.96
	(0.88, 1.00)	(0.86, 1.07)	(0.93, 1.15)	**(1.02, 1.24)**	(0.88, 1.05)

BOLD = p-value < 0.05. GEE models are fit using independent ("Ind"), exchangeable ("Exch), and AR-1 ("AR1") correlation structures.

Table 4.2. Estimates and 95% CIs: multivariable Panel models, ARIMA models, and synthetic control method

	All alcohol	Beer	Liquor	Wine	Cigarettes
Panel models					
Fixed effects	0.97	0.93	0.96	0.97	**0.87**
	(0.92, 1.01)	(0.83, 1.03)	(0.89, 1.03)	(0.88, 1.07)	**(0.77, 0.98)**
Random effects	0.96	0.93	0.96	0.97	**0.87**
	(0.92, 1.01)	(0.83, 1.03)	(0.89, 1.03)	(0.88, 1.07)	**(0.77, 0.98)**
GEE (Ind)[1]	0.99	0.93	0.93	1.07	**0.87**
	(0.82, 1.20)	(0.83, 1.03)	(0.76, 1.14)	(0.84, 1.37)	**(0.77, 0.98)**
GEE (Exch)	0.96	0.93	0.96	0.97	**0.87**
	(0.92, 1.01)	(0.83, 1.03)	(0.89, 1.03)	(0.88, 1.07)	**(0.77, 0.98)**
GEE (AR1)	**1.07**	0.96	1.05	**1.13**	**0.90**
	(1.01, 1.13)	(0.87, 1.05)	(0.97, 1.13)	**(1.01, 1.25)**	**(0.81, 0.99)**
ARIMA models					
FE ME	0.98	**1.07**	**1.07**	**1.12**	**0.90**
	(0.93, 1.02)	**(1.02, 1.12)**	**(1.03, 1,11)**	**(1.07, 1.16)**	**(0.86, 0.95)**
RE ME	0.98	**1.07**	**1.07**	**1.12**	0.90
	(0.92, 1.04)	**(1.01, 1.14)**	**(1.02, 1.13)**	**(1.04, 1.20)**	(0.79, 1.02)
Synthetic control method					
	1.02	0.97	0.98	1.07	0.85
	(0.81, 1.27)	(0.77, 1.24)	(0.82, 1.17)	(0.84, 1.37)	(0.66, 1.10)

BOLD = p-value < 0.05. GEE models are fit using independent ("Ind"), exchangeable ("Exch), and AR-1 ("AR1") correlation structures. [1] The GEE model fit with an independent correlation structure uses a robust sandwich estimator to account for autocorrelation. "FE ME" = fixed effects meta-analysis. "RE ME" = random effects meta-analysis.

Table 4.3. State-specific estimates and 95% CIs: ARIMA models

	All alcohol	Beer	Liquor	Wine	Cigarettes
California	0.83	1.14	1.01	1.00	**0.37**
	(0.60, 1.16)	(0.93, 1.40)	(0.81, 1.27)	(0.80, 1.25)	**(0.31, 0.44)**
Colorado	**0.77**	0.94	0.88	1.01	1.02
	(0.64, 0.93)	(0.77, 1.13)	(0.70, 1.11)	(0.83, 1.23)	(0.79, 1.30)
Maine	0.99	**1.12**	**1.17**	**1.21**	**1.51**
	(0.86, 1.16)	**(1.02, 1.22)**	**(1.05, 1.29)**	**(1.01, 1.46)**	**(1.29, 1.78)**
Massachusetts	1.18	1.00	0.97	1.26	**0.73**
	(0.88, 1.58)	(0.70, 1.45)	(0.70, 1.33)	(0.97, 1.65)	**(0.62, 0.87)**
Michigan	0.94	0.90	1.05	**0.84**	1.01
	(0.84, 1.05)	(0.81, 1.00)	(0.97, 1.14)	**(0.73, 0.96)**	(0.89, 1.16)
Nevada	1.18	1.04	**1.40**	0.84	0.98
	(0.86, 1.65)	(0.75, 1.44)	**(1.01, 1.95)**	(0.50, 1.41)	(0.83, 1.16)
Oregon	1.07	1.18	1.04	**1.48**	0.99
	(0.86, 1.32)	(0.90, 1.53)	(0.86, 1.26)	**(1.10, 2.00)**	(0.84, 1.17)
Vermont	0.96	1.14	1.09	1.04	0.70
	(0.77, 1.19)	(1.00, 1.30)	(0.91, 1.30)	(0.95, 1.14)	(0.49, 1.01)
Washington	1.06	**1.42**	1.09	**1.24**	0.85
	(0.90, 1.25)	**(1.23, 1.64)**	(0.98, 1.22)	**(1.14, 1.36)**	(0.59, 1.22)

BOLD = p-value < 0.05.

