THREE ESSAYS EVALUATING THE IMPACT OF PUBLIC POLICY ON PHARMACEUTICAL MARKETS AND PUBLIC HEALTH

by

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(Under the Direction of W. David Bradford)

ABSTRACT

Pharmaceuticals make up a large and growing portion of national health expenditures in the United States, and the market for prescription drugs is subject to a wide range of public policies. This work contains three essays analyzing the impacts of specific policies related to pharmaceuticals. First, I estimate the effect of protected classes on expenditures and utilization for drugs in the Medicare Part D program using the synthetic control method. I find a substantial increase in expenditures for drugs in protected classes—more than $1 billion more per class per year—relative to those in a matched synthetic control group. Second, using a difference-in-differences framework, I measure the changes in opioid painkiller prescribing among doctors in states that implemented prescription drug monitoring programs between 2010 and 2013. Despite the proliferation of these programs and the dire nature of the opioid epidemic, I find only small or insignificant effects for monitoring programs on prescribing. Finally, I develop measures of social capital at the county and state levels using factor analysis to better understand the relationship between vaccination rates and a community's level of social capital. The results of this study provide support that high levels of social capital can be important for encouraging activities like vaccinations that entail positive externalities. However, social capital can also be a

conduit for misinformation or anxiety, where such forces are strong, thus discouraging vaccination. Each of these essays addresses an issue that continues to garner significant public attention. These findings highlight some of the challenges and trade-offs that addressing these issues will entail.

INDEX WORDS: Pharmaceuticals, Prescription Drugs, Medicare Part D, Synthetic Control Method, Substance Abuse, Opioids, Prescription Drug Monitoring Programs, Immunization, Vaccination, Social Capital

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CHAPTER 1

INTRODUCTION

Access to and consumption of pharmaceuticals play an increasingly important role in health care. In 2014, Americans spent almost $298 billion on prescription drugs, which accounted for nearly 10% of total health care expenditure for the year and 1.7% of gross domestic product (Centers for Medicare and Medicaid Services, 2015). While health care expenditures overall increased by 5.3% from 2013, prescription drug spending increased at more than double that rate—12.2% (Martin, Hartman, Benson, Catlin, & National Health Expenditure Accounts Team, 2016). The United States is by far the largest consumer of pharmaceuticals worldwide, accounting for approximately half of all prescription drug sales (Morton & Kyle, 2012).

Clearly, prescription drugs are important economically and for health care delivery. In this dissertation, I intend to conduct quantitative analyses of three ways in which public policy intersects with pharmaceuticals in the U.S. and what the effects of these policies are. The policies I consider will be Medicare Part D protected classes, state prescription drug monitoring programs (PDMP), and state personal belief exemptions (PBE) for child vaccinations.

The pharmaceutical industry is a rich area for public policy research. The industry may appear, *prima facie*, to be a private market like many others, with producers and consumers conducting exchanges and achieving a competitive equilibrium. If this accurately described the world of prescription drugs, then government involvement would arguably be unnecessary and

even detrimental to achieving optimal outcomes. However, the list of ways in which the pharmaceutical market departs from the competitive optimum is long indeed.

To begin, new drug development is expensive and time-consuming such that pharmaceutical manufacturers incur significant upfront, fixed costs for research and development. Estimates suggest that bringing a successful drug through approval and onto the market costs an average of $800 million to $1.2 billion (DiMasi & Grabowski, 2007; DiMasi, Hansen, & Grabowski, 2003). However, marginal costs of production for most drugs are extremely low, perhaps pennies per pill for small molecule drugs (Berndt & Newhouse, 2010). In a competitive market where price equals marginal costs, the drug innovation pipeline, which benefits consumers by providing important new treatments, would dry up from firms being unable to recoup their investments.

This particularity of the pharmaceutical market obliges government action to shield pharmaceutical innovators from competitive copycats through an extended period of patent protection. The need for patent protection is exacerbated by requirements for manufacturers to disclose their product formulations entirely during the drug approval process, fully exposing their intellectual property to duplication by others (Morton & Kyle, 2012). Undermining competitive pressures with patents has the completely predictable effect, however, of undermining competitive pressures. The downsides of extended market exclusivity through patent protection is that it confers monopoly status to manufacturers, which these firms can and do use to increase prices and profits (Scherer, 1993). The rising costs of drugs for consumers is an ongoing concern for health care policy (Islam, 2015; Loder, 2015).

Monopoly producers are not the only mechanism by which competition is disrupted in pharmaceutical markets. Like other health care, prescription drugs are usually covered by

insurance, such that the insurer, as a third-party payer, intervenes in and distorts the relationship between supply and demand. Moral hazard issues are rife (Besanko, Dranove, & Garthwaite, 2016). Insurers employ deductibles, copayments, and formularies—which are lists of covered drugs and associated cost-sharing levels—to try to steer consumption toward favored products (Berndt, McGuire, & Newhouse, 2011). Physicians, as prescribers, are gatekeepers to pharmaceutical access and create an additional layer in drug transactions while also introducing principal-agent problems (Scherer, 1993). Information asymmetries exist between pharmaceutical manufacturers—which are aware of the effectiveness and risks of their products—and patients, creating a need for tight regulation. A number of prescription drugs carry a high potential for addiction and abuse, which produces negative externalities for society (Hernandez & Nelson, 2010). Conversely, vaccines for influenza, measles, and other infectious diseases provide significant positive externalities (Zhou et al., 2014). These and other market failures along with arguments concerned with social justice and unequal access to health care all create entry points for public policy involvement in the pharmaceutical sector.

Indeed, the public policy reach within pharmaceutical markets is extensive and expanding (Frank, 2003). Prescription drugs are heavily regulated by the U.S. Food and Drug Administration (FDA) to ensure efficacy and safety. The National Institutes of Health (NIH) provide funding for new drug discovery and innovation. Immunizations are overseen by the Centers for Disease Control and Prevention (CDC) and administered in large part by state and local public health agencies. The Drug Enforcement Agency (DEA) is tasked with limiting abuse of certain pharmaceuticals, known as controlled substances, which have the potential to help or harm. The list of government agencies responsible for some aspect of the pharmaceutical production or consumption is long and diverse.

Similarly, governments have a sizable involvement in payment for prescription drugs, and in many cases, are themselves the payer. For many years, prescription drug insurance coverage has been provided to millions of Americans through a patchwork of programs including Medicaid, the Children's Health Insurance Program (CHIP), and Veterans Affairs (VA) (Berndt, 2002). The number of individuals receiving drug coverage either sponsored or subsidized by the government has grown tremendously in the past decade (Centers for Medicare & Medicaid Services, 2016b). The Medicare Prescription Drug Benefit (or "Part D") began providing coverage to more than 40 million beneficiaries in 2006, and in 2014, the Patient Protection and Affordable Care Act (ACA) extended insurance coverage to millions more through expanded Medicaid eligibility and subsidized, government-run insurance exchanges. These public insurance programs have a profound impact on pharmaceutical utilization and pricing in the United States (Kesselheim, Avorn, & Sarpatwari, 2016).

As previously indicated, my dissertation will consist of three essays featuring quantitative analyses of public policies related to pharmaceuticals in the U.S. The first essay will address protected drug classes in the Medicare Part D program, a policy that was designed to prevent adverse selection against high-cost beneficiaries but also has implications for the competitive dynamic between drug manufacturers and insurers. There are six therapeutic drug classes designated as "protected" in the Medicare Prescription Drug Benefit (Part D)—anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants.

Under the rule generated by the Centers for Medicare and Medicaid Services (CMS), Part D drug plans—which are offered by private insurers—must cover "all or substantially all" FDA-approved drugs for these protected classes. This policy creates a significant wedge in the competitive negotiations between drug manufacturers and Part D insurers over drug price,

favoring the manufacturer by reducing the negotiating leverage of the insurer. I will explore what the effect of this protected class wedge is on total spending and utilization of drugs in the Medicare Part D program.

Analyzing this question is methodologically challenging for a number of reasons. First, the protected class policy went into effect nationwide and simultaneous to the Part D program in 2006. As a result, there is no intertemporal or geographic variation to exploit. From a practical perspective, there are also no Part D drug claims data that pre-date the protected class policy. Additionally, products in drug classes that were deemed protected likely differ from drugs in unprotected classes in meaningful ways such that treating outcomes in all unprotected classes as a counterfactual to the protected classes is not valid. In order to overcome these challenges, I rely on the synthetic control method (SCM). SCM is a variation on a difference-in-differences framework that provides a way of generating a valid counterfactual by creating a weighted combination untreated units that exactly matches the pre-treatment outcomes of the treated units (Abadie, Diamond, & Hainmueller, 2010).

On average, the SCM analyses show that the protected class policy is responsible for $1.02 billion per class per year more in total spending but had no impact on the quantity of drugs consumed. Policymakers continue to debate changes to this policy. This is the first study to estimate the effects of the policy on government and beneficiary spending, and it provides strong evidence that the policy exacts a significant cost. It will be up to policymakers to decide if any therapeutic benefits of improved drug access outweigh the financial cost of the policy.

Second, I will examine a policy that addresses an ongoing principal-agent problem in health care. Policymakers are increasingly concerned about overprescribing and abuse of prescription opioid analgesics. Opioid painkiller abuse was tied to almost 19,000 deaths in 2014,

a 16% increase over the previous year (Rudd, Aleshire, Zibbell, & Gladden, 2016). Policymakers' abilities to address the opioid crisis are limited, however, because these drugs are considered essential treatments for pain in some cases. Unlike illegal drugs, opioid painkillers are prescribed and dispensed by health care providers. Therefore, any attempt to limit their use must rely in large part on physicians to change their prescribing behaviors.

Prescription drug monitoring programs are a way for government officials to provide physicians with a tool for reducing inappropriate prescribing (Fishman, Papazian, Gonzalez, Riches, & Gilson, 2004). PDMPs keep records of prescriptions filled for controlled substances across all prescribers, which physicians can access to determine if their patients have overlapping prescriptions for opioids. PDMPs are designed to make it easier for physicians to recognize drug-seeking behavior in patients and restrict their prescribing to legitimate pain patients (Jones, Paulozzi, & Mack, 2014). Use of PDMPs is almost always voluntary for physicians, and it is unclear how effective the programs are in reducing prescribing.

I rely on a dataset of physician-level prescribing in the Medicare Part D program to examine the effect of PDMPs on the number of opioid and nonopioid painkiller prescriptions filled. I also examine changes in prescribing by type of opioid in order to see if PDMPs' effects are isolated to certain types of drugs. I separately examine drugs containing oxycodone and hydrocodone, which are the most commonly abused prescription opioids (Cicero, Ellis, Surratt, & Kurtz, 2013). I also look at other opioids by DEA controlled substances schedule. The results suggest that PDMPs have had only a small impact on prescribing, which is primarily limited to oxycodone, a high-profile drug in the opioid epidemic. However, PDMPs have been largely ineffective at reducing overall opioid prescribing, suggesting that policymakers need to find

ways to strengthen existing programs and enact additional policies to minimize the devastating effects of the opioid epidemic.

Lastly, I will explore the impact of social capital on the production of positive health externalities, in this case, through child immunizations. I will also measure the effects of state personal belief (a.k.a., "philosophical") exemption policies on vaccinations and how these policies interact with social capital to determine outcomes. Vaccination rates among children have declined in recent years as more parents are choosing not to follow the CDC's recommended immunization schedule (Kempe et al., 2015). All states require students to receive a certain number of vaccine doses for school enrollment; however, states also allow an array of exemption policies for medical, religious, and personal belief reasons (Omer, Richards, Ward, & Bednarczyk, 2012).

Consequently, parents have discretion about whether they will follow vaccine recommendations. As they make their decisions, they must weigh costs and benefits for both their own children at their communities overall. Vaccination confers a private benefit (personal immunity) in addition to a public benefit by enhancing "herd immunity" (Feikin et al., 2000). As such, vaccines offer positive externalities for society. Theoretically, activities that produce positive externalities occur at less than optimal levels because individuals make decisions strictly based on their private benefits. However, if parents are strongly connected to and engaged with their communities, they may be more likely to vaccinate because they will not neglect to consider the public benefits of immunization.

One way of operationalizing the strength of community ties and engagement is through the concept of social capital. Social capital refers to the value-added of "social networks and the associated norms of trust and reciprocity" that can be found in communities (Putnam, 2007). The

assumption is that if social capital is high, it can, in essence, "grease the wheels" of community action. This may be especially true in policy areas where collective action problems create a clash between individual and public interests. Hypothetically, increased social capital can help overcome these barriers, and vaccination is a public health area where such barriers exist.

I examine the correlation between social capital and vaccination rates at the school-level (using data from the California Department of Public Health) and the state-level (using data from the CDC). For the California data, I construct a county-level social capital index using factor analysis of a number of indicators of social capital. These include the number and resources of local nonprofit organizations, the number and employment in local civic organizations, voter turnout, and other variables. I similarly construct a state-level social capital index using comparable indicators in addition to other variables related to volunteering, trust, civic participation, and relationships between neighbors.

The results do not present a simple story for the association between community social capital and vaccination rates, but a more nuanced narrative emerges at closer inspection. The findings provide evidence that social capital can be a mechanism for improving or reducing vaccination coverage, depending on local context. In areas likely to have more anti-vaccination sentiment, more social capital is associated with lower rates of vaccination. In areas likely to be less skeptical of vaccinations, greater levels of social capital are positively associated with vaccination rates. One conclusion is that social capital can convey a variety of types of information and values in a community. Increasing social capital is not guaranteed to improve public health outcomes such as vaccinations. In fact, it can harm them.

These essays address three topics in health policy and public health that are currently some of the most salient. Rising drug prices, a destructive opioid epidemic, and declining rates of

vaccination are all areas of ongoing concern. Together, these essays conclude that policymakers have more work to do if they hope to address them. In the case of the protected classes, a policy that was designed to protect Medicare beneficiaries is likely substantially increasing pharmaceutical costs in the form of increased out-of-pocket spending and premium costs. One of the principal policies enacted to address prescription painkiller abuse has only a small impact on actual prescribing. Finally, public health officials may be failing to address the individual and community factors that encourage parents to skip vaccinating their children. These findings underscore the necessity of high-quality, objective policy analysis to help assess the effectiveness of policies and uncover better ways of achieving improved outcomes.

CHAPTER 2

HOW PROTECTED CLASSES IN MEDICARE PART D INFLUENCE DRUG SPENDING AND UTILIZATION: EVIDENCE FROM THE SYNTHETIC CONTROL METHOD

Introduction

Since going into effect in 2006, the Medicare Prescription Drug Benefit, known as "Part D," has provided millions of Medicare-eligible Americans with insurance coverage for prescription pharmaceuticals. Not all drugs, however, are treated equally by the program. From Part D's inception, six therapeutic drug classes—antidepressants, anticonvulsants, antipsychotics, antineoplastics, antiretrovials, and immunosuppressants—have enjoyed designation as protected classes according to Medicare rules. The private insurers offering plans through Part D must cover all FDA-approved drugs in the six protected classes; while they are only required to cover a minimum of two drugs in each of the many remaining unprotected classes.

The protected class policy was implemented to prevent insurers from designing plans in ways that deterred enrollment by Medicare beneficiaries who were likely to have above-average drug expenditures and to maintain access to a full range of therapies that might be imperfectly substitutable (Centers for Medicare & Medicaid Services, 2010). However, the policy also has the potential to carry unintended consequences for beneficiary utilization of drugs and overall spending by beneficiaries and the Medicare program. Class protection creates a wedge in the competitive negotiations between private Part D insurers and pharmaceutical manufacturers. The outcome of these negotiations ultimately determines prices paid for drugs, coverage on drug formularies, and cost-sharing levels required of beneficiaries. Protected status effectively

changes the terms of negotiations by eliminating drug coverage exclusion as a bargaining chip. As a consequence, drugs in protected classes may incur higher prices for beneficiaries and Medicare. Guaranteeing coverage of all drugs in these classes might also lower the average out-of-pocket prices faced by beneficiaries, thus increasing utilization for the drugs. Either effect could have profound impacts on Medicare spending in a program that cost the U.S. federal budget and beneficiaries $84.5 billion in 2011 (Medicare Payment Advisory Commission, 2013).

This paper is the first in the literature to directly address the effects of the protected class policy on drug utilization and overall spending in the Medicare program. The question of the impact of protected classes has gained renewed attention in recent years, as the Centers for Medicare and Medicaid Services have put forward (and subsequently retracted) proposals to remove certain classes from protection. It seems quite likely that changes in the list of protected classes will appear on the policy agenda in the near future, and this study can provide important insights into the consequences of a policy shift.

This question, however, is a difficult one to answer. The protected class policy went into effect simultaneously to the Part D program overall; therefore, there are no Part D claims data pre-dating the adoption of protected classes. Additionally, the protected classes have never changed and have always been in force nationwide, leaving no intertemporal or geographic variation to exploit. I overcome these methodological challenges using the synthetic control method (SCM), following Abadie and Gardeazabal (2003) and Abadie et al. (2010). Protected status is a policy that exerts its influence at the drug class-level, making class the appropriate level of analysis for this study. Because there are only six "treated" classes and a relatively small number of classes available to serve as controls, a comparative case study analysis is appropriate. The synthetic control method allows for a comparative case study analysis at the drug class-level

and has the advantage of building a counterfactual case of comparator classes selected on the data rather than researcher judgment. I use eleven years of observations (2001-2011) from the Medical Expenditure Panel Survey—a large, nationally representative survey—to observe trends in drug utilization and spending among Medicare beneficiaries prior to and following implementation of Part D. I examine the average treatment effect across all protected classes in addition to estimating the impacts in each of the six protected classes individually.

My results suggest that protected class status significantly increased overall spending for drugs in these classes. For the average protected class, spending increased $1.02 billion (in 2011 dollars) over comparable classes also covered under Part D. I also observe increases in the quantity of drugs consumed; however, the effect is not statistically significant.

Background

Medicare Part D

In 2003, Congress enacted the Medicare Prescription Drug, Improvement, and Modernization Act (MMA), legislation that created the Medicare Part D prescription drug benefit and set in motion some of the most significant changes to the Medicare program since its inception nearly four decades earlier (Lichtenberg & Sun, 2007). Previously, Medicare served as a public health insurance program that provided medical coverage for Americans 65 years and older and disability-eligible beneficiaries. Self-administered pharmaceuticals (as opposed to those administered by a health care provider in a hospital or other medical setting) were not a covered benefit, and Medicare beneficiaries either had to pay for prescription drugs out-of-pocket or obtain prescription insurance through another source (e.g., retiree benefits, a supplemental Medigap policy, some Medicare Part C managed care plans, or Medicaid for the dually eligible). Only 66% of Medicare's more than 40 million beneficiaries had access to any

insurance coverage for prescription drugs through such sources prior to the availability of Part D. By the end of 2006, 90% of Medicare beneficiaries had drug coverage, either through Part D or some other source (Neuman & Cubanski, 2009).

Congress created Medicare Part D as an optional benefit that would subsidize approximately 75% of beneficiary drug expenses. Unlike Medicare Parts A and B—which cover hospital and outpatient medical care, respectively, and operate according to a single-payer model, whereby the Medicare program administers and pays claims directly to providers—the Part D prescription drug benefit would be provided through a multitude of private insurers. These insurers would be given the latitude to design a variety of insurance plans—within established CMS guidelines—with different features and cost-sharing arrangements. Furthermore, the MMA's "noninterference clause" specifically (and controversially) prohibited the Centers for Medicare and Medicaid Services from negotiating directly with pharmaceutical manufacturers on drug prices. Instead, Part D would rely on private insurers, as "large, sophisticated purchasers" to leverage their market power in order to obtain favorable pricing (in the form of "rebates") from manufacturers (Frank & Newhouse, 2008). Thus, Part D was unique relative to other aspects of Medicare in its use of competition among private insurance plans. By design, Part D plans would compete against each other to enroll Medicare beneficiaries and receive premium payments, and they would engage in competitive negotiations with drug companies to achieve lower prices for pharmaceuticals.

Pharmaceutical manufacturers can be formidable adversaries in these negotiations. They enjoy a degree of monopoly power granted from patent protection for their branded products over a certain period of time. As such, the more distinctive, medically effective, and needed their products are, the greater their ability to extract high reimbursement prices from insurers (Berndt

et al., 2011). It is this monopoly power—coupled with the presence of insurance that distorts the out-of-pocket prices paid by patients—that leads some critics of the pharmaceutical industry to argue that drug prices exceed the therapeutic value they deliver.

Insurers attempt to counteract these competitive pressures by exerting their own market power as buyers of pharmaceuticals with some degree of monopsony power. Insurers, with the help of pharmacy benefit managers (PBM), engage in their own competitive strategies, primarily related to plan design. They develop drug formularies, that is, lists of drugs eligible for coverage. More generous plans feature comprehensive formularies that include all or nearly all pharmaceuticals approved by the FDA. Most Part D plans offer more restrictive formularies that only provide coverage for a limited number of drugs within each therapeutic class. With the ability to restrict formulary access, an insurer can issue a credible threat to drug companies that, unless they agree to an acceptable reimbursement price, they stand to effectively lose access to the beneficiaries covered under the insurer's plan.

In practice, insurers do indeed flex their muscle through formulary exclusion. The Medicare Payment Advisory Commission (MedPAC) estimates that in 2011, Part D plans covered an average of 84% of total chemical entities. As for branded drugs specifically, plans covered an average of 77% of branded drugs and as few as 64% of branded products, indicating that, on average, plans excluded nearly a quarter of brand name drugs entirely from coverage (Hoadley, Hargrave, & Merrell, 2011).

Insurers can further subdivide formularies into tiers that assign drugs to various cost-sharing levels. For example, generic drugs might be available for a very low copayment, while branded drugs are classified as preferred or nonpreferred, with drugs on preferred tiers requiring significantly less out-of-pocket than those on nonpreferred tiers. In Part D's first year, median

copayment amounts were $5 for generic drugs, $25 for preferred brand drugs, and $53 for nonpreferred brand drugs (Hoadley, Hargrave, Cubanski, & Neuman, 2006). The tiering architecture enables insurers to relegate higher-cost drugs to the nonpreferred tier and use the preferred tier as an enticement for manufacturers to offer them lower prices. Overall, in the competitive landscape of Part D, manufacturers have an incentive to set more generous prices for insurers that grant their drugs, first, inclusion on the formulary, and second, more favorable tier placement within the formulary (Berndt & Newhouse, 2010).

These market conditions—with a monopoly supplier and monopsony buyer—characterize a bilateral monopoly. Economic theory predicts some outcome on negotiated price between the high price of a pure monopoly and a low, monopsony price. The actual predicted outcome is somewhat ambiguous, depending on the elasticities of demand and the relative market power of the insurers and manufacturers (Berndt & Newhouse, 2010; Pauly, 2004).

As a result of this competitive, private market-driven system, Medicare Part D's burden on the federal budget relies significantly on insurers' abilities to limit high drug prices using these tactics. High reimbursements would in large part be passed on to Medicare and beneficiaries through higher plan premiums. Consequently, CMS rules regarding plan requirements largely support this form of bargaining between insurers and manufacturers. Attempting to strike a balance between maintaining necessary access to drugs and holding down program costs, CMS only requires that Part D plan formularies cover at least two drugs in most therapeutic classes. Plans are free to choose which drugs will be covered and exclude those that are considered too costly. Research shows that, in general, private Part D plans have been successful at using negotiations to hold down prices and spending for branded drugs that face within-class competition (Frank & Newhouse, 2008). Yet, there remain two instances when

negotiations by private plans may still fall short in keeping drug prices down. The first is when innovator products enter the market, creating new therapeutic classes within which there is little or no competition. The second is in the protected classes, where CMS rules have hampered insurers' bargaining power by curtailing plans' abilities to exclude drugs from formularies (Lee, Gluck, & Curfman, 2016). This paper explores the effect of the latter on Part D drug spending and utilization.

Protected Classes

Allowing insurers to have discretion over plan design and drug coverage presents added challenges with respect to adverse selection. Insurers are incentivized to seek out healthier enrollees who will provide insurers with a more favorable risk pool and lower their drug reimbursement payments. From the perspective of the insurer, more generous coverage has the potential to induce high-cost beneficiaries "adversely select" into those plans; however, offering paltry coverage overall is likely to repel all potential enrollees—both the healthy and the sick. Insurers may then resort to "cream skimming," that is, identifying therapeutic drug classes used by beneficiaries with above-average drug costs and targeting those classes with poor coverage in order to discourage high-cost enrollees.

CMS—desiring to deter such behaviors, ensure access to quality coverage for all beneficiaries, and prevent therapeutic disruption for vulnerable patients—singled out six classes as potential targets for cream-skimming behavior and designated them "protected" (Donohue, 2006). Formularies "must include all or substantially all drugs" in the antidepressant, antipsychotic, anticonvulsant, antiretroviral, antineoplastic, and immunosuppressant classes (Centers for Medicare & Medicaid Services, 2010). "Substantially all" is defined as all drugs and unique dosage forms, with some specific exceptions. For example, plans can exclude a branded

version of a drug if a generic equivalent is available, and they can exclude an extended release product if an immediate-release version of the drug is covered.

In the six protected classes, the competitive dynamic between insurer and manufacturer is disrupted. Although insurance providers still have the flexibility to assign drugs in protected classes to different cost-sharing tiers, they are no longer free to exclude drugs from their formularies. Manufacturers know that insurers are hamstrung by this rule and have more leverage to demand higher prices for their drugs without fear of being kicked off the formulary.

The Department of Health and Human Services (HHS) Office of Inspector General (2011) issued a report that drew on anecdotal evidence and explored the potential impacts of the protected classes policy on Part D rebates. Part D insurers they interviewed asserted that insurers were able to receive "no or minimal rebates" for drugs in the protected classes. Due to the insurers' limited bargaining power, if they did obtain a rebate, it was very likely to be of a lower percentage than otherwise would have been obtained. In another study (also relying on Part D plan self-reports), Part D plan administrators estimated that drug rebates would be approximately 15% higher if classes did not have protected status, for total of $511 million in lost rebates per year (Kipp & Ko, 2008).

If these assertions are accurate, the protected class policy is a wedge in manufacturer-insurer negotiations and serves to enhance the relative market power of the manufacturer over the insurer. Compared to the base case, bilateral monopoly outcome determined by negotiations in unprotected classes, CMS effectively has put its thumb on the scale for the six protected classes, reducing the monopsony power of the insurers. The effect is likely that negotiated prices are higher than what they otherwise would have been in absence of class protection.

The questions asked in this study have a high degree of salience today amidst recent proposals to make significant changes to the Part D protected classes policy. The protected class designation was first established through the CMS rule-making process after enactment of the MMA and was only intended remain in place for the first year or two while the Part D plans became established (Centers for Medicare & Medicaid Services, 2013). It became permanently enshrined in statute when Congress passed the Medicare Improvements for Patients and Providers Act (MIPPA) in 2008 and again in the Patient Protection and Affordable Care Act (ACA) of 2010. In these two pieces of legislation, CMS established two criteria for determining if drug classes should maintain (or newly receive) protected status. They are 1) whether restricting access to a subset of available drugs would lead to major clinical consequences and 2) whether the drugs in the class displayed significant heterogeneity in chemical actions and pharmacological effects, such that some individuals would need access to multiple drugs.

In 2013, CMS convened an expert panel to apply these criteria and determine if there should be more or fewer protected classes. It found that three classes, antidepressants, antipsychotics, and immunosuppressants did not meet the criteria. Subsequently, CMS issued a proposed rule in January 2014 to remove protection from antidepressants and immunosuppressants and to reassess protection for antipsychotics in the following year, stating, "We are concerned that requiring essentially open coverage of certain categories and classes of drugs presents both financial disadvantages and patient welfare concerns for the Part D program *as a result of increased drug prices and overutilization* [emphasis added]" (Centers for Medicare & Medicaid Services, 2014, p. 1937). In response to CMS's recommendations, patient and health care provider advocacy groups moved swiftly in opposition to the proposed changes, and CMS retreated from its position, issuing its final rule in May 2014 that made no changes to protected

classes (Spatz, 2014). However, in its most recent report to Congress, MedPAC (2016) recommended that the Secretary of Health and Human Services proceed with removing antidepressants and immunosuppressants from protection. Clearly, the debate over this policy continues.

Conceptual Model

As indicated above, the protected classes policy has the potential to impact total drug spending in two ways—through both price and quantity. With respect to price, insurers—removed of the possibility of excluding protected drugs from coverage—are likely less able to receive lower prices through their negotiations with branded manufacturers. Typically, the impact of higher prices on overall expenditures would be ambiguous. Spending is the product of price and quantity, and drugs being ordinary goods, their utilization should decline if the protected class policy induces their prices to increase. In this case, the overall effect on spending would depend on the relative magnitudes of the shifts, which would be determined by the price elasticities of demand.

However, the interference of insurance has the potential to disrupt the inverse relationship between price and quantity, and it would be possible to see simultaneous increases in both utilization and price. Such an effect would arise from the distinction between the smaller out-of-pocket price incurred by patients and the larger actual price paid for a drug by all parties. It is hypothesized that health insurance induces moral hazard (Pauly, 1974). As revealed in numerous empirical studies, including the well-known RAND Health Insurance Experiment, insurance promotes increased use of health care goods and services by reducing the out-of-pocket costs faced by consumers (Manning et al., 1987).

Moral hazard likely affected utilization in most if not all drug classes after Part D expanded access to prescription drug coverage. One study estimated that, among individuals who previously lacked any prescription coverage, total spending on drugs across all classes increased by 74% two years after Part D went into effect (Zhang, Donohue, Lave, O'Donnell, & Newhouse, 2009). Like other kinds of health care, demand for prescriptions is largely inelastic to price; however, consumers still demonstrate some sensitivity to changes in out-of-pocket spending, with price elasticities of demand in the range of -0.209 (Gemmill, Costa-Font, & McGuire, 2007) to -0.23 (Gilman & Kautter, 2008) or higher, depending on the drug class and patient characteristics (Goldman, Joyce, & Zheng, 2007). Lower out-of-pocket spending from insurance is also related to increased drug consumption arising from higher rates of medication adherence (Chernew et al., 2008).

The effect of moral hazard on drug utilization may be even greater for the protected classes. By requiring that all drugs be covered, the policy could result in lower out-of pocket costs for patients if their drug would have been excluded from coverage in absence of the policy. Within a given therapeutic class, certain patients will respond more amenably to particular drugs, achieving a better drug-patient match. In the protected classes, patients are potentially more likely to seek and continue drug treatment due to more affordable access to the therapy that best fits their needs in terms of active ingredient, mode of administration, side-effect profile, etc. Therefore, protected status may increase drug consumption, despite the policy also increasing overall price. However, it is not entirely certain whether out-of-pocket will be lower on average in the protected classes, since plans could respond by placing a protected drug on a higher cost sharing tier.

These hypothesized relationships lead me to the following conceptual model,

$$EXPEND_{idt} = Pr_{idt}[Q_{dt} > 0] \times P_{dt}(protection_{dt}) \times Q_{idt}(OOP_{dt}(protection_{dt})),$$

where $EXPEND_{idt}$ is the i^{th} Medicare beneficiary's spending on drug d in time t. The variable $protection_{dt}$ indicates if the drug is in a protected class. Expenditures depend on the probability of the person using any of the drug (based on her medical condition), the price (P_{dt}) of the drug, and the quantity consumed (Q_{idt}). Both price and quantity are a function of protected class status (for quantity, indirectly via out-of-pocket price).

Based on the arguments above, I hypothesize the following relationships:

$$\frac{\partial P_{dt}}{\partial protection_{dt}} > 0$$

and

$$\frac{\partial Q_{idt}}{\partial OOP_{dt}} < 0$$

$$\frac{\partial OOP_{dt}}{\partial protection_{dt}} >=< 0$$

such that

$$\frac{\partial Q_{idt}}{\partial OOP_{dt}} \times \frac{\partial OOP_{dt}}{\partial protection_{dt}} >=< 0$$

According to these arguments, total expenditures are likely to be greater for drugs in protected classes relative to the counterfactual of no protection since price will increase in response to protected status, and the effect on quantity, while less certain, has the potential to increase as well.

The magnitude of the effect is unclear, but the impact could be consequential for Medicare's financial sustainability. These protected classes are far from being a niche part of the Medicare Part D program. Four of the six classes (antipsychotics, antidepressants, anticonvulsants, and antiretrovirals) were among the top 15 therapeutic classes in Medicare in terms of spending in 2007, accounting for 19.6% of program spending (Medicare Payment Advisory Commission, 2010). The drugs in all six protected classes make up between 16.8% and 33.2% of drug spend for insurers, according to one 2008 survey of Part D plan administrators (Kipp & Ko, 2008). Ultimately, it is likely that the value of these lost rebates is passed on in the form of higher costs for the Medicare program and higher premiums for beneficiaries.