Table 4.4. State-specific estimates and 95% CIs: synthetic control method

	All alcohol	Beer	Liquor	Wine	Cigarettes
California	0.94	0.98	-	-	**0.74**
	(0.88, 1.01)	(0.92, 1.05)			**(0.67, 0.81)**
Colorado	0.93	0.91	0.98	0.99	**0.84**
	(0.85, 1.02)	(0.81, 1.01)	(0.86, 1.11)	(0.85, 1.16)	**(0.78, 0.91)**
Maine	1.09	**0.62**	**1.21**	1.12	1.00
	(0.97, 1.23)	**(0.52, 0.74)**	**(1.02, 1.43)**	(0.97, 1.29)	(0.80, 1.25)
Massachusetts	1.02	1.06	0.93	**1.18**	**0.79**
	(0.93, 1.11)	(0.94, 1.20)	(0.82, 1.06)	**(1.07, 1.31)**	**(0.70, 0.90)**
Michigan	0.92	0.96	1.03	**0.81**	1.04
	(0.82, 1.02)	(0.87, 1.05)	(0.89, 1.20)	**(0.70, 0.95)**	(0.93, 1.16)
Nevada	1.00	**1.17**	0.96	**1.19**	**0.73**
	(0.91, 1.11)	**(1.01, 1.35)**	(0.83, 1.11)	**(1.05, 1.34)**	**(0.62, 0.86)**
Oregon	**1.12**	0.94	0.93	**1.21**	**1.13**
	(1.03, 1.22)	(0.85, 1.05)	(0.81, 1.07)	**(1.08, 1.35)**	**(1.01, 1.27)**
Vermont	0.92	**0.80**	0.86	1.03	**0.50**
	(0.78, 1.09)	**(0.65, 0.99)**	(0.69, 1.07)	(0.74, 1.42)	**(0.36, 0.71)**
Washington	1.07	**1.12**	1.04	0.94	0.96
	(0.99, 1.16)	**(1.04, 1.20)**	(0.91, 1.18)	(0.84, 1.04)	(0.86, 1.07)

BOLD = p-value < 0.05. "-" represents a model that did not achieve convergence. This is likely the result of a lack of appropriate donors in the donor pool to construct a synthetic control.

Supplementary Table 4.1. Estimates and 95% CIs: crude panel models, ARIMA models, using ARIMA controls

	All alcohol	Beer	Liquor	Wine	Cigarettes
Panel models					
Fixed effects	0.96	0.94	1.03	0.99	**0.81**
	(0.86, 1.07)	(0.85, 1.04)	(0.94, 1.13)	(0.90, 1.08)	**(0.71, 0.94)**
Random effects	1.00	0.94	1.03	0.99	**0.81**
	(0.94, 1.06)	(0.85, 1.04)	(0.94, 1.13)	(0.90, 1.08)	**(0.71, 0.94)**
GEE (Ind)[1]	1.03	0.99	1.00	1.08	0.84
	(0.81, 1.31)	(0.75, 1.31)	(0.79, 1.28)	(0.90, 1.44)	(0.70, 1.01)
GEE (Exch)	1.00	0.94	1.03	0.99	**0.79**
	(0.94, 1.06)	(0.85, 1.04)	(0.94, 1.13)	(0.90, 1.08)	**(0.65, 0.97)**
GEE (AR1)	0.98	**0.74**	**1.13**	1.01	**0.87**
	(0.93, 1.03)	**(0.70, 0.78)**	**(1.04, 1.22)**	(0.90, 1.13)	**(0.82, 0.93)**
ARIMA models					
FE ME	0.98	**1.07**	**1.07**	**1.12**	**0.90**
	(0.93, 1.02)	**(1.02, 1.12)**	**(1.03, 1,11)**	**(1.07, 1.16)**	**(0.86, 0.95)**
RE ME	0.98	**1.07**	**1.07**	**1.12**	0.90
	(0.92, 1.04)	**(1.01, 1.14)**	**(1.02, 1.13)**	**(1.04, 1.20)**	(0.79, 1.02)

Control units used in the panel models are the same as those selected for the ARIMA models based on parallel trends in the outcome prior to recreational marijuana legalization. ARIMA models and estimates here are identical to those reported in Table 4.2. Panel models are unadjusted.

Supplementary Table 4.2. Estimates and 95% CIs: multivariable panel models, ARIMA models, using ARIMA controls