Literature

The extant empirical literature on protected classes is extremely limited and therefore does little to support or contradict CMS concerns about increases in spending and utilization. The above referenced reports by Kipp & Ko (2008) and the HHS Office of Inspector General (2011) provide anecdotal evidence of increased prices due to class protection.

Madden et al. (2015) use interrupted time series analysis to examine claims from dual eligibles[1] with a diagnosis of schizophrenia or bipolar disorder and observe changes in their utilization of antipsychotics and anticonvulsants before and after Part D's launch. Under Part D, they find significantly increased utilization for patients who were in states with strict caps on utilization for their Medicaid programs—35.5% higher prescription fills for bipolar patients and 17.7% more fills for schizophrenia patients—but no significant differences for patients in no-cap Medicaid states. This suggests that quantity effects are potentially significant—especially for

[1] Dual-eligible beneficiaries are those who receive both Medicare and Medicaid. Prior to the implementation of Part D, dual eligibles received prescription drug coverage through Medicaid; however, their coverage shifted to Medicare once Part D came online in 2006.

patients who previously had no or limited prescription coverage—however, it does not provide any insights into the extent to which being a protected class drove the increases in utilization of antipsychotics and anticonvulsants.

Duggan and Morton (2010) use 2003-2006 MEPS data to examine drug-level pharmaceutical price and utilization changes related to the Part D program overall, while also attempting to measure those changes for protected classes specifically. Their results suggest that although Part D was successful in lowering drug prices in general, prices in protected classes were either unchanged or increased. However, due to a small sample size, their estimates lack precision, and several are not statistically significant. Their findings for utilization in protected classes are inconclusive. Additionally, they rely on a very short panel and only observe one year of post-Part D data; therefore, their study does not take into account outcomes that occurred in subsequent years after Part D's first, somewhat tumultuous year of implementation.

This study seeks to fill the gap in our knowledge about how the designation of six classes as protected has affected Medicare beneficiaries' access to these drugs by measuring changes in the quantity of the drugs consumed as well as estimating the impact on total spending for the drugs. Although CMS abandoned its latest effort to make changes to the protected class policy, the agency has signaled that it will revisit the issue in the future (Medicare Payment Advisory Commission, 2016). Having a fuller understanding of the policy's impacts will be beneficial for informing the debate going forward and helping to ensure that the Part D prescription benefit strikes a satisfactory balance between access to needed drugs and cost.

Methods

Analyzing the effect of protected status entails a number of methodological challenges. First, protected status and overall Part D coverage share the same birthday; they both went into

effect on January 1, 2006, making it difficult to separate out the effects of expanded pharmaceutical coverage through Part D from the independent effects of class protection. This also means that there are (obviously) no Part D program or claims data prior to the program's launch in 2006, which makes it necessary to find other data sources that can track both the pre- and post-Part D time periods. Third, protected class status has always been a nationwide policy and no drug classes have either gained or lost protection over time, eliminating the ability to exploit variation either between geographic areas or within drug classes over time. Finally, protected status is conferred at the therapeutic drug class level, which makes the aggregated class the appropriate level of empirical analysis. The number of classes available to use as potential control group comparators to the six protected classes is relatively small, and any analysis at the class-level must grapple with a modest sample size.

An obvious methodological approach—assuming access to an appropriate dataset that spans the treatment implementation—is a difference-in-differences (DID) estimation. Such a strategy would compare changes in average pre- and post-Part D outcomes between the protected (treated) classes and the unprotected (control) classes. The DID method rests on the assumption that the treatment and control groups would follow parallel trends in absence of the intervention. In this case, the approach is appealing because it would take into account that both treated and control groups experience Part D expansion at the same time, but only the treated classes receive the extra policy "shock" of having protected status.

A DID approach has shortcomings in general and in this study in particular. First, researchers often assume that the parallel trends requirement has been satisfied with little justification for why. Sometimes researchers rely on visual inspection of the pre-period trends or they assert that a regression on pre-treatment observations shows no statistically significant

difference in the time trends between treated and control groups. This is perhaps too low of a bar in order to allege that the two groups were likely to follow the same trajectory post-treatment.

In this study, an apparent barrier to use of the DID method is that simultaneous treatments occurred on January 1, 2006—Part D coverage availability and protected classes. Parsing the independent effects of each is difficult. However, since all drug classes included in the study experience Part D coverage availability—protected and unprotected alike—this confounder should be differenced out using a DID approach.

What remains quite tricky in this study is the choice of a comparator, and this challenge particularly is what makes a traditional DID approach potentially inappropriate. The characteristics of different drug classes vary a great deal, and there is no obvious reason *a priori* to believe that antipsychotic drugs would follow the same trends in utilization and spending as drugs for, say, acid reflux or diabetes. CMS did not assign the protected class designation at random. The agency chose the six protected classes deliberately because of their use by high-cost, vulnerable patients. These classes will differ systematically from the average unprotected class. Consequently, using all unprotected classes in the control group is unlikely to provide a valid counterfactual. I could attempt to refine my control group by selecting comparator classes that exhibit similar observable characteristics and treat a similar severity of illness but that were, for whatever reason, not chosen for protection by CMS. However, doing so runs the risk of introducing a researcher's subjective judgment into the analysis, which could bias the results.

Following the lead of Abadie and Gardeazabal (2003) and Abadie et al. (2010), I rely on the synthetic control method (SCM) as a data-driven approach to constructing a valid comparator. SCM matches treatment and control groups on observable, pre-treatment characteristics. Instead of attempting to demonstrate similar trends in a difference-in-differences

framework or identifying a single unit to serve as the control in a comparative case study, the synthetic control method creates a weighted combination of comparison groups such that the trends in the weighted combination itself very closely match the trends in the treated group. For example, in Abadie et al. (2010), the researchers estimate the effect of California's 1988 tobacco control program on cigarette sales by constructing a "synthetic California" from a weighted average of five other states without such programs—Colorado, Connecticut, Montana, Nevada, and Utah. In the pre-treatment period, cigarette sales in California and synthetic California follow an identical, overlapping path, and the divergence between the two after introduction of the policy represents the effect of the tobacco control program. Similarly, Powell (2016) employs SCM to predict the impact of state minimum wage law changes on employment; Cavallo, Galiani, Noy, and Pantano (2013) measure the effects of natural disasters on economic growth, and Kreif et al. (2015) create a synthetic control to understand the relationship between hospital pay-for-performance initiative in England with mortality reductions.

There are several other advantages of the synthetic control method over a difference-in-differences framework. As discussed, SCM constructs a control group without introducing possible bias from researcher discretion. While DID models will be biased if unobserved variables affect the dependent variable differentially over time, SCM allows the effects of unobservables to vary over time (Abadie, Diamond, & Hainmueller, 2015). Additionally, SCM can accommodate (in fact, it requires) a small sample size, whereas a DID approach will suffer from a lack of precision in small-n studies. This provides an advantage in this study, which has only 126 observations per year. Finally, in this study in particular, where some potential control classes are quite unlike the treated classes, the method is intuitively attractive. SCM identifies similar classes from the pre-treatment data and weights them in order to recreate the trajectory of

the protected class and construct a strong counterfactual case. The ability to visualize the pre-treatment overlap in trends and the post-treatment divergence provides more confidence in the validity of the observed effect.

Synthetic Control Method Implementation

To implement the synthetic control method, I measure the effect of protected status for each of the six protected classes independently in separate models. I also conduct a seventh model to measure the overall effect of class protection on an aggregate protected class. This aggregate protected class is composed of the average values of all of the six protected classes. This last model will provide an estimate of the protected class effect in general and will be the focus of this analysis. In addition to estimating seven separate models for each of the six protected classes and for the aggregate protected class, I also measure the policy effects on two dependent variables—utilization and total spending. Therefore, I conduct 14 separate models—7 for each treated group with two dependent variables.

Closely following the synthetic control method as presented by Abadie et al. (2010), I define my sample as containing $J + 1$ drug classes. The first class will experience the treatment—in this case, protected status in Part D formularies. The remaining J unprotected classes constitute the "donor pool." They are the classes from which the synthetic control group will be constructed. The outcome of interest is Y, and Y_{it}^{N} is the value that would be observed in an untreated state (i.e., without class protection) for the i^{th} class in year t. The sample thus consists of classes $i = 1, \ldots, J + 1$ and years $t = 1, \ldots, T$.

In this study, there are two outcome variables that will be used in separate analyses—total utilization and total spending. I define T_0 as the number of time periods before the implementation of the protected class policy, such that $1 \leq T_0 < T$. While Y_{it}^{N} is the outcome of

interest without exposure to the treatment, Y_{it}^{P} is the value of the outcome when a class has received protected status, and treatment remains in place in all years of the post-treatment period, from $T_0 + 1$ through T. In the pre-treatment period, Y_{it}^{N} and Y_{it}^{P} are the same. The treatment effect in year t and class i, defined as α_{it}, then equals $Y_{it}^{P} - Y_{it}^{N}$.

An indicator variable, D_{it}, has a value of 1 if i is designated a protected class in t and 0 if not, such that D_{it} only equals 1 when $i = 1$ and $t > T_0$. Consequently, the observed value of Y for class i in year t is:

$$Y_{it} = Y_{it}^{N} + \alpha_{it} D_{it}.$$

The ultimate objective is to estimate the post-treatment policy effects, $\alpha_{1T_{0+1}}, \ldots, \alpha_{1T}$. For all $t > T_0$,

$$\alpha_{1t} = Y_{1t}^{P} - Y_{1t}^{N} = Y_{1t} - Y_{1t}^{N}.$$

While I do observe, Y_{it}^{P}, I do not observe the counterfactual, untreated world that produces Y_{1t}^{N}. I must generate an unbiased estimated value of Y_{1t}^{N} in order to measure α_{1t}. Continuing to follow Abadie et al. (2010), I assume that Y_{1t}^{N} can be defined by a factor model,

$$Y_{it}^{N} = \delta_t + \theta_t Z_i + \lambda_t \mu_i + \varepsilon_{it},$$

where Z_i is a vector of observed exogenous characteristics of i, λ_t is a vector of unknown common factors and μ_i are the unknown class-specific factor loadings, δ_t is an unknown time-variant factor that is constant between classes, and ε_{it} is the stochastic error term.

It is unlikely that a single untreated unit or group of units will be able to exactly recreate this counterfactual, Y_{1t}^{N}. However, it is possible that a weighted combination of untreated units from the donor pool can approximate Y_{1t}^{N}. Therefore, I create a J × 1 vector of weights $W = (w_2, \ldots, w_{J+1})'$, where $0 \leq w_j \leq 1$ for $j = 2, \ldots, J + 1$ and $\sum_{j=2}^{J+1} w_j = 1$. The goal is to select an optimal set of weights $(w_2^*, \ldots, w_{J+1}^*)$ such that

$$\sum_{j=2}^{J+1} w_j^* Y_{j1} = Y_{1,1}$$

$$\vdots$$

$$\sum_{j=2}^{J+1} w_j^* Y_{j,T_0} = Y_{1,T_0}$$

$$\sum_{j=2}^{J+1} w_j^* Z_j = Z_1,$$

that is, the pre-treatment values of the outcome variable and the control variables are weighted to match those of the protected class (Cavallo et al., 2013). In order to estimate the effect α_{1t} for the post-treatment period (T_0+1, . . . , T), I use

$$\hat{\alpha}_{1t} = Y_{1t} - \sum_{j=2}^{J+1} w_j^* Y_{jt}.$$

Using these weights, $\sum_{j=2}^{J+1} w_j^* Y_{jt}$ becomes an unbiased estimate of Y_{1t}^N.

Selection of the optimal weights arises from a straightforward linear algebra problem that minimizes the geometric distance between vectors of pre-treatment outcome and control variables. A (k × 1) vector of all pre-treatment outcome and control variables for the treated class is defined as $X_1 = (Z_1'; Y_{1,1}, \ldots, Y_{1,T_0})'$. A ($k$ × J) matrix, defined as X_0, contains the same variables for all of the donor classes (that is, a combination of J k × 1 vectors, one vector from each unprotected class). The values of w_j^* in the (J × 1) vector W^* are then generated by minimizing the distance, $\|X_1 - X_0 W\|$, between X_1 and $X_0 W$. As done in Abadie et al. (2010), I will seek to minimize $\|X_1 - X_0 W\|$ subject to

$$\|X_1 - X_0 W\|_V = \sqrt{(X_1 - X_0 W)' V (X_1 - X_0 W)}$$

where V is a ($k \times k$) symmetric and positive semidefinite matrix. V gives weights to a linear combination of the variables in X_1 and X_0 such that the mean square prediction error of the synthetic control estimator is minimized.

In this study, I use 11 years of MEPS data; five years (2001-2005) in the pre-treatment period ($T_0 = 5$) and six years in the post-treatment period (2006-2011). There are six protected classes, and I separately estimate the effects of protection in individual models for each of the six. I also estimate a model using an aggregated treated class created by averaging the outcome and control values from all six classes, following Kreif et al. (2015). In the aggregated model, I can observe the overall effect of protected class status on the dependent variables. However, it is also advantageous to estimate separate models for the individual protected classes because some of the treated classes may respond differently to protection than others. If some classes respond more strongly to protection than others, the effects on those classes may be attenuated in an aggregated model. Understanding the differential effects of the six protected classes is also important from a policy perspective. CMS has revealed its intention to remove protected status from targeted classes; therefore, understanding how the impact of the policy on spending or consumption of antidepressants, for example, compared with antineoplastics is an important distinction.

Inference Using Placebo Tests

The method described above does not allow for the computation of traditional standard errors. I again follow Abadie et al. (2010) and estimate a series of placebo tests for each of the 14 models to establish statistical significance. This process entails acting as though each of the *untreated* classes in the sample had been treated with protected status in 2006 and iterating the

synthetic control method for each of the untreated units. As with the treated, protected classes, each of the untreated classes from the donor pool is matched with a synthetic control, generated from the remaining donor pool. In other words, I observe what the pseudo-effect size would be if each of the unprotected classes was designated as a pseudo-protected class in 2006. From these placebo tests, I generate a distribution of estimated treatment effects calculated from a data generating process where the null hypothesis of zero treatment effect is known to be true. This process allows me to compare the magnitude of the estimated effects from the actual protected classes to the magnitude of the estimated effects from the pseudo- (or placebo-) protected classes. As a corollary to the typical 95% confidence interval, for the effect size of the protected class to be considered significant in the SCM model, the magnitude of the effect would need to be among the largest 5% in absolute value compared to the placebo effects.

This inferential method is particularly important in this study because all drug classes—not only the protected ones—underwent a substantial shock in 2006 with the expansion of prescription drug coverage through the launch of Part D. The placebo tests serve to capture and separate out the base effect of Part D coverage. If the protected classes show effect sizes that are among the largest when compared the placebos, it would provide support that there is an independent impact of the protected class designation on utilization or spending separate from the overall effect of Part D.

I execute each of these 14 models in Stata SE 13 using two modules developed for the synthetic control method—the `synth` package (Hainmueller, Abadie, & Diamond, 2014) and the `synth_runner` package (Quistorff & Galiani, 2016). `synth_runner` operates through `synth` but offers additional output options that make it desirable. For example, `synth_runner` provides the effect sizes for the placebo tests. However, only `synth` provides

the weight vectors used to construct the synthetic control. Therefore, I run identical commands through both packages to obtain the complete set of parameters presented in the Results section.

Data

To examine the effects of protected drug classes, I use eleven years of data from the Medical Expenditure Panel Survey (MEPS) from 2001 to 2011. The MEPS is a long-running, nationally representative survey of individuals and their health care providers conducted by the HHS Agency for Healthcare Research and Quality (AHRQ). It follows survey participants during five data collection periods over two-year, overlapping panels. Each year, there are approximately 30,000-35,000 survey respondents in the sample, which includes individuals of all ages and diverse backgrounds. The survey collects information about health status and behaviors, insurance coverage, health care utilization and spending, and demographic characteristics.

I rely most on the MEPS Prescribed Medicine files. These annual files contain data collected from the survey respondents and their pharmacies on prescriptions used during the year. The data include the 11-digit National Drug Code (NDC) and drug name, the quantity (in units, such as pills) of the drug dispensed, the drug's therapeutic class based on the Multum Lexicon database (a widely used proprietary drug classification system), and the total amount paid to the pharmacy for the drug from all payers. I adjust the spending variable for inflation using the Bureau of Labor Statistic's Consumer Price Index for medical care to 2011 dollars.

I also obtain the individual's insured status and insurance type (e.g., private payer, Medicare, Medicaid, etc.) from the MEPS Household Component Full-Year files. I generate an indicator variable for a person being dually enrolled in both Medicare and Medicaid. Finally, I use the Risk Adjustment Scores file to obtain the relative risk scores for each of the survey participants. The MEPS generates these scores based on each individual's gender, age, and

diagnostic status across a number of conditions to develop a score that represents the propensity for a person to utilize health services. The scores are normalized such that a value of 1.0 predicts spending equal to the average in the Medicare population; therefore, a value of 1.2 would indicate spending predicted at 20% higher than average and 0.8 would indicate spending 20% lower than average.

I merge each these individual-level datasets together. Because my aim is to study changes in drug spending and utilization among Medicare beneficiaries, I drop all of the observations for individuals who did not have Medicare coverage in the year. Then, using the survey sample weights to create nationally representative estimates, I collapse the individual-level data to the drug class-year level. I identify the six protected classes in the data—anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants—and create dichotomous variables designating them as the treated groups. Following Kreif et al. (2015), I also create a seventh treated group whose values were the averages of all the protected classes, which allows me to estimate the overall effect of protected status. I created a post-treatment period variable for all observations from 2006 and later.

My final dataset contains two dependent variables—total quantity of units consumed in the drug class and total spending (from all sources, out-of-pocket and insurers) in the class. My control variables include the percent of Medicare users who were dual eligibles and the average relative risk score for Medicare beneficiaries taking drugs in the class. The percent of dual eligibles variable helps to identify drug classes that are used by a high proportion of low-income, more socioeconomically vulnerable patients. The average relative risk score provides a way to compare drug classes whose users have similar health statuses, severity of illness, and expected health care spending.

Over the 11-year study period, there were 246 drug classes present in the data. First, I excluded 17 classes that are not eligible for coverage under Part D, such as prescription cold and cough remedies or vitamins, because the purpose of the analysis is to compare protected classes that gained Part D coverage in 2006 with control classes that gained Part D coverage without protection. Additionally, I excluded classes that were not present in the data for all 11 years of the study period in order to achieve a balanced panel, which is required for implementation of the synthetic control method. Many of the drug classes are either only intermittently present in the sample (because they include drugs that are not widely used) or the class was newly created during the study period (when some innovator drug came to market). These 98 excluded classes account for less than 5% of the drugs consumed in the data. The final dataset used in the synthetic control analyses includes the six treated drug classes plus the aggregated protected class along with 125 control classes in the donor pool. Each of the 14 synthetic control models, which include a single treated class, has a sample size of 1,452.

Table 1 displays the summary statistics for the entire sample and for the sample divided by protected and unprotected classes. Average total spending for all classes was approximately $749 million; however, spending was almost four times higher for the protected classes than the unprotected classes. Finally, average utilization was substantially higher for the protected classes.

Results

Figure 1 displays the average pre-treatment values of the dependent variables for the treated and synthetic controls over time along with the average values for all of the control classes if they were weighted evenly, as would be the case in a normal difference-in-differences model. The graphs demonstrate the advantage of the synthetic control method in this analysis.

Not only do the average values between the protected classes and the average of all controls have very different intercepts, they also follow different slopes. For both of the dependent variables, the pre-treatment trends for the protected classes have steeper slopes than the average of the control classes, which would violate the parallel trends assumption of DID. In comparison, the trends for the synthetic controls exactly match the protected class values in magnitude and slope.

The results of the synthetic control models are best presented graphically. To simplify the analysis of 14 separate models, I present the main results from the two aggregated models in Figure 2 (for drug utilization) and Figure 3 (for drug spending). The results for the models measuring the effects on anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants alone are provided in the Appendices A-F.

The graphs displayed on the left sides of Figure 2 and Figure 3 are the line graphs showing the 11-year trends in the outcome variables for the protected classes (solid red lines) compared with their matched synthetic controls (dashed blue lines). The dotted vertical line separates the data points collected before and after the implementation of both Part D and the protected class policy.[2] In each case, the lines clearly track uniformly over the pre-treatment period and diverge in the post-treatment period. This vertical divergence between protected class and synthetic protected class in the post-treatment period represents the estimated effect of protected class status.

The left-side graph in Figure 2 examines the effect of protected class status on the total number of drug units consumed by Medicare patients. The estimates show a gradual and modest increase in consumption in the protected classes that exceeds the growth of the unprotected Part D drugs included in the synthetic control. Table 2 shows the numeric results of the synthetic

[2] Because Part D implementation occurred on January 1, 2006, the vertical dotted line falls on the graph at 2005 because the 2006 values are post-implementation data points.

control model measuring the effect on units consumed for the aggregated protected class by year and for the post-treatment period average. By 2011, there are almost 400 million more units consumed in the aggregate protected classes than in its synthetic control. The average post-treatment effect size for the protected class policy is 212 million additional units consumed, which represents a 15.7% increase over the synthetic control. Table 4 displays the results of the SCM models for individual protected classes and shows that the effect seems to have been driven by the antidepressant, antineoplastic, and immunosuppressant classes.

The left-side panel in Figure 3 shows the effect of protected status on total spending (in millions of 2011 dollars) for the aggregated protected classes. There is a clear separation between the protected class and the synthetic control that begins in 2006, the first post-treatment period, and diverges sharply beginning in 2007. The protected classes show rapidly increasing spending over the synthetic control, whose spending remains relatively flat post-Part D. By 2011, there is approximately a $1.4 billion difference between the average protected class and the synthetic control. Looking at the individual class models presented in the Appendices, this trend in total spending holds for all of the protected classes. Each of the graphs shows increased spending relative to the synthetic control. Only for the anticonvulsant and immunosuppressant classes does this seem to be a merely modest increase.

The question remains if these observed effects of protected class status are "large" enough to be considered significant. To answer, I turn to the results from the placebo tests. The graphs displayed on the right sides of Figure 2 and Figure 3 provide the results of the main SCM models estimating the effects for protected classes (red line) along with the results of the placebo tests conducted on each of the control classes (blue lines). In the pre-2006 period, these differences in all cases should be zero or very close to zero, as the synthetic controls were

intentionally constructed to match the pre-treatment trends of the treated group. The positive and negative differences shown in the post-treatment period display the divergence between the treated and synthetic controls for the actual protected class and the placebo protected classes. In order to consider the estimated effect for the protected class to be significant, it would need to have one of the highest or lowest lines—depending on the direction of the effect—compared with the placebo classes.

Some of the control classes simply do not find a close pre-treatment match using the SCM approach, and therefore are not valid comparators for the treated protected classes as placebo tests. As noted in the Methods section, the synthetic controls are matched by minimizing the pre-treatment root mean squared prediction error (RMSPE). In order to retain only those placebo tests that do have strong enough pre-treatment matches, I exclude placebo tests with RMSPEs greater than 20 times the RMSPE from the protected class model (Abadie et al., 2010).

The placebo graph in Figure 2 (right-side) reveals how the observed effects of aggregate protected class on total utilization compare with those of the placebo tests. The increases experienced in the protected classes are large compared to most of the placebo tests; however, a significant number of placebo control classes experienced even larger increases in the post-Part D period. The treatment and placebo effects for drug spending are in the right-side panel of Figure 3. Indeed, the positive effects shown in the panel to the left prove to be quite large when examined next the placebo tests in the graph on the right. This provides strong evidence that total spending has risen substantially in the protected classes relative to comparable unprotected classes since the implementation of the Medicare Part D program. For most post-treatment time periods, only one drug class saw bigger increases in utilization after 2006.

Visualizing the treatment and placebo effect lines is helpful but does not provide a quantitative measure of the improbability of observing a certain effect for the treated group. In order to generate such a value, I follow the example of Kreif et al. (2015) and calculate p-values for each of the leads (i.e., years post-treatment) and for the average of the treatment effects in the post-treatment period (2006-2011). For each protected class and dependent variable, I then determine the percent of placebo effect values that were *at least as great* as the effect value for the protected class in absolute value. The resulting value is a "p-value" that is very small if the protected class effect size is very large relative to the placebo values (in absolute value terms). I conduct a two-tailed significance test since I do not assume *a priori* if the effects will be positive or negative. Following convention, I consider a result to be significant at the 99% if the p-value is less than or equal to 0.01, at the 95% level if it has a p-value less than 0.05, and at the 90% level if it has a p-value less than 0.1.

These p-values are presented for the aggregated models in Table 2 for the utilization dependent variable and in Table 3 for the spending dependent variable. As suggested by the visual representations in Figure 2, the p-values for the utilization model are too large to be considered significant across all leads and for the post-treatment average. Table 4 displays the p-values for the utilization models looking at the individual protected classes. Like the aggregated model, the individual class models are almost across the board insignificant. Only antidepressants show statistically significant increases in utilization after 2006.

Table 3 shows the p-values for the aggregated model estimating effects on drug spending. The outcome here is different than for the utilization models. The p-values are small and statistically significant in all post-treatment years except the first lead, 2006. The average post-treatment effect size is also significant, with a p-value of 0.027. Table 5 displays these spending

results for the individual class models. They show that increases in spending were significant for four of the six classes across nearly all years and on average over the post-treatment period. Only anticonvulsants and immunosuppressants did not show statistically significant results.

Discussion

These 14 synthetic control models examined the effect of the protected class policy on the spending and utilization of the drugs in these protected classes. The findings suggest that the protected class policy is very costly to the Medicare program and consumers. Total spending (from all sources) increased for the aggregated protected class and for all but two individual protected classes when the classes are examined separately. For the aggregated model, the estimated effect size (as seen in Table 2) was $1.02 billion in 2011 dollars, that is, compared to a matched synthetic control, the protected classes saw an average increase of this magnitude. Without question, this is a substantial effect, not only in statistical significance, but also in economic significance. As seen in Table 3, the effect represents a 50.6% increase over the synthetic control counterfactual.

This large effect on total spending can arise from increases in quantity of drugs consumed, price, or both quantity and price. While this study is not able to measure changes in price of drugs in the protected classes, the findings suggest that increased prices are the most likely drivers of this raise in spending. There were generally no statistically significant increases in quantity consumed for the synthetic control models. Additionally, even the statistically insignificant estimate for change is quantity was a 15.7% increase, which could not entirely explain the larger 50.6% increase in overall spending.

The pharmaceutical market is diverse and subject to fluctuations in price and utilization due to factors that can be difficult or impossible to observe, especially on an industry-wide scale.

These factors could include updated safety warnings from the FDA, drug shortages from production disruptions overseas, new research findings on drug efficacy, new product entry on the market, or patent loss by a prominent product. It is possible that the placebo classes that showed effect sizes larger in magnitude than the protected classes (thus lowering the estimates' p-values) encountered idiosyncratic changes that produced abnormally sized jumps in utilization. Fundamentally, comparing the activity of one drug class to another, even a well matched one, is not comparing two otherwise identical entities, and there can be changes that occur to one for which a researcher cannot account. With this in mind, the p-value less than 0.2 for the aggregated protected class model measuring utilization could still merit attention even though it does not meet conventional standards for statistical significance.

Robustness Checks

These results from the synthetic control models above provide compelling evidence that the protected class policy increased spending for the Medicare Part D Program. However, there are a number of robustness checks that I can conduct to increase confidence in these results. First, I want to test my hypothesis that the increases in spending derive from an increase in the relative market power of drug manufacturers when their drugs are in protected classes. This advantage should accrue only to on-patent, branded products. When generic equivalents are available on the market, the branded manufacturer should have very little market power to exploit, whether their products are protected or not. Therefore, I conduct the same SCM analysis as in my previous models; however, I restrict the sample to only drugs that had generic equivalents available during the entire study period—that is, only drugs that had lost patent protection prior to 2001. If the protected class policy is operating through changes in market power, the effect of protected classes should disappear in this specification. Figure 4 displays the

graphs for the effects and placebo tests for this specification on the aggregated protected class, and Table 6 provides the effect sizes and p-values. As predicted the effect size is substantially smaller and statistically insignificant when only off-patent products are used.

For a second robustness check, I recalculate the effects of protected classes on the aggregate protected class excluding antineoplastics. There are several reasons for wanting to exclude this class. First, as shown in Table 5, the effect size for antineoplastics is very large ($2.6 billion per year, on average) compared to the rest of the classes. So it is important to know the extent to which this class is driving the overall results. In addition, antineoplastic drugs, which include chemotherapy for the treatment of cancer, are sometimes covered by Medicare Part B instead of Part D, dependent on whether they are self-administered or given in a medical facility. Since there may be measurement error in knowing whether these drugs were always subject to Part D's rules, it is useful to exclude them. Finally, there has been a great deal of innovation in this class during the post-treatment period, including the introduction of new products that treat new indications of cancer. This may violate the spirit of the difference-in-differences framework and bias the results away from zero.

Figure 5 displays the results from an SCM model measuring the effect of protected classes on total spending for an aggregated protected class that excludes antineoplastics, and Table 7 presents the effect sizes and p-values. The result is lower than what is estimated when all six classes are included but is still quite large and statistically significant. This specification estimates the effect of protected class status to be $647 million per class per year on average over the post-treatment period.

I also want to be confident that the results estimated are not due to measurement error from the MEPS survey or problems with the sample weights used to make nationally

representative estimates of drug spending and utilization. For this reason, I conduct SCM models using alternative datasets measuring drug sales and utilization. I use 2001-2010 data from IMS Health on sales of pharmaceuticals for the top 1,000 drugs (by U.S. sales). In also use 2003-2010 Verispan VOTA data on drugs sales and quantity consumed for the top 200 drugs (by U.S. sales). For the aggregate protected class, I get qualitatively similar results in these models as I do in my original models using MEPS data (results in Appendices G and H). There are large and statistically significant increases in drug sales for the protected classes, and using the Verispan utilization data, I do not find statistically significant effects for utilization.

Finally, I conduct a standard difference-in-differences regression model on the MEPS data with class and year fixed effects (and the same controls as used in the SCM models) to see if my results are produced by the SCM methodology rather than actual empirical effects. The results (available in Appendix I) for drug spending are remarkably similar in magnitude and significance to those from the synthetic control models. The principal difference is that the results for quantity consumed are statistically significant in the DID regression while they are not in the SCM models.

Each of these tests strengthens the findings from the main synthetic control models. They support the conclusion that the protected class policy has resulted in increased total spending for drugs in the protected classes, and there is inconclusive evidence to suggest that utilization may have increased as well.

Conclusion

The launch of the Medicare Part D prescription drug benefit in 2006 heralded a major change in the pharmaceutical and insurance markets. It expanded access to comprehensive prescription drug coverage for millions of seniors and others eligible for Medicare. Protected

classes have been a part of the Part D program from the beginning, yet we have little understanding of their impact on drug spending and utilization. Part of the reason that protected classes have received almost no attention in the literature is due to the difficulty in isolating their effects. The policy has not varied over geography or time, and it went into effect at the same time as the original Part D "policy shock." It is difficult to generate a valid counterfactual with unprotected drug classes that could differ in important ways from the protected classes. Additionally, if examined at the level of the policy action—the drug class level—analyses will be small-n studies.

This study engages the question over whether protected classes have affected spending and utilization with a comparative case study approach at the drug class level. It uses an innovative methodology to produce a well-matched counterfactual by relying on the synthetic control method to construct a weighted average of unprotected classes that follow the same pre-Part D trajectory on the outcome variables. Doing so makes it possible to estimate the policy effect by measuring the divergence between the protected classes and the synthetic control in the period after policy implementation.

Hypothetically, there is good reason to anticipate that the protected class policy produces increased spending, perhaps through increased quantity consumed or increased prices (or both). By mandating that all approved drugs be covered in these classes, the policy creates a wedge in the competitive negotiations between two parties, each with significant market power. The monopsonist private insurers attempt to use inclusion on their formularies as a way to extract price concessions from the monopolist pharmaceutical manufacturers. The protected class policy shifts the balance of power in these negotiations in favor of the manufacturer such that, in comparison with other classes that gained coverage under Part D, it is reasonable to expect that

prices would be higher. The quantity of drugs consumed in protected classes could increase significantly compared with drugs from unprotected classes as well since cost-sharing arrangements in plans are likely to make Part D beneficiaries largely insensitive to price. For these reasons, overall spending could increase from simultaneous increases in price and quantity consumed.

The findings present robust evidence that spending increased sharply for drugs in the protected classes after Part D's launch relative to spending in similar unprotected classes. Across almost all of the protected classes, spending increased. For the aggregated protected class model, the effect was $1.02 billion (in 2011$) per class per year higher spending in the protected classes than in the matched synthetic control. To put this result in perspective, gross drug spending in Part D by all payers and beneficiaries was $84.9 billion in 2011 (Medicare Payment Advisory Commission, 2013). Therefore, these estimates represent a 7.2% increase in Medicare Part D spending. Due to concerns about the anti-cancer drugs (i.e., antineoplastics) biasing results upward, a lower bound estimate is that protected classes increased total spending by $647 million per class year. This would represent a 4.6% increase in spending. (The results of the study suggest that increases in price were largely responsible for the growth in expenditures; although, utilization may have also increased).