	All alcohol	Beer	Liquor	Wine	Cigarettes
Panel models					
Fixed effects	1.01	0.97	1.02	0.99	0.87
	(0.95, 1.07)	(0.86, 1.09)	(0.94, 1.10)	(0.90, 1.09)	(0.75, 1.01)
Random effects	1.01	0.97	1.02	0.99	0.87
	(0.94, 1.08)	(0.86, 1.10)	(0.94, 1.11)	(0.90, 1.10)	(0.75, 1.01)
GEE (Ind)[1]	1.01	0.97	0.98	1.10	0.87
	(0.83, 1.25)	(0.77, 1.22)	(0.78, 1.23)	(0.86, 1.40)	(0.75, 1.01)
GEE (Exch)	1.01	0.97	1.02	0.99	0.87
	(0.94, 1.08)	(0.86, 1.10)	(0.94, 1.11)	(0.90, 1.10)	(0.75, 1.01)
GEE (AR1)	1.06	**0.73**	**1.24**	1.08	**0.87**
	(0.99, 1.13)	**(0.65, 0.83)**	**(1.12, 1.37)**	(0.97, 1.20)	**(0.76, 0.99)**
ARIMA models					
FE ME	0.98	**1.07**	**1.07**	**1.12**	**0.90**
	(0.93, 1.02)	**(1.02, 1.12)**	**(1.03, 1,11)**	**(1.07, 1.16)**	**(0.86, 0.95)**
RE ME	0.98	**1.07**	**1.07**	**1.12**	0.90
	(0.92, 1.04)	**(1.01, 1.14)**	**(1.02, 1.13)**	**(1.04, 1.20)**	(0.79, 1.02)

Control units used in the panel models are the same as those selected for the ARIMA models based on parallel trends in the outcome prior to recreational marijuana legalization. ARIMA models and estimates here are identical to those reported in Table 4.2. Panel models are adjusted for state-level year-specific poverty and unemployment rates, the proportion of people under the age of 30, and state population size.

CHAPTER 5: Medicaid Expansion and Substance Use

Introduction

The Affordable Care Act (ACA) includes a provision to expand Medicaid coverage, made optional by the 2012 Supreme Court Ruling in *National Federation of Independent Business v. Sebelius*.[176] Under this provision, states can expand their Medicaid eligibility to adults with a household income below 138% of the federal poverty level (FPL). Currently, 38 states and the District of Columbia have expanded Medicaid. States that have expanded Medicaid coverage have seen greater declines in uninsured rates compared to states that have not expanded.[177–180]

There is evidence that Medicaid expansion is related to reductions in substance use and use-related health problems. In Oregon, Medicaid expansion was associated with a six percentage-point increase in alcohol use disorder treatment rates and a 150% increase in Medicaid enrollees with alcohol use disorder.[181] Medicaid expansion has also increased access to smoking cessation treatments.[182] Expansion has not only resulted in an increase in the number of insured people, but is associated with greater odds of being screened for smoking status and of making attempts to quit smoking when compared to states that did not expand Medicaid.[183] Using Nielsen consumer data from 2011 to 2015, Cotti et al. found reductions in cigarette, snuff (a smokeless form of tobacco), beer, and liquor purchases following Medicaid expansion across 31 states.[184] We extend this work by examining the association between Medicaid expansion and

alcohol, cigarette, and e-cigarette product purchases using a longer timespan and incorporating states that have more recently expanded Medicaid.

The effects of policies like Medicaid expansion can vary across racial and ethnic groups. Historically, Hispanic and non-Hispanic Black people had much higher uninsured rates compared to white people.[185,186] The ACA, and closely-related laws such as the Mental Health Parity and Addiction Equity Act (MHPAEA), have helped to address this disparity and have been shown to differentially impact substance use treatment rates with greater benefits for people of color.[187] Medicaid expansion has increased coverage rates across all racial and ethnic groups, but disparities in coverage rates between groups remain.[188, 189] While the benefits of Medicaid expansion disproportionately apply to racial and ethnic marginalized groups,[190] in practice, many of the health benefits from expansion (e.g., having a source of usual care, having health needs met, having an annual health check-up), may be restricted to white low-income childless adults based on previous findings.[191] This raises the question of whether changes in substance use following Medicaid expansion are consistent across race and ethnicity, or whether certain demographic groups are more likely to be affected as this would have ramifications for substance use-related health disparities.

In the current study we examine whether Medicaid expansion is associated with the purchasing of alcohol, cigarettes, smoking cessation products, and e-cigarettes. We also examine whether the effects of Medicaid expansion on purchasing of these products varies across household racial and ethnic identity. Based on previous studies, we

hypothesize that Medicaid expansion is associated with decreases in some product purchases, particularly alcohol and cigarettes. We also hypothesize that reductions in purchasing are primarily among white households, given these households are more likely to have a greater number of resources and more privilege to benefit from the policy change.

Methods

Study Design and Data Sources

This study used a controlled interrupted time series (CITS) design with multiple treated and comparison groups. We combined data from the 2011 to 2019 panels of the Nielsen Consumer Panel (NCP) dataset across the 48 contiguous states and the District of Columbia. Briefly, the NCP is an open cohort of households that record daily purchases intended for personal use from any outlets (e.g., grocery stores, convenience stores), including online purchases. Participating households use in-home scanners to record their purchases after each shopping trip. Households in the dataset are sampled proportionately across several demographic characteristics (e.g., household income, number of children, race/ethnicity). The dataset includes survey frequency weights that allow for calculations of national, state, and market area-level projections. Annually, the dataset contains approximately 60,000 households and uses on-going recruitment to replace households that drop out (approximately 80% of households each year continue to participate in the panel the following year).