These increases in spending are likely passed on by the plans to the Medicare Part D program and beneficiaries in the form of higher premiums. Given the fact that plan premiums are subsidized at approximately 75% by Medicare, a very simple back-of-the-envelope estimate is that Medicare's costs are $2.9-4.6 billion higher per year due to the protected class policy. Meanwhile, beneficiaries are shouldering an additional $973 million-1.5 billion extra in higher

premiums. On a per capita basis, this translates to $30.89-48.57 per enrollee per year (based on the 31.5 million enrollees in the program in 2011).

Impacts of this magnitude are important to acknowledge as the deliberations over whether to preserve, reduce, or expand protected classes in Medicare Part D continue. In 2014, the Centers for Medicare and Medicaid Services proposed eliminating two classes from protection—antidepressants and immunosuppressants, and the agency marked antipsychotics as a future target for losing its protected status. CMS's recommendations were motivated by analyses that questioned whether those classes deserved to be distinguished from other classes based on therapeutic justifications. This study did not ascertain whether protected status delivered better medical results for beneficiaries.

However, the present findings add to the debate by quantifying the financial consequences of maintaining protected classes in Part D. These results suggest that the Medicare program and consumers have significantly higher expenditures due to the policy. Perhaps policymakers will consider this level of additional expenditures warranted compared with the therapeutic benefits of maintaining the protected classes. Whatever the case, this study's findings enable a discussion about the value of continuing the policy in its current form, adapting it, or eliminating it.

Therapeutic concerns are not the only considerations related to this decision. There is also the danger that private Part D plans could, if protection was eliminated from these classes, live up to the CMS's original fears and adversely select against vulnerable patients by offering inadequate coverage for drugs in these classes. However, there are reasons to believe that sufficient risk-sharing protections are in place to protect plans against high-cost beneficiaries, which should guard against adverse selection. When beneficiaries have annual drug costs that

exceed the catastrophic coverage threshold ($6,447 in 2011), Medicare covers 80% of all drug costs above this level. In addition, Part D provides risk adjustment payments for plans that experience overall losses. Risk corridors prevent excessive plan losses (and gains). Finally, plans that enroll dual eligible beneficiaries (who are more likely to have above-average expenditures) receive additional Low Income Subsidies (LIS) (Medicare Payment Advisory Commission, 2015).

All of these concerns—financial and clinical—are relevant to the continuation of the protected class policy. This study advances the literature by providing the most comprehensive and recent analysis of the expenditure and utilization impacts of the policy. When CMS inevitably revisits the protected class policy in the near future, it should take account of all these considerations and carefully balance the priorities of preserving access to needed drugs and controlling spending.

Tables and Figures

Table 1: Variable Means and Standard Deviations

	All Classes	Protected Classes	Unprotected Classes
Average Risk Adjustment Score	1.192	1.416	1.181
	(0.286)	(0.700)	(0.245)
Percent Dual Eligible	0.181	0.273	0.176
	(0.121)	(0.149)	(0.118)
Total Spending (in millions of $2011)	748.8	2543.7	662.7
	(1505.5)	(1605.0)	(1446.1)
Total Units Consumed (in millions)	590.8	1372.3	553.3
	(974.5)	(1515.8)	(925.1)
Observations	1441	66	1375

Standard deviations in parentheses

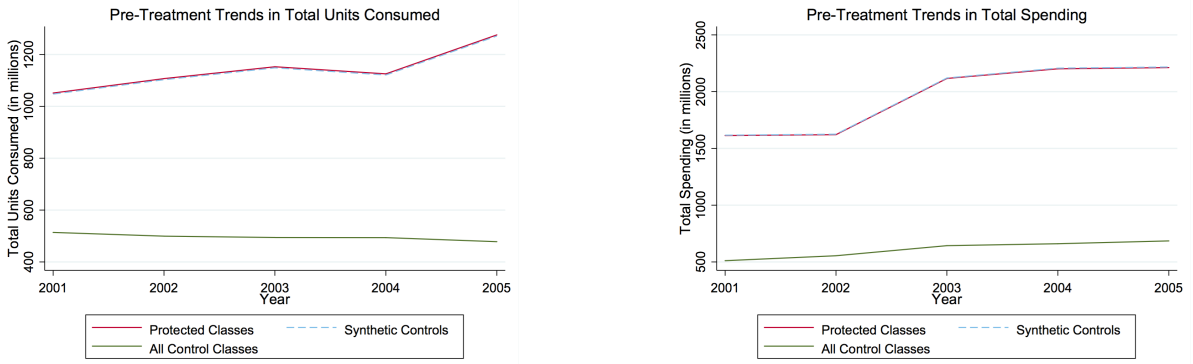
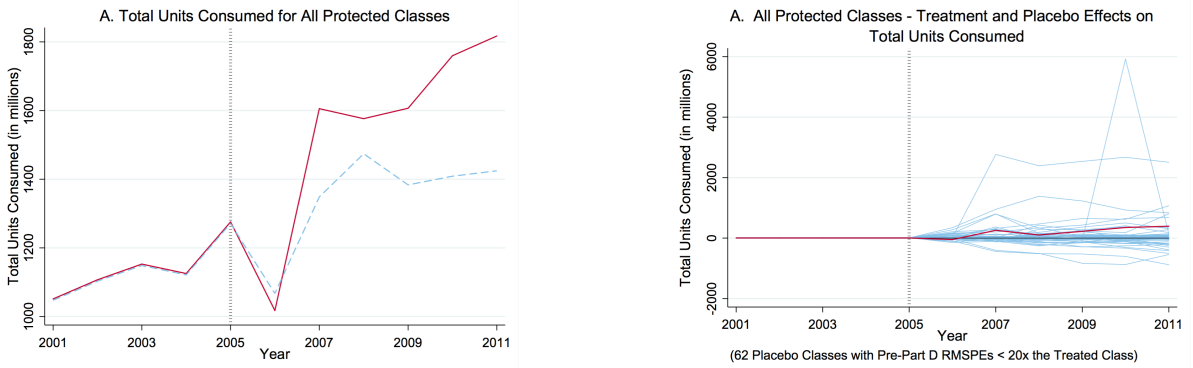


Figure 1: Average Pre-Part D Trends in the Dependent Variables for Protected Classes, the Matched Synthetic Control Classes, and All Control Classes



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 2: Effects of Protection on Drug Utilization for the Aggregate Protected Class and Placebo Effects

Table 2: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Total Units Consumed for the Aggregate Protected Class

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Lead 6	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006-2011**
Tx Value	1017.42	1605.48	1576.35	1606.73	1759.57	1817.12	1563.78
S.C. Value	1067.26	1348.41	1474.11	1383.48	1408.77	1424.58	1351.1
Effect Size	**-49.84**	**257.07**	**102.24**	**223.25**	**350.8**	**392.54**	**212.68**
P-Value	**(.27)**	**(.159)**	**(.317)**	**(.206)**	**(.159)**	**(.143)**	**(.19)**
% Change	-4.7%	19.1%	6.9%	16.1%	24.9%	27.6%	15.7%

* p<0.10, ** p<0.05, *** p<0.01

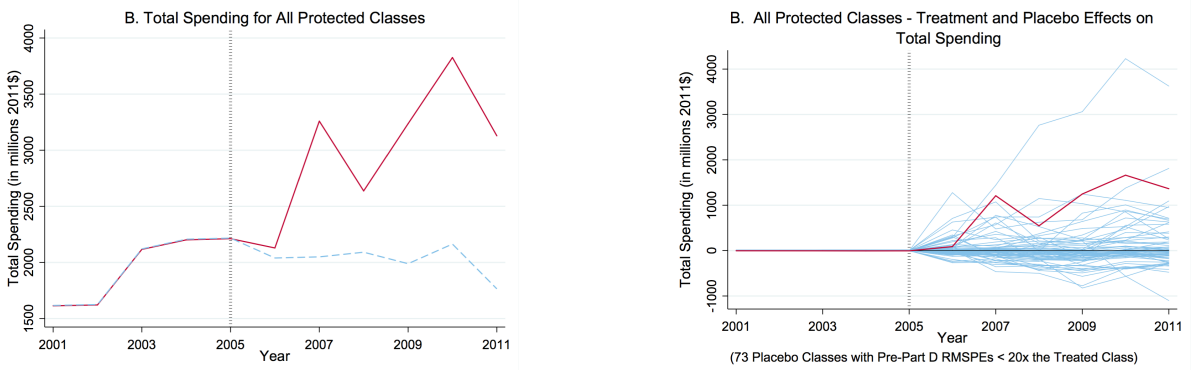


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Figure 3: Effects of Protection of Drug Expenditures for the Aggregate Protected Class and Placebo Effects

Table 3: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Total Expenditures for Aggregate Protected Class

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Lead 6	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006-2011**
Tx Value	2128.83	3259.18	2637.27	3236.55	3826.07	3128.43	3036.05
S.C. Value	2039.58	2049.71	2091.26	1988.89	2163.83	1764.76	2016.34
Effect Size	**89.25**	**1209.47****	**546.01***	**1247.66****	**1662.24****	**1363.67****	**1019.72****
P-Value	**(.27)**	**(.014)**	**(.054)**	**(.014)**	**(.014)**	**(.027)**	**(.027)**
% Change	4.4%	59%	26.1%	62.7%	76.8%	77.3%	50.6%

* p<0.10, ** p<0.05, *** p<0.01

Table 4: Effect Sizes and P-Values for Total Units Consumed from Synthetic Control Models by Year and Post-Treatment Average and by Protected Class

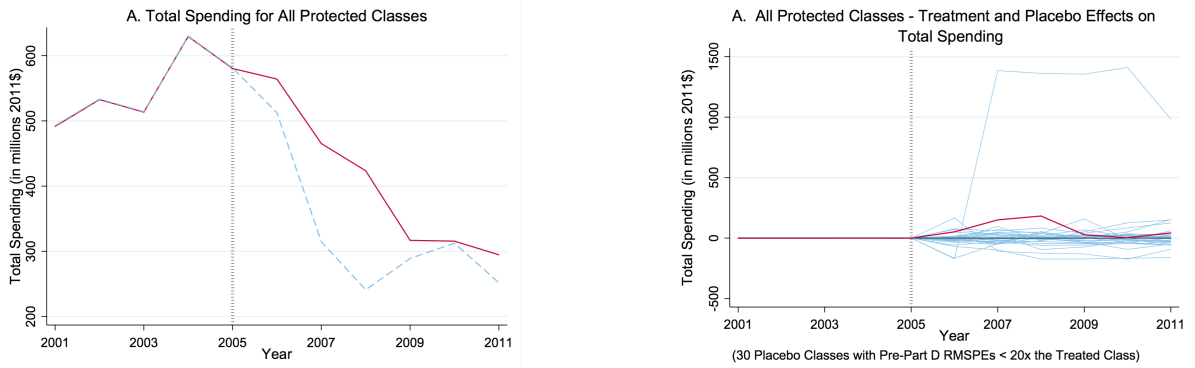
	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Lead 6	Post-Tx Average
Protected Class	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006-2011**
All Protected Classes	**-49.84**	**257.07**	**102.24**	**223.25**	**350.8**	**392.54**	**212.68**
	(.27)	(.159)	(.317)	(.206)	(.159)	(.143)	(.19)
Anticonvulsants	**-863.11*** **	**-485.49**	**-482.07**	**-227.84**	**347.2**	**105.25**	**-267.68**
	(0)	(.111)	(.127)	(.246)	(.206)	(.429)	(.198)
Antidepressants	**189.47**	**1032.96****	**379.79**	**379.19**	**923.57***	**1030.52***	**655.92***
	(.135)	(.024)	(.159)	(.159)	(.087)	(.056)	(.079)
Antineoplastics	**169.51**	**396.45**	**371.68**	**452.94**	**144.08**	**248.21**	**297.14**
	(.143)	(.151)	(.167)	(.119)	(.341)	(.294)	(.175)
Antipsychotics	**118.09**	**160.1**	**41.83**	**61.72**	**87.33**	**93.17**	**93.71**
	(.172)	(.19)	(.586)	(.466)	(.397)	(.466)	(.328)
Antiretrovirals	**-68.44**	**-88.03**	**-25.75**	**54.45**	**143.35**	**-19.08**	**-.58**
	(.254)	(.27)	(.619)	(.476)	(.254)	(.73)	(.968)
Immunosuppressants	**111.25**	**77.06**	**417.03**	**352.34**	**133.87**	**360.55**	**242.02**
	(.254)	(.381)	(.151)	(.167)	(.341)	(.222)	(.214)

* p<0.10, ** p<0.05, *** p<0.01

Table 5: Effect Sizes and P-Values for Total Spending from Synthetic Control Models by Year and Post-Treatment Average and by Protected Class

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Lead 6	Post-Tx Average
Protected Class	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006-2011**
All Protected Classes	**89.25**	**1209.47****	**546.01***	**1247.66****	**1662.24****	**1363.67****	**1019.72****
	(.27)	(.014)	(.054)	(.014)	(.014)	(.027)	(.027)
Anticonvulsants	**63.82**	**89.92**	**355.62**	**978.77***	**32.08**	**356.16**	**312.73**
	(.385)	(.475)	(.172)	(.074)	(.77)	(.262)	(.18)
Antidepressants	**756.2****	**1478.99*****	**543.18****	**1099.27****	**2405.03****	**2225.65****	**1418.06****
	(.014)	(0)	(.043)	(.029)	(.014)	(.014)	(.014)
Antineoplastics	**311.07***	**5374.87*****	**1566.77****	**2954.73****	**3789.16****	**1735.67****	**2622.05*****
	(.071)	(0)	(.014)	(.014)	(.014)	(.029)	(0)
Antipsychotics	**303.46**	**1656.01****	**866.91***	**1523.84****	**3239.63****	**2888.82****	**1746.45****
	(.128)	(.016)	(.08)	(.024)	(.016)	(.016)	(.016)
Antiretrovirals	**-611.84***	**-133.9**	**426.44**	**1225.39***	**3591.11****	**2146.12****	**1107.22****
	(.088)	(.336)	(.144)	(.064)	(.016)	(.032)	(.048)
Immunosuppressants	**-227.84**	**-592.03**	**551.58**	**-339.74**	**-820.1**	**121.54**	**-217.76**
	(.183)	(.111)	(.111)	(.238)	(.103)	(.508)	(.325)

* p<0.10, ** p<0.05, *** p<0.01



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 4: Effects of Protection on Drug Expenditures for the Aggregate Protected Class and Placebo Effects, Off-Patent Drugs Only

Table 6: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Total Expenditures for Aggregate Protected Class, Off-Patent Drugs Only

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Lead 6	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006-2011**
Tx Value	564.14	465.24	423.59	316.8	315.63	294.74	396.69
S.C. Value	512.48	314.76	241.05	289.09	312.56	251.92	320.31
Effect Size	**51.67**	**150.48****	**182.54****	**27.72**	**3.07**	**42.82**	**76.38**
P-Value	**(.226)**	**(.032)**	**(.032)**	**(.516)**	**(.871)**	**(.387)**	**(.129)**
% Change	10.1%	47.8%	75.7%	9.6%	1%	17%	23.8%

* p<0.10, ** p<0.05, *** p<0.01

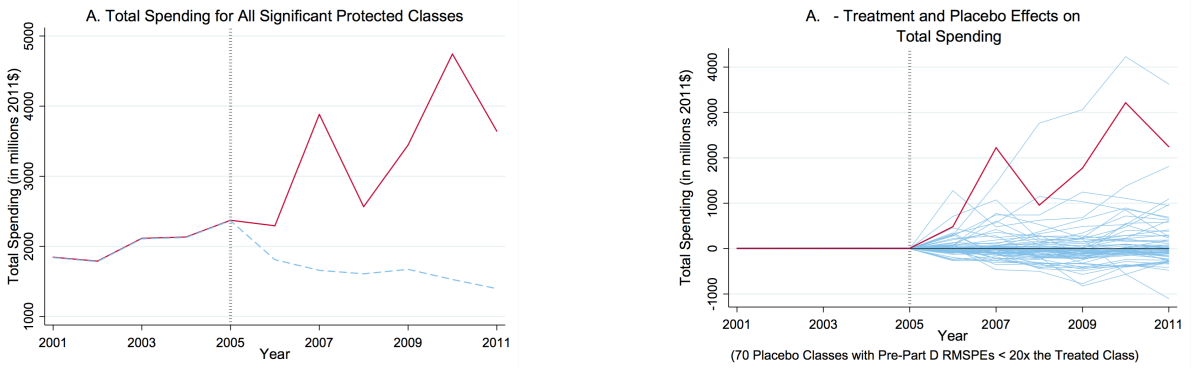


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Figure 5: Effects of Protection on Drug Expenditures for the Aggregate Protected Class and Placebo Effects, Excluding Antineoplastics

Table 7: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Total Expenditures for Aggregate Protected Class, Excluding Antineoplastics

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Lead 6	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006-2011**
Tx Value	2285.11	2650.25	2679.31	3109.45	3659.93	3246.07	2938.35
S.C. Value	2271.23	2361.25	2402.89	2256.59	2482.19	1976.58	2291.79
Effect Size	**13.88**	**289**	**276.43**	**852.87****	**1177.74****	**1269.49****	**646.57****
P-Value	**(.774)**	**(.189)**	**(.264)**	**(.019)**	**(.038)**	**(.038)**	**(.038)**
% Change	.6%	12.2%	11.5%	37.8%	47.4%	64.2%	28.2%

* p<0.10, ** p<0.05, *** p<0.01

CHAPTER 3

PRESCRIPTION DRUG MONITORING PROGRAMS PRODUCE A LIMITED IMPACT ON PAINKILLER PRESCRIBING IN MEDICARE PART D

Introduction

A four-fold increase in deaths attributable to prescription painkiller overdose in the United States since 1999 has caught the attention of state policymakers. Opioid painkiller abuse was tied to more than 22,500 deaths in 2015 (Rudd, Seth, David, & Scholl, 2016). Opioid-related emergency department visits and substance abuse treatment admissions have also sharply increased (CDC, 2013), and an estimated 4.5 million Americans currently use these prescription drugs for nonmedical purposes (SAMHSA, 2015). These are some of the alarming trends underlying results from a recent study by Case and Deaton (2015) that revealed an unprecedented *increase* in mortality for middle-aged, non-Hispanic whites, driven substantially by rises in drug poisonings, especially from opiates.