Data were aggregated to the household and month level, creating separate time series for each household. Because the amount of time a household spent in the NCP varied, the number of monthly observations each household provided ranged from twelve to 108.

Measures

Exposure: Medicaid expansion

State-level expansion of Medicaid eligibility was parameterized as a binary variable. The variable was a time-variant indicator of which months a given state had expanded Medicaid. For households in states that had expanded Medicaid, the months prior to expansion were coded as "0" while months following expansion were coded as "1." Households in states that did not expand Medicaid during the study period were coded as "0" for the entirety of the series.

Outcome Variables: Substance Use

Substance use was measured across four individual products: alcohol, combustible cigarettes, smoking cessation products, and e-cigarettes. Alcohol products were further divided into beer, liquor, and wine. For each product category, we first created a binary variable to indicate whether a household had purchased that product in each month. We also created variables measuring the amount of each product that a household purchased over each month.

Alcohol

The total amount of alcohol, as well as the amount from each type of alcoholic products (beer, liquor, and wine) was measured in milliliters of pure ethanol. This was calculated by multiplying the milliliters of liquid in each container by the number of containers, and then by a static proportion for each type of alcohol (0.045 for beer, 0.129 for wine, and 0.411 for liquor).[192]

Combustible cigarettes

Monthly combustible cigarette purchases were measures as the number of individual cigarettes. Cigars and non-combustible tobacco products (e.g., chewing tobacco) were not included. The NCP includes information on the number of product units (i.e., individual cigarettes) within multi-packs and the quantity of multi-packs purchased. For example, a household that buys two 20-packs of cigarettes in a month would be recorded as having purchased 40 cigarettes.

Smoking cessation products

Products to assist with smoking cessation (e.g., nicotine gum, nicotine patches) were measured as the number of product units purchased each month. We used the same strategy as with combustible cigarettes by dividing multi-packs into individual product units and multiplied by the number of products purchased.

E-cigarettes

We measured e-cigarette purchases as the milliliters of liquid nicotine solution in each product. This measure was developed by Cotti et al. and described more in-depth in

their study of cigarette and e-cigarette purchasing.[193] In brief, e-cigarette products come in a variety of forms (disposable e-cigarettes, refill cartridge packs, starter kits). Because these products vary in length of use and the product quantity, they must be standardized while taking into account product type, number of product units, and amount of liquid in each product.

Interaction Measure: Household Race and Ethnicity

The NCP includes a measure of race that identifies the "racial identity of the household" (white, Black, Asian, or a non-specified racial identity) and a measure that indicates whether members of the household are of Hispanic origin. These two variables were combined into a measure of race and ethnicity, where 1=Black non-Hispanic, 2=Asian non-Hispanic, 3=white non-Hispanic, 4=Racial identity not provided, and 5=Hispanic.

Covariates

All models were adjusted for a number of potential household-level and state-level confounding variables. Household-level variables were the marital status of the heads of household, educational attainment of heads of household, household income, whether the household had an internet connection, the ages of the heads of household, and whether the household included children. At the state-level we included time-variant indicators for whether recreational cannabis had been legalized and whether the state had an excise tax on e-cigarettes. States that have expanded Medicaid are also more likely to have an excise tax on e-cigarettes and to have legalized recreational marijuana than states that have not expanded. These policies may also affect substance purchases

through increased pricing of products (i.e., a higher cost for e-cigarette products) and through substitution or complementarity relationships with products not directly targeted by the policy. We also included state fixed effects to account for any unmeasured differences across states that may affect substance purchases.

Analysis

The sample was restricted to households where all heads of household were older than 18 and younger than 65, to avoid overlap eligibility for Medicare and other government-provided health insurance programs (e.g., Children's Health Insurance Program) (n=3,123,321 observations). We also removed households with incomes between 100% and 138% of the FPL (n=328,855 observations), as households in this range became eligible for health insurance subsidies in 2014.[116] The final study sample consisted of 25,054 households with 4,381,775 observations. Of those, 1,596,868 observations were from households in states that expanded Medicaid at some point within the study timeframe and 2,784,907 were from households in states that did not expand within the study timeframe.

We used a difference-in-difference (DiD) approach when examining whether Medicaid expansion is associated with substance purchases. To measure the probability of purchasing a given product we fit logistic regression models for each binary outcome variable and calculated average predicted probabilities for Medicaid expansion vs not. To measure the amount of a product purchased we fit negative binomial models for count outcomes (i.e., cigarettes, smoking cessation products) and linear models for

continuous outcomes (i.e., milliliters of ethanol from all alcoholic products combined, beer, liquor, wine; and for milliliters of e-cigarette liquid). Models examining amount of a product were restricted to households that were not abstainers of that product (i.e., had purchased that product at least once in the time period). To determine whether the association between Medicaid expansion and product purchases varied across household race and ethnicity, we interacted the Medicaid expansion and race/ethnicity variables. This is analogous to a difference-in-difference-in-differences (DDD) approach. We generated stratified DiD estimates for each product by race/ethnicity from the interaction term models. All models used the frequency weights provided by Nielsen. Robust standard errors allowing for within household correlation were used to account for serial correlation from repeated observations within the same household.[194,195]