Despite the high potential for harm and addiction inherent in opioid painkiller use, the drugs are prescribed extensively in the U.S. as pain management therapies. In the early 1990s, U.S. health care practitioner groups began to call attention to the problem of unmanaged pain by labeling pain as the "fifth vital sign" (Lucas, Vlahos, & Ledgerwood, 2007). The desired effect was to encourage doctors to be more deliberate about evaluating, diagnosing, and treating patient pain. Simultaneously, Purdue Pharma received FDA approval for its soon-to-be blockbuster opioid analgesic Oxycontin (the extended-release formulation of oxycodone) in 1996 and proceeded to market it extensively to physicians as a safe treatment for chronic pain with low addiction risk (Van Zee, 2009). Subsequently, Oxycontin and other opioid painkillers such as

Vicodin (containing hydrocodone) gained wider acceptance among physicians as appropriate treatment options for millions of sufferers of chronic, non-cancer pain, and the opioid painkiller market experienced dramatic increases in sales.

Fast-forward to more recent years—at their peak, health care providers issued for 259 million prescriptions for opioids in 2012, a quantity sufficient to medicate every American adult for a month (CDC, 2014). Between 2000 and 2015, opioid overdose deaths rose 382% for men and 473% for women (National Institute on Drug Abuse, 2016). The most recent estimates from the Drug Abuse Warning Network indicate that opioids were also involved in approximately 488,000 emergency department visits in 2011, nearly twice the number from 2004 (Substance Abuse and Mental Health Services Administration, 2013). Furthermore, abuse of and deaths from heroin are also on a dramatic rise, and research suggests that substantial numbers of heroin users have a prior history of prescription opioid abuse (Muhuri, Gfroerer, & Davies, 2013).

These damaging trends have demanded a policy response from both public health and law enforcement officials to reduce the supply of opioids and curtail abuse. However, in contrast to the outright bans adopted to combat problems related to illicit drugs (e.g., cocaine or methamphetamine), policymakers have had to proceed with a lighter touch with respect to opioids. They potentially face a trade-off between two competing public health priorities when they regulate opioid painkillers—preventing abuse and overdoses and ensuring access to appropriate pain management therapies. Pain is a bitter reality in lives of many individuals. The Institute of Medicine (2011) estimates that more than 100 million Americans are afflicted with chronic pain, with associated costs between $560-635 billion a year. Opioid painkillers are considered essential for pain management in many individuals, especially for vulnerable individuals such as cancer and HIV patients. Therefore, policies that inhibit access to opioids

could have profound spillover effects on pain management, requiring a nuanced approach that allows physician flexibility to treat patient pain while reducing inappropriate prescriptions.

Physicians encounter difficulties in identifying drug-seeking patients from legitimate pain patients because many opioid abusers engage in a practice known as doctor shopping—that is, concealing their addiction by visiting multiple doctors and pharmacies to obtain numerous prescriptions (Fishbain, Johnson, Webster, Greene, & Faysal, 2010). Doctor shopping is the most common method of drug procurement for the heaviest-use opioid abusers (Jones et al., 2014), making this behavior an essential target for public policy.

Currently, 49 states (all but Missouri) have enacted prescription drug monitoring programs (PDMP) as a primary tool for curtailing the illegitimate use of opioids obtained by prescription (NAMSDL, 2015). These online databases keep records of prescriptions filled by patients for controlled substances, including opioid painkillers. Physicians can use them to more easily recognize doctor shopping by accessing the records to determine if their patients have overlapping prescriptions for opioids (Perrone, DeRoos, & Nelson, 2012). Ideally, a physician would refrain from prescribing to a drug-seeking patient and refer him to substance abuse treatment. Indirectly, PDMPs might result in fewer prescriptions written for opioids by creating undesirable administrative hurdles for prescribers or by reinforcing the message to providers and patients that the drugs have a high potential for harm. PDMPs could also encourage physicians to rely more heavily on substitute pain therapies or analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs).

Whether prescription drug monitoring programs are effective tools for reducing high-risk opioid prescribing remains uncertain. In most states, physician use of a PDMP is entirely voluntary. PDMP data are largely not integrated with electronic medical records, making PDMP

consultation a time-consuming task (Perrone et al., 2012). Many programs experience very low use; one study found a median rate of PDMP registration of only 35% for physicians who had issued at least one controlled substance prescription (Kreiner, Nikitin, & Shields, 2013). Only in the most recent years have a few states begun requiring registration and, in some cases, mandating that physicians access PDMPs prior to issuing opioid prescriptions (NAMSDL, 2015). In contrast to this more rigorous approach to PDMP administration, 16 states included language in their statutes as of 2015 *explicitly not requiring* a physician to utilize the PDMP. Because such a legal statement strongly reinforces the message to physicians that PDMP access is purely voluntary, PDMPs in these states may be underutilized and less impactful. I will control for such statutory language in the models to measure its impact.

Although states have invested millions of dollars into PDMP development and administration, little evidence exists evaluating the programs' effectiveness in changing prescribing practices. Most studies of PDMPs have analyzed the policies' effects on possible downstream outcomes such as opioid-related deaths or addiction treatment facility admissions (Paulozzi, Kilbourne, & Desai, 2011; Radakrishnan, 2014; Reifler et al., 2012); however, their empirical findings have been mixed, with some studies observing modest improvements in outcomes related to PDMPs and others failing to find significant impacts (Gugelmann, Perrone, & Nelson, 2012). Recent work by Rutkow et al. (2015) finds small decreases in physician-level opioid prescribing in Florida after the implementation of both a PDMP and pill mill legislation; however, it is unclear if these results are generalizable to other states or in absence of pill mill laws. (Such laws regulate so-called "pill mills," or pain management clinics that inappropriately prescribe and dispense large quantities of opioids.) I expand on this line of inquiry by examining the effects of PDMPs on physician opioid prescribing behavior across many states using data

from the Medicare Part D prescription drug benefit. I also look for changes in prescribing of nonopioid analgesics as evidence of substitution to other pain therapies.

Furthermore, this study explores more nuanced changes in opioid prescribing based on results from Radakrishnan (2014), who observes reduced abuse of the particular opioid Oxycontin, and Paulozzi et al. (2011), who find evidence of switching from Schedule II to Schedule III opioids in states with PDMPs. This study separately estimates the effects of PDMPs on prescribing drugs containing oxycodone and hydrocodone (e.g., Vicodin), which are the most commonly abused opioids (Cicero, Ellis, Surratt, & Kurtz, 2014), and during a recent period that had some of highest levels of opioid abuse, 2010-2013. Finally, this study looks at prescribing of opioid painkillers according to the Drug Enforcement Agency's (DEA) Controlled Substances Schedules II-IV separately.

Methodology

Medicare Prescribing Data

The primary data source measures physician-level prescribing for patients enrolled in the Medicare Prescription Drug Benefit, or "Part D." Part D is the optional pharmaceutical insurance program for Medicare beneficiaries that launched in 2006 and provided drug coverage to 37 million Americans in 2013 (CMS, 2016a). The first year available for these data is 2010. They were compiled for 2010-2012 by the nonprofit news organization, ProPublica, and provided as the Prescriber Checkup database. For 2013, the Centers for Medicare and Medicaid Services (CMS) released the data itself. In both cases, the data report all prescriptions written by physicians and filled through Medicare Part D. All providers with at least 50 Medicare prescriptions were included. Drugs for which a provider wrote fewer than 10 prescriptions each

year were suppressed to protect patient confidentiality. Each observation describes the total days supply of prescriptions written for each drug by each provider in a given year.

Although illicit drug abuse is not a problem commonly associated with individuals in Medicare, *prescription drug* abuse and misuse is an area of rising concern for this population (SAMHSA, 2012)—as evidenced by numerous policies recently adopted by the Department of Health and Human Services trying to combat problematic prescribing in Medicare (*Opioid Use Among Seniors*, 2016). Individuals become Medicare Part D-eligible either by age (i.e., 65 years or older) or disability (through Social Security Disability Insurance). In 2013, nearly 7 million of Part D enrollees were under the age of 65 and eligible for the program due to disability status (CMS, 2016a). These disabled beneficiaries accounted for more than 25% of the drug claims used in this study. Not only is this population more likely to abuse drugs based on their younger age, approximately 34% of them qualified for disability benefits due to musculoskeletal conditions—often chronic back pain (SSA, 2012)—and these types of patients are prescribed opioid medications in significant numbers. In 2011, almost 44% of disabled Medicare beneficiaries received at least one opioid prescription, and 23% were chronic users (Morden et al., 2014).

Doctor shopping remains a problem within the Medicare population. A third of total Part D beneficiaries—10 million individuals—filled at least one opioid prescription in 2011 due to the high incidence of chronic pain (MedPAC, 2014). The Government Accountability Office (GAO) (2011) examined Part D claims from 2008 and found 170,000 cases of doctor shopping, 80% of which were associated with the opioids oxycodone and hydrocodone. Beneficiaries suspected of doctor shopping represented 1.8% of the Medicare population with prescriptions for these drugs.

While research finds that the 65 and older Medicare population abuses prescription drugs at a significantly lower rate than younger individuals, abuse does still occur among this older cohort and has grown in recent years as the baby boom generation has aged into Medicare eligibility (Colliver, Compton, Gfroerer, & Condon, 2006; Han, Gfroerer, Colliver, & Penne, 2009). Inpatient hospital stays related to opioid overuse by Medicare beneficiaries increased 10.6% annually between 1993 and 2012 (MedPAC, 2014). There are also clinical reasons to monitor their opioid prescription history for older patients, who show increased sensitivity to opioids and can experience adverse drug events. These patients' greater use of pharmaceuticals in general present more opportunities for dangerous interactions between opioids and drugs such as sedatives (SAMHSA, 2008). Overall, the Medicare Part D program data provide an interesting way to analyze the effects of PDMPs on opioid prescribing. However, to the extent that the older population abuses drugs at lower rates, the estimated effects of PDMPs found in this study may be lower than what would be observed using data of prescribing for younger patients.

Dependent Variables

There are seven dependent variables used in the models to measure multiple dimensions of the effect of PDMPs on prescribing patterns. Using the drug-specific values for the number of days supply prescribed per physician, I aggregated up to the following analgesic categories—total days supply prescribed per physician for all opioids, nonopioid analgesics, oxycodone-containing products, hydrocodone-containing products, and opioids categorized in DEA Schedules II-IV. The dependent variables are log-transformed to account for skewness. As a result, the models include only physicians with nonzero prescribing in the given categories. The total sample included 789,569 physician-year observations, 451,583 (57%) of which had at least one opioid prescription. I identified opioid and nonopioid pain relievers based on classifications

from the Medicare Formulary Reference File. There were 208 painkillers identified in the data, of which 122 were opioids.

The first two models examine the effects of PDMPs on opioid and nonopioid analgesic prescribing broadly, while the oxycodone and hydrocodone models home in more closely on the two high-profile drugs associated with prescription painkiller abuse. If PDMPs have any effects on prescribing, I would expect them to be most pronounced for these specific drugs. Finally, I examine changes in prescribing for different schedules of controlled substances to observe potential substitution from higher Schedule II drugs (considered by the DEA to have a greater potential for harm and addiction) to lower Schedule III and IV drugs. During this study period, the DEA classified oxycodone as a Schedule II drug. Hydrocodone was designated a Schedule III drug with fewer restrictions (but was reclassified to Schedule II in 2014). The Schedule II and III categories are exclusive of oxycodone- and hydrocodone-containing products, respectively, since the effects on these drugs are measured separately in the other models.

Table 8 shows the means of the dependent and independent variables for the sample grouped by states with and without PDMPs. Observations are included under the "States with PDMP" category if they were from a state and year when a PDMP was operational for part of that year. There are statistically significant differences in prescribing between states with and without PDMPs for all analgesic categories. The logged values are higher for observations in PDMP states, which highlights the need to account for endogeneity of PDMP status. This study attempts to do so with a difference-in-differences framework and through the use of physician-level fixed effects.

Prescription Drug Monitoring Programs

This paper is specifically interested in the effect of monitoring programs that allow health care providers real-time access to patient information. The only practical way to accomplish this is to provide physicians with online PDMP access. Early PDMPs relied on fax or other cumbersome modes of communication, and especially prior to widespread high-speed internet access, they did not allow timely access to prescribers wanting information. Therefore, I only consider a state to have a PDMP in time *t* if their program met all of three conditions: 1) prescriber and dispenser access (as opposed to only law enforcement, for example), 2) online access, and 3) required reporting of all prescriptions dispensed by the pharmacy. Under these circumstances, prescribers have a tool available that offers both complete and timely information. In the models, I include a variable with a value of 1 if a state had an online PDMP operational for the entire year in time *t*, 0 if a state had no PDMP during the year, and a value between 0 and 1 representing the proportion of the year the PDMP was operational if the state launched its PDMP in time *t*.

PDMP's vary in their implementation, making some more binding and more likely to have an impact on physicians' PDMP use and prescribing behaviors. As previously mentioned, several states have recently begun requiring physicians to access the PDMP prior to issuing opioid prescriptions. These regulations almost all went into effect after the end of this study period and are promising topics for future research as new data become available. I do control for states that have statutes that specifically do not require physicians to utilize PDMPs. Of the physicians subject to a PDMP in the sample, 27% of them practiced in such states.

Because I am using a difference-in-differences framework to observe the effect of introducing a PDMP in a state, I limit my analysis to those states that either implemented a new online PDMP during 2011-2013 (the first year of data availability, 2010, serving as a pre-

treatment time period) or who had still not implemented one by 2013. I exclude the 29 states that already had PDMPs in place prior to 2011. (Massachusetts is maintained in the dataset because its PDMP began only in December 2010.) The 21 states included in the analysis and their dates of PDMP adoption are displayed in Figure 6. PDMP dates of operation came from the National Alliance for Model State Drug Laws (NAMSDL) and were supplemented by correspondence with state PDMP administrators. Care was taken to ensure that the dates used to determine a state's PDMP status reflected when PDMPs were actually operational online and available for physician use.

Following the introduction of the Massachusetts PDMP in late 2010, three states—Florida, Kansas, and Oregon—had programs become operational in 2011, followed by eight more in 2012, and another four in 2013. A final five states had no PDMP operational online by the end of the study period. On average, 30.6% of providers in the sample practiced in states where they had online access to a PDMP. Two states—Texas and Rhode Island—had older PDMPs in place prior to the study period but began offering online access between 2011 and 2013.

Covariates

I obtain county-level economic and demographic variables from the U.S. Census Bureau American Community Survey, including median household income and percent of population by race and ethnicity. I also control for the size and characteristics of the county Medicare population using CMS-provided data. I control for the number of Medicare Part D enrollees and the standardized per capita Medicare costs of beneficiaries in the county.