To address concerns of bias in estimates due to the staggered timing of Medicaid expansion, we conducted a sensitivity analysis restricting to states that either did not expand Medicaid or expanded Medicaid on January 1, 2014. States that expanded Medicaid within the study time period on a date other than January 1, 2014 were excluded. Staggered treatment timing in difference-in-difference models can bias effect estimates by subtracting the treatment effect of "early adopters" from groups that receive the treatment later.[160] Stata version 17 was used for all analyses.

Results

Descriptive household characteristics of the study sample are shown in Table 5.1. The majority of the households in the sample included married individuals, had heads of

household at least 45 years old, had no children under 18, had an internet connection at home, and identified as white non-Hispanic. There were no notable differences between households in states that did and did not expand Medicaid, except that a greater percentage of the sample in the states that did not expand Medicaid was Black (14.61% versus 8.66%).

Table 5.2 shows predicted probabilities for monthly purchasing and amounts purchased of each product by state Medicaid expansion status (i.e., whether a state expanded Medicaid, and the period before expansion versus after expansion). The right-most column shows the difference-in-difference estimate comparing change in the outcome between households in expansion states and households in control states. On average, households were more likely to purchase liquor (0.44 percentage points) and e-cigarette products (0.08 percentage points) following Medicaid expansion, and less likely to purchase combustible cigarettes (-0.46 percentage points). The amount of e-cigarette products purchased increased by 0.28 milliliters following expansion. To give an example of how to interpret these estimates: for e-cigarettes, households in states that expanded Medicaid saw a greater increase in both the probability of purchasing e-cigarette products and the amount purchased compared to households in states that did not expand Medicaid.

Stratified difference-in-difference estimates and 95% CIs for each product across household race and ethnicity are shown in Table 5.3. Following Medicaid expansion, Black households saw increases in the probability and amount of alcohol purchased

(1.94 percentage points and 49.92 milliliters) and an average decrease of five smoking cessation products per month. The only change among Asian households was an average of 13.95 more milliliters of pure ethanol from liquor products. Hispanic households saw decreases in ethanol purchased, driven primarily by decreases in wine (-1.81). Among white households, both the probability of purchasing cigarettes (-0.82) and the amount of smoking cessation products (-5.43) decreased. Table 5.3 also indicates whether an estimate differed from white household estimates statistically significantly (denoted with an asterisk).

We conducted additional analyses with models restricted to states that either did not expand Medicaid or expanded Medicaid on January 1, 2014 (results not shown). Results between restricted and un-restricted samples differed in a few cases. In the restricted sample, the overall probability of purchasing alcohol became statistically significant (0.70) while the probability of purchasing e-cigarette products and the amount purchased both became non-significant (-0.01 and 0.05, respectively). When stratified by race, among the restricted sample, the probability of white households purchasing any alcoholic beverage, the total amount of ethanol purchased, and amount of ethanol from wine all became statistically significant (-0.77, -23.85, and -7.74, respectively).

Discussion

Our findings show that Medicaid expansion was associated with changes in purchasing of harmful substances across several products. Specifically, the probability of purchasing cigarettes and the amount of smoking cessation products purchased decreased, and the

probability of purchasing liquor and e-cigarettes (and the amount of e-cigarette liquid purchased) increased. When the effect of Medicaid expansion was examined across racial and ethnic groups, overall findings suggested that white households were the primary beneficiaries of Medicaid expansion when it comes to substance use. With the exception of e-cigarettes, white households consistently showed decreases in the amount of harmful substances purchased in an average month (though not all decreases were statistically significant). Lee and Porrell similarly found that white adults saw greater gains in healthcare access (e.g., having a source of usual care, having an annual check-up, reporting an overall good health status) following Medicaid expansion compared to Black and Hispanic adults.[191]

Our results quantifying the relationship between Medicaid expansion and substance purchasing were consistent in directionality with a previous study using the same dataset, which found reductions in cigarette, beer, and liquor purchases following Medicaid expansion.[184] However, estimates from our study were not statistically significant. One reason for this may be study sample differences. Given several years had passed since the prior study, we were able to use more years of data (up to the year 2019) and include states that had expanded Medicaid more recently. Increases in product purchases immediately following Medicaid expansion may be followed by a decline in the effect and a movement toward pre-expansion levels of purchasing. However, examination of trends in purchasing following Medicaid expansion showed no evidence of regression to the mean. Bias from negative weighting due to staggered timing of policy implementation can also attenuate estimates towards the null,[160]

however results from our sensitivity analyses to account for this issue remained consistent. Other studies using different datasets have shown sustained decreases in alcohol and cigarette use following Medicaid expansion,[196] as well as increased treatment uptake for alcohol and opioid misuse.[197]