Finally, I account for the concentration of the county physician market by constructing a Herfindahl–Hirschman Index (HHI) equal to the sum of the squared values of each physician's

percentage of countywide prescribing. A larger measure indicates that more prescribing is concentrated in fewer doctor's practices in a county. Because doctor shopping relies on the ability to visit multiple doctors, a more concentrated market might make doctor shopping more difficult.

Models

To understand the potential effect of PDMPs, I employ a series of difference-in-differences regression models using ordinary least squares with physician and year fixed effects to predict the different outcome variables as a function of state PDMPs, statutes not requiring PDMP access, and the controls described above. I also employ cluster-robust standard errors (clustered by physician) to adjust for heteroskedasticity and correlation in the individual errors (Cameron & Travedi, 2005).

As specified, the models are the equivalents of difference-in-differences estimation because all of the states included in the analysis either implement a PDMP during the study period (i.e., the treatment group) or never have a PDMP (i.e., the control group). These treatment and control group identifiers are captured in the physician fixed effects. The year indicator variable measures the pre- and post-treatment identifiers. The PDMP variable then becomes the algebraic equivalent of the interaction term in a DID model. The DID approach helps to reduce endogeneity concerns. Inclusion of physician fixed effects further reduces the potential bias of PDMP status being nonrandomly assigned by measuring within-physician variation and controlling for time-invariant prescriber characteristics, such as medical specialty. Finally, the year fixed effects control for secular time trends in opioid prescribing patterns.

In order for a difference-in-differences estimator to be unbiased, the assumption must hold that the trends in the outcome variable for the treatment and control groups would have

followed the same pattern in absence of the policy intervention. Typically, visual inspection of a pre-trend analysis will provide evidence of this counterfactual. With no pre-2010 observations available in the dataset, I rely instead on CMS's State Drug Utilization Data (SDUD)—which provides state-level measures of Medicaid prescribing—to compare trends for the treatment and control states in the years preceding the study period. Figure 7 displays the numbers of opioid prescriptions filled through Medicaid per 100,000 beneficiaries from 2005-2009 for the 21 states analyzed in this study. The trends are parallel in the period leading up to this study, providing support that the DID models will produce unbiased estimates of the effect of PDMPs.

Table 9 displays the unadjusted differences in prescribing for the treatment and control groups between the pretreatment period, 2010, and the final treatment period, 2013. These estimates show small deviations between the two groups and prescribing decreases for only oxycodone and Schedule III opioids. Values are positive for opioids, nonopioids, hydrocodone, and Schedules II and IV. As such, I proceed with the following model specifications:

$$lnRX_{icst} = \beta_1 + \beta_2 PDMP_{st} + \beta_3 STATUTE_{st} + \beta_4 Z_{ct} + \delta_i + \tau_t + \varepsilon_{icst}$$

where the unit of analysis for all models is prescriber *i* in each time period *t*. $lnRX_{icst}$ represents the logged days supply of opioid analgesics, nonopioid analgesics, oxycodone, hydrocodone, and opioids in DEA controlled substances schedules II-IV prescribed by provider *i* in the c^{th} county and the s^{th} state in time *t*. The predicted values of $lnRX_{icst}$ are estimated as a function of a state's PDMP status in time *t*, $PDMP_{st}$, if the state's statute explicitly does not require physician use of the PDMP, $STATUTE_{st}$, along with county and individual characteristics and time. County characteristics, Z_{ct}, include median income (in $1,000s), number of Part D enrollees (in 1000s), per capita Medicare spending (in $1,000s), percent of population by race and ethnicity, and the

HHI measure of physician market concentration. Physician fixed effects are captured in δ_i, τ_t comprises the year dummies, and the error term is ε_{icst}.

Results

The coefficients and confidence intervals for the two main variables of interest—PDMP and statutory language not requiring PDMP use ("PDMP Statute")—are represented in Figure 8. Complete regression results for these seven DID regressions are presented in Table 10. With logged dependent variables, the coefficients are interpreted as the percent change in prescribing among physicians with nonzero prescribing. Only three categories of analgesics—opioids, oxycodone, and hydrocodone—show statistically significant decreases in days supply prescribed associated with the presence of a PDMP. The larger oxycodone result is consistent with the raw DID estimates from Table 9. Prescriptions containing oxycodone reduced by an average of 5.2% per physician. Prescribing for opioids overall and for hydrocodone products show declines of a much smaller magnitude at 2% and 2.8%, respectively.

PDMPs are not associated with greater prescribing of nonopioid analgesics. However, they are correlated with a small 1.4% increase in prescribing for Schedule IV opioids, a category that includes opioids such as tramadol. There were no statistically significant differences in days prescribed for Schedule II or III opioids (excluding oxycodone and hydrocodone) associated with PDMPs.

Figure 8 illustrates an interesting relationship between the model coefficients for PDMPs and the coefficients for the PDMP Statute variable. These coefficients are essentially mirror images of each other. For oxycodone, hydrocodone, and opioids overall, a significant negative coefficient for PDMP is matched with a positive coefficient with a similar magnitude for the statute.

Results from fixed effects models employing untransformed, Winsored dependent variables yielded qualitatively similar results as these models with logged dependent variables, with the exception that the significant but small effects observed for opioids overall and hydrocodone products in the logged models become insignificant in the nonlogged specifications. As an additional robustness check to rule out Type 1 errors, I conduct a series of placebo tests by randomizing PDMP treatment by state and year. The models for oxycodone and opioids overall easily pass this falsification test, providing additional credence to the estimated effects. The model for hydrocodone only marginally passes the test, and the model for Schedule IV opioids does not pass, indicating these findings may be less robust. As a result, the estimates from these models may be considered associations rather than causal effects.

Discussion

These findings show that PDMPs have significant but limited impacts on physician prescribing behaviors among the Medicare Part D population. The regression results provide evidence that PDMPs have had some success in a targeted way by reducing prescribing for one of the most abused and publicized drugs of the opioid epidemic—oxycodone. The 5.2% average decrease indicated by the model represent 83.6 fewer days supply (or slightly less than three 30-day prescriptions) of oxycodone prescribed per physician. This is a meaningful effect but is still modest when compared to the widespread increases in oxycodone use.

Despite being a more extensively prescribed drug than oxycodone, hydrocodone prescriptions showed only a small response to the introduction of a PDMP. Certainly, hydrocodone is also a highly addictive and widely abused drug in its own right. The average reduction for hydrocodone was 53.1 days supply. Furthermore, it does not seem to be the case that PDMPs have a large, generalized effect on overall opioid prescribing. The 2% average

decline estimated here for opioids represents only 77 fewer days supply prescribed, that is, approximately 2.5 30-day prescriptions per doctor per year.

An expected and perhaps desired response was not observed for nonopioid painkillers, prescribing for which did not show significant changes following PDMP implementation. However, the coefficient might underestimate the full effect because many options for these drugs are available over-the-counter and would not appear in the claims data. Switching away from oxycodone and hydrocodone appears to move some consumption toward Schedule IV opioid painkillers. Prescribing for these drugs rose by approximately 25.3 days supply. This supports the idea that there is substitution occurring to the supposedly less harmful Schedule IV drugs when PDMPs are introduced. It is possible that interfacing with PDMPs makes physicians more aware of the relative risks of opioid painkillers and has encouraged greater reliance on lower-schedule drugs. The extent to which these shifts are welfare enhancing is not possible to ascertain from the data.

The second main finding relates to the impact of statutory language designed to protect physicians by asserting that they are under no obligation to utilize the PDMP and its data. In the models, the "PDMP Statute" variable acts as an interaction term denoting that a state has both a PDMP *and* such a statute. As Figure 8 makes clear, changes produced by the PDMP are negated by the presence of such a statute. For example, the 5.2% days supply decline in oxycodone related to PDMP implementation is met with a 5.1% days supply increase when the law absolves doctors from the need to use the PDMP. In practice, it seems that the suggestive power of this aspect of the PDMP legislation sends a powerful message to physicians that negatively influences their use of the databases.

Limitations

There are several limitations of the study that must be considered when drawing conclusions based on its findings. First, the prescribing data used do not provide information on dosage strength, making it impossible to determine if average prescription strength changed post-PDMP implementation. Secondly, the current study does not track other interventions that may have been implemented simultaneously with PDMPs and been responsible for changes in opioid prescribing, such as "pill mill" restrictions. The sharp increase in opioid abuse in recent years provoked various policy responses, many of which would be difficult to identify and track. (However, a nationwide policy change would be controlled for in the year fixed effects.)

In some cases, drug-seeking individuals may respond to PDMPs by visiting doctors across state borders in states without PDMPs. To the extent this occurs, these models may overstate the benefits of the programs. Another limitation, already discussed, is the use of Medicare data. It is possible that studies looking at prescribing outside the Medicare program may uncover more pronounced impacts for PDMPs. Perhaps physicians are more likely to access the PDMP for non-Medicare patients, who they might consider to be more likely to abuse drugs.

I explored estimating a hierarchical model that accounted for the variation present multiple levels in the data—physicians within counties within states. Due to the short nature of the panel, a fully hierarchical model proved infeasible. Additionally, the use of a DID estimator and physician fixed effects control for unobservable time-invariant sources of endogeneity; however, to the extent that time-variant sources of endogeneity may still be present, results can be considered correlations and not causal.

Another limitation arises from the use of pharmaceutical claims data to study prescribing. If drug-seekers feared their behaviors would be uncovered from monitoring of their insurance claims and they attempted to hide their behaviors by paying out-of-pocket for prescriptions,

those transactions would not appear in these Medicare data. However, the possibility of being identified as a drug-seeker from Part D claims was very low during this study period, as CMS did not require Part D insurers to conduct utilization review for opioid misuse until July of 2013 (McCutcheon, 2014).

Finally, recent changes in PDMP requirements may make these programs more effective tools as time goes by. Registration requirements and access mandates have been adopted in a few states and should reduce the problem of PDMP underutilization by physicians. Future research with more up-to-date data should explore these policy details.

Conclusions

Today nearly every American lives in a state where filling a prescription for an opioid painkiller means being tracked by a prescription drug monitoring program. The reach of these programs is expansive; therefore, their effects are quite relevant to health care policy research. While PDMPs are seen as promising tools for reducing opioid abuse, the literature has produced conflicting findings on their actual effectiveness.

This study adds to the literature in a number of ways. It relies upon a large, recent dataset of physician-level prescribing. Second, it gets to the potential core effect of monitoring programs by examining the number of prescriptions filled for opioids. Finally, this study employs a difference-in-differences approach and physician fixed effects to address the potential for endogeneity in program adoption.

The findings present a nuanced picture of physician response to PDMP implementation within a specific patient population. Decreases are most concentrated on oxycodone; however, even these changes are small when compared to the large increases in oxycodone use during recent years. Changes for opioid prescribing in general and for hydrocodone specifically are even

more modest. These findings suggest that PDMPs are effective in reducing opioid prescribing in a limited and targeted capacity. Physicians seem to be changing their behaviors primarily with respect to the drug most commonly associated with prescription abuse.

These reductions in prescribing are met with corresponding increases in prescribing for Schedule IV opioids. A similar effect was observed by Paulozzi et al. (2011). The results indicate that PDMP administrators should make efforts to broaden the perceived opioid threat beyond oxycodone. Furthermore, the results present compelling evidence that statutes that explicitly do not require physicians to access PDMP data largely eliminate the impacts of monitoring programs on prescribing. The 16 states with such statutes on the books should consider revising them to increase program utilization. Additionally, researchers should account for this variable in their studies, since it serves to attenuate PDMP effectiveness.

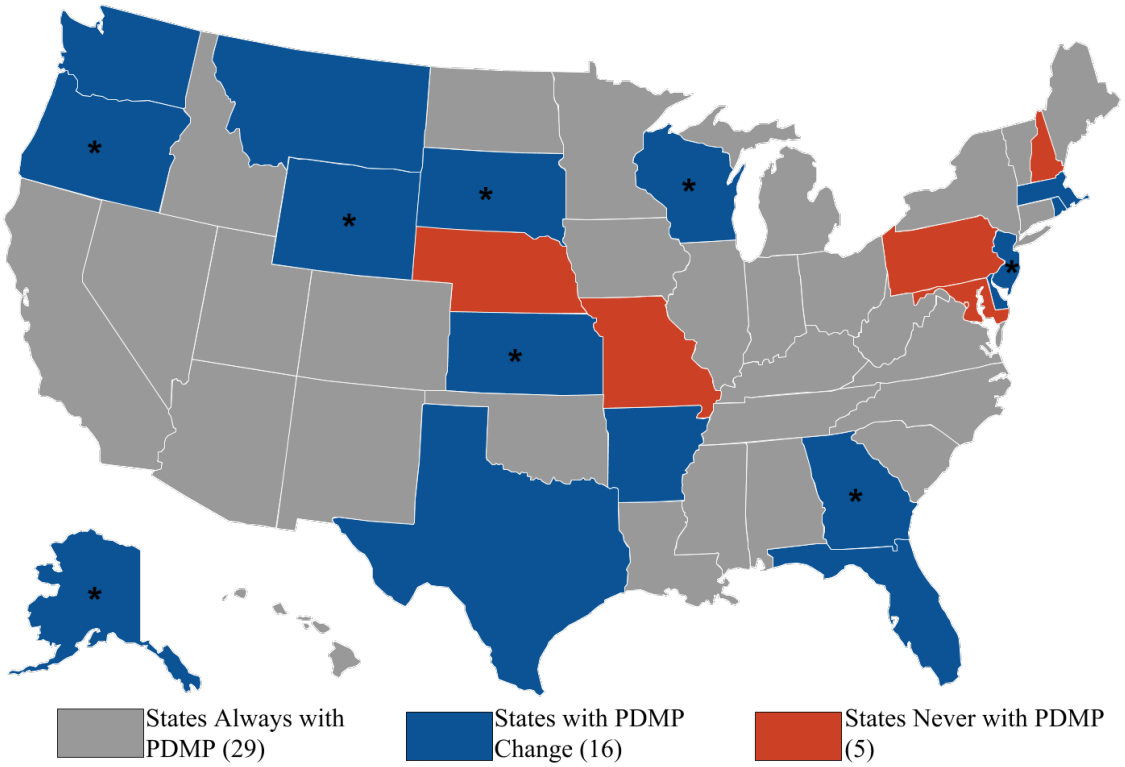
Ultimately, both pain and drug abuse will continue to be serious public health threats in the foreseeable future. Federal and state policymakers have the difficult task of trying to balance their management of these threats and ensure that victories in one arena do not produce suffering in the other. These findings suggest that a key tool in combatting the prescription abuse epidemic does not operate in straightforward ways. Future research should continue to look for ways to improve existing PDMPs and for alternative policies to reduce opioid abuse.

Tables and Figures

Table 8: Variable Means and Proportions by PDMP Status

Variable	Variable Definition	States without PDMP	States with PDMP
Independent Variables			
PDMP	State has an operational, online PDMP	-	0.785 (0.313)
		-	[0.08, 1]
PDMP Statue	Statute explicitly does not require PDMP	-	0.217 (0.381)
	access	-	[0, 1]
Dependent Variables			
Opioids	Logged days supply opioids	6.858 (1.766)	6.891* (1.765)
		[2.485, 13.05]	[2.398, 13.08]
Nonopioids	Logged days supply nonopioid analgesics	7.378 (1.280)	7.402* (1.319)
		[2.485, 11.78]	[2.398, 11.88]
Oxycodone	Logged days supply oxycodone	6.283 (1.469)	6.320* (1.493)
		[2.398, 12.12]	[2.398, 12.26]
Hydrocodone	Logged days supply hydrocodone	6.403 (1.506)	6.440* (1.537)
		[2.565, 12.10]	[2.398, 12.19]
Schedule II	Logged days supply Sch. II opioids (not	6.923 (1.065)	6.943* (1.142)
	oxycodone)	[2.398, 11.95]	[2.485, 12.23]
Schedule III	Logged days supply Sch. III opioids (not	5.723 (0.927)	5.803* (0.924)
	hydrocodone)	[2.639, 9.549]	[2.197, 10.26]
Schedule IV	Logged days supply Sch. IV opioids	6.801 (1.228)	6.827* (1.213)
		[2.398, 11.47]	[2.485, 11.29]
Control Variables			
Enrollment	County Part D enrollment (in 1000s)	59.36 (62.70)	87.19* (84.09)
		[0, 305.2]	[0.00858, 350.9]
Medicare Costs	Per capita Medicare costs (in 1000s)	9.290 (1.540)	9.677* (1.871)
		[2.862, 15.43]	[3.384, 16.70]
Median Income	County median income (in 1000s)	51.86 (13.29)	53.22* (12.56)
		[20.58, 108.5]	[21.57, 107.2]
HHI	County HHI for physician prescribing	193.0 (511.8)	138.1* (437.7)
		[7.544, 10000]	[6.955, 10000]
White	Percent county population white	66.14 (21.65)	61.05* (20.51)
		[2.860, 98.65]	[3.170, 97.78]
Black	Percent county population black	14.60 (15.02)	11.95* (10.20)
		[0, 73.59]	[0.0200, 72.68]
Hispanic	Percent county population Hispanic	13.23 (15.00)	20.08* (17.33)
		[0.340, 95.71]	[0.630, 95.67]
Asian	Percent county population Asian	3.717 (3.457)	4.414* (3.843)
		[0, 29.55]	[0, 31.48]
Other Race	Percent county population other races	2.305 (2.650)	2.501* (2.779)
		[0.0900, 94.53]	[0.100, 92.24]
	Observations	269,888	212,279

Standard deviations in parentheses; minimum and maximum values in brackets.
Significantly different from the "States without PDMP" category (* $p < 0.01$).
Note: The data represent measures of Medicare Part D prescribing and other variables from 2010 to 2013. The table includes summary statistics for all observations that are included in at least one of the seven study models. Values under "States without PDMP" include statistics from time periods when a state had no online PDMP operational during the year. The number of states falling under this category ranged from 20 states in 2010 to 5 states in 2013.Values under "States with PDMP" include statistics from time periods when a state had an online PDMP operational for at least part of the year. "HHI" refers to a Herfindahl–Hirschman Index.