There are several possible explanations for why the relationship between Medicaid expansion and substance use varied across race and ethnicity. While Medicaid expansion removes one structural obstacle to better health by providing an affordable pathway to healthcare coverage, marginalized racial and ethnic groups still disproportionately face other structural obstacles to accessing healthcare. Counties with a higher proportion of black residents are less likely to have a substance use disorder treatment facility that accepts Medicaid.[198] Having to travel a greater distance to access routine or specialized healthcare, and a lack of culturally relevant or tailored treatments for marginalized racial and ethnic groups, can also contribute to a lack of engagement with healthcare treatment.[199,200]

Importantly, we found that only white households had the same pattern of changes in substance use purchasing as the models that did not take racial and ethnic heterogeneity into account. White households represented the majority of our sample, and thus exerted more influence on our regression estimates. If studies of policy effects do not take into account policy effect heterogeneity across racial and ethnic groups, then the results used to inform policymakers may only reflect the experiences of a majority group. In the case of our study, the majority group in our sample (white

households) is also one with the greatest amount of privilege and resources to benefit from Medicaid expansion. Our results support this: white households were the primary beneficiaries of Medicaid expansion through reductions in all products purchases (save e-cigarettes). Researchers must be aware that policies may appear beneficial to health and well-being at a population level, but in reality may only benefit certain groups and ultimately widen health disparities.

Strengths and limitations

The study sample is an unbalanced panel, where households may be missing an entire year of data upon leaving and re-entering the panel. While these missing waves represent missing data, it is not clear whether current methods to account for missing data (e.g., multiple imputation) offer any improvements for unbalanced panels.[201] Despite efforts to adjust for differences between households in states that expanded Medicaid versus households in states that did not expand, controls likely remain non-equivalent. Our study is strengthened by the quantity of data available in the NCP, allowing for a longer time series with finer-grained (i.e., household-level) data. The NCP also uses in-home scanners to track product purchases rather than relying on recollection and maintains a database of product information that standardized across all years of data.

Future directions

The strength of Medicaid expansion and overall change in benefits may impact changes in substance use. Prior to expansion, some states had implemented reforms to expand

Medicaid coverage and thus saw a smaller change in healthcare access following expansion. Future studies should examine this policy heterogeneity, taking into account both the extent of expansion benefits as well as the magnitude of change in benefits pre- versus post-expansion. We were unable to examine the effects of Medicaid expansion on youth. While Medicaid is targeted toward adults younger than 65, expansion has had spillover effects for children – particularly children in low-income families – called a "welcome mat" effect.[202] Given that people under the age of 18 have seen the greatest rate of increase in e-cigarette use in the last few years, studies should examine the role of Medicaid expansion in youth e-cigarette use. Medicaid expansion may affect the use of substances that were not included in the NCP, such as marijuana, opioids, and illicit drugs.

Conclusions

The current study shows that Medicaid expansion is associated with an overall decrease in alcohol, cigarettes, and smoking cessation products, and an increase in e-cigarette purchases. When examining this association across different racial and ethnic groups, these decreases are primarily seen among white households. Our results underscore the importance of considering how population-level health interventions like policies impact health disparities. Black, Hispanic, and Asian households may benefit less from Medicaid expansion compared to white households when it comes to substance use, despite a greater need for healthcare access among these groups. These disparities must be addressed to ensure better health for all and a reduction in health disparities.

Table 5.1. Household demographic characteristics by Medicaid expansion status (%)

	Households in expansion states N=2,784,907 observations	Households in control states N=1,596,868 observations
Marital status		
Married	65.23	67.19
Widowed	2.98	3.25
Divorced/Separated	14.16	14.62
Single	17.62	14.94
Age (female head)		
No female head	10.36	9.44
<25	0.44	0.56
25-29	2.78	3.20
30-34	6.44	7.08
35-39	8.93	9.53
40-44	10.62	11.00
45-49	13.25	13.55
50-54	16.48	16.27
55-64	30.70	29.37
Age (male head)		
No male head	24.77	24.27
<25	0.26	0.29
25-29	1.73	1.98
30-34	4.51	5.13
35-39	6.76	7.33
40-44	8.65	9.15
45-49	10.91	11.15
50-54	13.39	13.28
55-64	29.02	27.44
Age of children		
<6	4.17	4.60
6-12	7.43	7.64
13-17	8.96	9.00
<6 & 6-12	3.75	4.03
<6 & 13-17	0.51	0.70
6-12 & 13-17	4.73	5.11
<6 & 6-12 & 13-17	0.73	0.92
No children under 18	69.72	67.99
Has internet connection	96.06	96.13
Race/ethnicity		
White non-Hispanic	77.26	72.30

Black non-Hispanic	8.66	14.61
Asian non-Hispanic	4.60	2.49
Hispanic	2.57	2.60
Not reported	6.91	8.00

Table 5.2. Adjusted Difference-in-Difference Estimates of Product Purchases Before and After Medicaid Expansion (Main Effects Models)

Outcome	Pre-expansion	Post-expansion	DiD estimate Pre vs. Post
Any alcohol			
Purchased (%)	25.43 (24.95, 25.91)	25.75 (25.38, 26.12)	-0.33 (-0.98, 0.33)
mL	310.88 (300.07, 321.69)	308.08 (293.92, 322.24)	-2.79 (-21.89, 16.30)
Beer			
Purchased (%)	13.00 (12.71, 13.29)	12.77 (12.39, 13.16)	-0.23 (-0.76, 0.30)
mL	91.52 (86.76, 96.28)	91.08 (84.42, 97.74)	-0.44 (-9.49, 8.61)
Liquor			
Purchased (%)	9.47 (9.24, 9.70)	9.93 (9.63, 10.23)	**0.46** **(0.05, 0.88)**
mL	146.41 (138.78, 154.03)	146.85 (137.56, 156.15)	0.45 (-12.40, 13.29)
Wine			
Purchased (%)	12.01 (11.76, 12.26)	11.64 (11.32, 11.96)	-0.37 (-0.81, 0.07)
mL	72.95 (68.80, 77.10)	70.15 (64.11, 76.18)	-2.80 (-10.83, 5.22)
Cigarettes			
Purchased (%)	7.45 (7.59, 7.20)	6.92 (6.57, 7.27)	**-0.53** **(-0.99, -0.08)**
Count	75.00 (71.18, 78.83)	73.11 (66.60, 79.62)	-1.89 (-9.62, 5.83)
Smoking cessation			
Purchased (%)	0.38 (0.33, 0.43)	0.33 (0.27, 0.39)	-0.05 (-0.14, 0.03)
Count	13.29 (9.63, 16.96)	8.45 (6.17, 10.73)	**-4.84** **(-9.01, -0.68)**
E-cigarettes			
Purchased (%)	0.14 (0.12, 0.16)	0.21 (0.14, 0.28)	**0.08** **(0.00, 0.15)**
mL	0.25 (0.17, 0.32)	0.53 (0.28, 0.78)	**0.28** **(0.05, 0.51)**

DiD estimates are coefficients and 95% confidence intervals from difference-in-difference models. Covariates to adjust for confounding were marital status of the heads of household, educational attainment of heads of household, household income, whether the household had an internet connection, the ages of the heads of household, whether the household included children, whether recreational cannabis had been legalized, and whether the state had an excise tax on e-cigarettes.

Table 5.3. Adjusted Difference-in-Difference Estimates of Product Purchases Before and After Medicaid Expansion Stratified by Race and Ethnicity (Interaction Term Models)

Outcome	Black DID estimate Pre vs. Post	Asian DID estimate Pre vs. Post	Hispanic DID estimate Pre vs. Post	Not provided DID estimate Pre vs. Post	White (ref) DID estimate Pre vs. Post
Any alcohol					
Purchased (%)	**2.16* (0.75, 3.57)**	-0.37 (-1.98, 1.23)	**-2.27* (-3.66, -0.88)**	-0.40 (-2.80, 2.00)	-0.26 (-0.97, 0.45)
mL	**51.57* (12.18, 90.96)**	-5.05 (-36.98, 26.89)	2.85 (-29.21, 34.90)	14.18 (-46.75, 75.11)	-11.62 (-32.31, 9.07)
Beer					
Purchased (%)	0.40 (-0.61, 1.41)	-0.26 (-1.37, 0.85)	-0.86 (-2.02, 0.31)	0.66 (-1.32, 2.63)	-0.19 (-0.77, 0.39)
mL	12.72* (-0.69, 26.14)	11.80* (-2.03, 25.63)	8.12 (-10.38, 26.62)	16.03 (-7.93, 40.00)	-5.27 (-14.93, 4.39)
Liquor					
Purchased (%)	**1.09 (0.14, 2.03)**	0.52 (-0.31, 1.35)	0.02 (-0.78, 0.81)	0.26 (-1.30, 1.82)	**0.47 (0.02, 0.92)**
mL	27.76 (-4.50, 60.01)	-10.77 (-31.17, 9.62)	-3.02 (-21.50, 15.47)	4.30 (-35.95, 44.55)	-2.01 (-15.83, 11.82)
Wine					
Purchased (%)	**1.61* (0.72, 2.51**)	-0.92 (-2.12, 0.27)	**-1.61* (-2.54, -0.68)**	-1.00 (-2.66, 0.66)	-0.33 (-0.81, 0.15)
mL	11.09* (-0.85, 23.02)	-6.08 (-19.34, 7.18)	-2.26 (-15.39, 10.87)	-6.15 (-29.21, 16.91)	-4.34 (-13.01, 4.33)
Cigarettes					
Purchased (%)	0.80* (-0.29, 1.88)	0.05 (-0.71, 0.82)	0.12 (-0.77, 1.01)	-0.80 (-2.36, 0.76)	**-0.85 (-1.37, -0.33)**
Count	3.87 (-8.34, 16.08)	20.59 (-12.46, 53.64)	-5.91 (-17.54, 5.71)	5.52 (-12.86, 23.90)	-4.95 (-14.44, 4.54)
Smoking cessation					
Purchased (%)	-0.05 (-0.13, 0.03)	-0.03 (-0.18, 0.12)	0.01 (-0.12, 0.14)	-0.24* (-0.49, 0.02)	-0.06 (-0.17, 0.05)
Count	**-4.55* (-7.95, -1.15**)	3.85 (-4.87, 12.57)	3.16 (-7.56, 13.88)	-8.97 (-18.14, 0.21)	**-5.60 (-10.46, -0.73)**
E-cigarettes					
Purchased (%)	0.07 (-0.03, 0.17)	-0.02 (-0.09, 0.05)	0.31* (-0.01, 0.62)	-0.07 (-0.36, 0.23)	0.06 (-0.02, 0.13)
mL	0.14 (-0.18, 0.46)	0.02 (-0.36, 0.39)	1.63 (-0.11, 3.37)	-0.14 (-0.62, 0.34)	0.14 (-0.05, 0.33)

DiD estimates quantify the difference in purchasing changes following the time Medicaid expansion between states that did expand and states that did not. Bolded values are statistically significantly different from zero (p-value<0.05). Asterisks (*) denote coefficients that were statistically significantly different from the reference group. White households were set as the reference group for interaction terms. Covariates to adjust for confounding were marital status of the heads of household, educational attainment of heads of household, household income, whether the household had an internet connection, the ages of the heads of household, whether the household included children, whether recreational cannabis had been legalized, and whether the state had an excise tax on e-cigarettes.

CHAPTER 6: Synthesis and Conclusions

Disparities in health status across racial and ethnic groups are partially explained by differential access to quality healthcare.[203] Racial and ethnic minority groups are more likely than white people to have a major chronic disease, including cancer,[204] and are less likely to have insurance coverage.[205] Because in the United States the most prevalent source of health insurance is private employment-based insurance, lack of access to healthcare is often tied to economic conditions like employment status and income.

The link between health and healthcare access is explored indirectly in Chapter 3, by examining whether post-treatment cancer survivors use alcohol as a way to self-medicate cancer pain. While we do not explore the direct effects of any measure of healthcare access, the assumption is that survivors may use substances like alcohol to address their pain if they are not receiving adequate pain management through the healthcare system. As described earlier, our findings were that cancer pain was associated with less alcohol consumption when using the entire sample of survivors. However, there were important differences in this association across race and ethnicity; specifically, Black, Asian, and multiracial survivors with cancer pain tended to drink more alcohol than those without pain. This finding echoes the findings of chapter 5 in several ways: the overall estimate for cancer pain and alcohol use was driven primarily by white cancer survivors, who represented the majority of the sample and exerted more influence on the regression estimate. White cancer survivors may also be more likely to

receive adequate pain management and care, thus masking a heterogeneous effect and a disparity in cancer pain self-medication behaviors.

Given that health disparities caused by systems that allow greater access to healthcare for some demographic groups, differences in healthcare access are a population-level problem. Policies are well-suited to address one of the root causes of these disparities: affordability of health insurance. Following the implications of chapter 3 – that inadequate pain management may explain increased alcohol use among Black, Asian, and multiracial cancer survivors – we examined the heterogenous effects of Medicaid expansion on substance use across racial and ethnic groups. Because Medicaid expansion theoretically increases access to healthcare through closure of the Medicaid gap, one might expect to see reductions in substance use among racial and ethnic groups that are disproportionately uninsured. The results from chapter 5 instead show that Medicaid expansion primarily benefited white households; specifically, white households saw decreases in alcohol and cigarette purchasing following Medicaid expansion whereas Black households saw increases in alcohol purchases.

Because policies may inadvertently worsen health disparities, their effects on both targeted and correlated health outcomes must be rigorously evaluated. Chapter 4 demonstrates this by examining how recreational marijuana legalization is associated with substance use using several statistical modeling approaches. We did not evaluate these effects across different racial and ethnic groups, however the approaches used do not change when looking across different strata or using interaction terms for the

groups of interest. Specific to cancer pain, Medicaid expansion, and substance use, the modeling approaches most appropriate must account for staggered policy implementation timing, incorporate comparison groups to mimic the counterfactual (i.e., the effect with no policy), and leverage the advantages of a long time series of data.

The greatest hope with this dissertation is that some of these insights – particularly those concerning policy evaluation and health disparities – are relevant to fields outside of substance use. Policies remain one of our most effective, if challenging to wield and evaluate, tools for creating population-level change. Their impact on substance use and other health problems is well-documented, and they will continue to impact our health and wellbeing for as long as our societies rely on governance to organize our social systems and institutions.

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