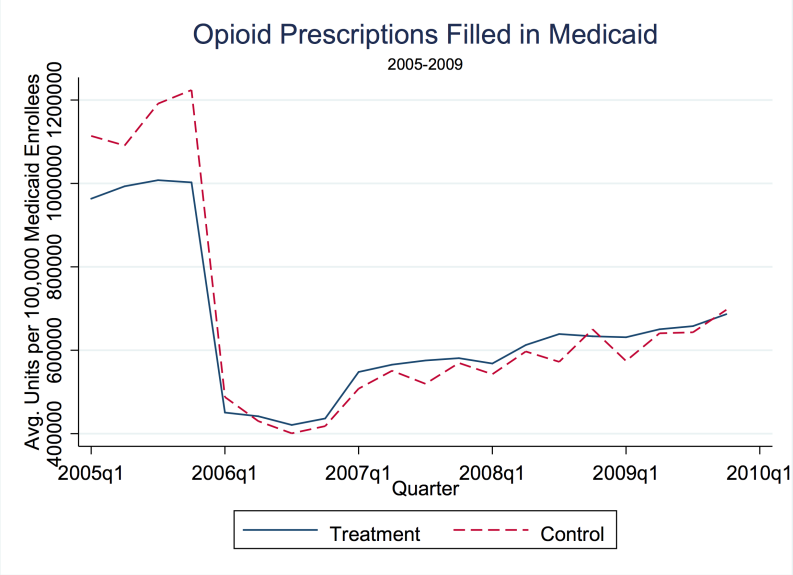


Year of Online PDMP Implementation	
2010	MA
2011	FL, KS*, OR*
2012	AK*, DE, MT, NJ*, RI, SD*, TX, WA
2013	AR, GA*, WI*, WY*
Control	MD, MO, NE, NH, PA

Source: National Alliance for Model State Drug Laws (NAMSDL) with supplementary data collected by author in communication with state PDMP coordinators

* indicates that the state's PDMP statute contains language explicitly not requiring physicians to utilize the program.

Figure 6: State Status for Operational Online Prescription Drug Monitoring Programs, 2010-2013



Source: Centers for Medicare & Medicaid Services States Drug Utilization Data
Note: The sharp decline in prescriptions between 2005 and 2006 is explained by the transfer of prescription drug coverage for dual-eligible Medicare and Medicaid enrollees from Medicaid to the Medicare Part D program beginning in 2006.

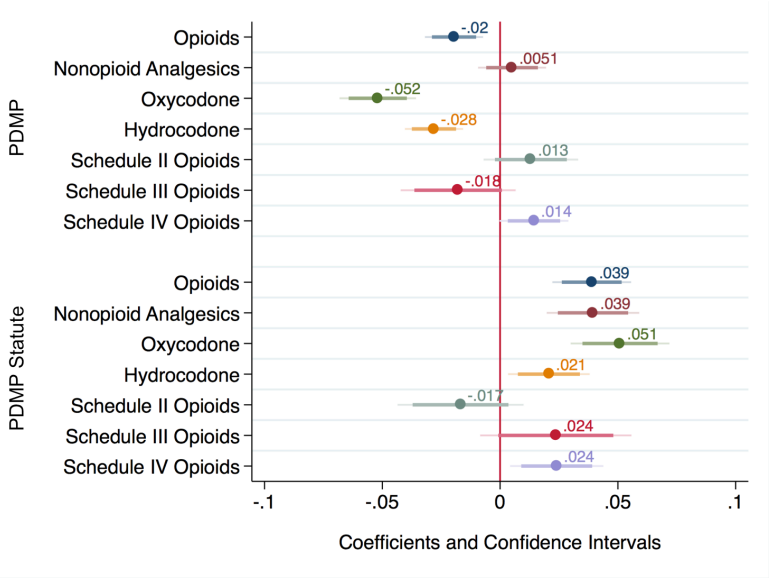
Figure 7: Pre-trend Analysis of Opioid Prescribing in Treatment and Control States, 2005-2009

Table 9: Raw Difference-in-Difference Estimates for Logged Days Supply of Opioid and Nonopioid Analgesics between 2010 and 2013

	Opioids	Nonopioids	Oxycodone	Hydrocodone	Schedule II†	Schedule III†	Schedule IV
Treatment Group 2013	6.920	7.452	6.346	6.466	6.972	5.820	6.849
Treatment Group 2010	6.801	7.302	6.260	6.353	6.877	5.708	6.744
Treatment Group Difference	*0.119*	*0.151*	*0.085*	*0.112*	0.095	0.111	*0.106*
Control Group 2013	6.956	7.487	6.351	6.472	6.994	5.777	6.881
Control Group 2010	6.878	7.388	6.222	6.375	6.909	5.655	6.802
Control Group Difference	*0.077*	*0.099*	*0.129*	*0.098*	0.085	0.122	*0.080*
Raw Difference-in-Differences	***0.041***	***0.052***	***-0.043***	***0.014***	**0.009**	**-0.011**	***0.026***

† Schedule II and Schedule III models measure days supply of opioids prescribed in the schedules exclusive of oxycodone- or hydrocodone-containing drugs, respectively.

Note: Values represent the average logged days supply of the analgesic categories among physicians with any prescribing in those categories.



Note: Confidence intervals indicated at 99% and 95% levels.

Figure 8: Coefficient Plots for PDMP and PDMP Statute Variables in Difference-in-Differences Models Estimating Changes in Logged Prescribing Dependent Variables

Table 10: Coefficients for Difference-in-Differences Models Predicting Logged Days Supply Prescribed for Opioid and Nonopioid Analgesics (Conditional on Any), Physician and Year Fixed Effects

	(1) **Opioids**	(2) **Nonopioids**	(3) **Oxycodone**	(4) **Hydrocodone**	(5) **Schedule II†**	(6) **Schedule III†**	(7) **Schedule IV**
PDMP	-0.020**	0.0051	-0.052**	-0.028**	0.013	-0.018	0.014*
	(-4.09)	(0.91)	(-8.24)	(-5.87)	(1.68)	(-1.88)	(2.54)
PDMP Statute	0.039**	0.039**	0.051**	0.021**	-0.017	0.024	0.024**
	(6.00)	(5.18)	(6.26)	(3.09)	(-1.62)	(1.90)	(3.13)
Enrollment (in 1000s)	0.0018**	0.0019**	-0.00058	0.0011**	0.0017**	0.00080*	0.0018**
	(10.10)	(9.03)	(-1.74)	(6.54)	(4.74)	(2.11)	(8.60)
Medicare Costs (in 1000s)	0.0037	0.0072	0.016*	0.0069	-0.0016	0.023*	-0.011
	(0.71)	(1.28)	(2.51)	(1.29)	(-0.21)	(2.39)	(-1.90)
Median Income (in 1000s)	-0.0018*	-0.00088	-0.0018	-0.0021**	-0.00068	-0.0049**	-0.0010
	(-2.46)	(-1.02)	(-1.88)	(-2.89)	(-0.57)	(-3.20)	(-1.18)
HHI	-0.00013**	-0.000024	0.000032	-0.00011**	0.0000028	0.000024	-0.0000074
	(-4.60)	(-0.99)	(0.98)	(-4.22)	(0.13)	(0.55)	(-0.29)
Black	-0.011	0.012	0.0012	0.0091	0.040**	0.026*	-0.023**
	(-1.73)	(1.69)	(0.14)	(1.42)	(3.44)	(2.03)	(-3.23)
Hispanic	0.0034	0.0022	-0.0055	-0.017**	0.0077	0.0046	0.010*
	(0.89)	(0.53)	(-1.15)	(-4.11)	(1.32)	(0.51)	(2.45)
Asian	0.032**	0.0044	-0.0054	-0.026**	-0.066**	-0.040*	0.097**
	(3.58)	(0.43)	(-0.44)	(-2.69)	(-3.97)	(-1.99)	(8.44)
Other Race	-0.065**	-0.063**	-0.031	-0.034	-0.034	-0.0080	-0.11**
	(-2.88)	(-2.69)	(-1.00)	(-1.53)	(-1.37)	(-0.20)	(-4.48)
Constant	6.84**	7.04**	6.29**	6.61**	6.76**	5.58**	6.85**
	(54.39)	(50.97)	(37.65)	(51.00)	(34.38)	(19.60)	(46.90)
Year Dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes
F-Statistics	735	697	429	559	109	91	617
Observations	451,583	277,080	224,830	362,092	129,624	83,477	251,445

† Schedule II and Schedule III models measure days supply of opioids prescribed in the schedules exclusive of oxycodone- or hydrocodone-containing drugs, respectively.

Notes: HHI = Herfindahl-Hirschman Index

* p<0.05, ** p<0.01

CHAPTER 4

THE IMPORTANCE OF COMMUNITY FOR IMMUNITY: IS SOCIAL CAPITAL RELATED TO VACCINATION COVERAGE?

Introduction

The rise of public health campaigns such as those in the late-eighteenth and early-twentieth centuries that promoted healthier air, water, living conditions, food quality, and personal hygiene are responsible for important advances in well being and decreases in morbidity and mortality. Public health officials have long heralded the advent of immunizations as one of the singular public health victories in the past century (Centers for Disease Control and Prevention, 1999). The ability to vaccinate a population against once prevalent and dangerous diseases has increased longevity and prevented unknowable levels of pain and suffering for people of all ages. Edward Jenner, the "father of immunology," introduced vaccination with his discovery of the smallpox vaccine in the late-eighteenth century. A century later, wide-spread vaccination began against a host of infectious diseases—rabies (1885), diphtheria (1924), pertussis (a.k.a., whooping cough) (1926), tuberculosis (1927), tetanus (1927), yellow fever (1935), polio (1955), measles (1964), mumps (1967), rubella (1970), and hepatitis B (1981) (Cutler, Deaton, & Lleras-Muney, 2006).

Despite the health gains obtained through mass immunization campaigns in the United States, vaccination rates among children have declined steadily in recent years. Although most states require a number of vaccinations for entry into kindergarten, parents are increasingly opting out of having their children vaccinated altogether or are selectively choosing vaccines and timing of vaccination rather than relying on the established, recommended immunization

schedule (Gust, Darling, Kennedy, & Schwartz, 2008). There are a number of possible explanations for this downward trend in immunization rates. For example, some experts believe that parents feel less urgency about preventing diseases that, thanks to immunological successes, are almost entirely eradicated from the population. Parents may not realize the severity of the health effects that these diseases produce, or they might believe that they can rely on society's herd immunity for protection. Since most other individuals are immunized, the chances of disease transmission are low. Additionally, many parents have heard reports—despite scientific evidence to the contrary—pointing to a relationship between vaccination and serious side effects, specifically, development of autism (Kennedy, LaVail, Nowak, Basket, & Landry, 2011).

Vaccination against infectious disease is a prime example of a positive externality in public health. A high immunization rate conveys a higher degree of protection from disease to the vaccinated as well as the unvaccinated. Conversely, lower vaccination rates put communities a greater risk of disease outbreak. As such, economic theory predicts that vaccines will be underutilized relative to the social optimum.

Since the private decision about vaccination has public ramifications, government polices attempt to address the underproduction of positive externalities. At the federal level, the Centers of Disease Control and Prevention (CDC) are charged with tracking immunization coverage and disease outbreaks and coordinating efforts to encourage vaccination. State and local public health departments provide subsidized or free vaccinations for children. All states mandate that children receive a prescribed number of vaccine doses prior to enrolling in school. However, states also vary in terms of allowable exemptions to the requirements. All states make exceptions for children who have medical reasons for not getting vaccinated. Currently, all but three states—California, Mississippi, and West Virginia—allow parents to opt out of immunizing their

children based on religious objections. Eighteen states[3] also allow personal belief, or philosophical, exemptions, a looser constraint that allows parents to opt out based on little more than a stated aversion to vaccines (Goodwin, 2015).

As more parents avail themselves of permissive exemption policies, it is important to understand what other, nongovernmental mechanisms can influence vaccination rates. In recent decades, researchers in sociology, economics, and other disciplines have studied the impact on social capital on the abilities of communities to generate public goods. As described in more detail below, social capital is a concept with many definitions, but it is typically characterized as the levels of values such as trust and reciprocity present in a community that are produced by informal networks between people. Social capital could relate to vaccination coverage because scholars hypothesize that communities with greater levels of social capital will be more likely to engage in activities that entail positive externalities. Because individuals in places with more social capital are more connected and attuned to their neighbors and the underlying wellbeing of their neighborhoods, they will place more value on what is in the public interest, not focusing exclusively on private benefits.

This paper is the first to examine the relationship between community social capital and vaccination rates. It approaches the research question using two different datasets. The first analysis uses school-level vaccination rates from all California public and private schools from 2010-2015 and a county-level, longitudinal index of social capital. This social capital index is constructed from variables measuring a number of aspects of community cohesiveness and civic engagement, including the presence of civic groups and nonprofit organizations, voter turnout, and more. The second analysis measures the correlation between a state-level, longitudinal index

[3] Arizona, Arkansas, Colorado, Idaho, Louisiana, Maine, Michigan, Minnesota, New Mexico, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, Utah, Washington, and Wisconsin (California and Vermont eliminated personal belief exemptions beginning with the 2016-17 school year.)

of social capital (constructed with similar variables to the county-level index) and state vaccine coverage rates published by the CDC.

The California school-level models are useful for examining the relationship between vaccination decisions and social capital at a more micro-level. In addition, California schools provide an interesting setting for exploring child vaccination issues. Until the current 2016-17 school year, California had some of the most lenient exemption policies in the country and relatively low rates of vaccination overall. Moreover, it contained geographic pockets where vaccine coverage fell well below CDC targets. I can exploit this variation to try to identify the different characteristics of counties with high and low vaccination rates. Finally, a high-profile measles outbreak in 2014 led the California state legislature to dramatically tighten its exemption restrictions. Joining Mississippi and West Virginia, it became the third state to only allow exemptions for medically certified reasons. Follow-up studies should be able to observe how the state policy change interacts with local characteristics to produce different responses.

The second analysis—using data at the state-level—does not have the advantage of the more granular approach to measuring social capital, but it provides other advantages to building a more complete picture of the relationship between vaccination, social capital, and public policy. First, the results of the state-level models are more generalizable because they do not apply only to the California context (which, as just described, is distinctive). Secondly, a state-level analysis can integrate aspects of public policy into vaccine outcomes, specifically, differences in state exemption policies. In these models, I control for the presence of religious and personal belief exemption policies to see how vaccination rates respond to the policy environment.

I analyze eight school-level outcome variables in the California models. These are the percent of enrolled kindergarteners who are up-to-date on the required doses of all five mandated vaccines in addition to the percent up-to-date for each of the five vaccines individually. The final two outcomes are the percent of enrolled kindergarten students with medical exemptions and personal belief exemptions. For the state-level models, I estimate the relationship between social capital and the percent of kindergarteners who are up-to-date on the five required vaccines. I also include an interaction between the social capital score and an indicator for states allowing personal belief exemptions.

Overall, the results present seemingly conflicting results. The California school-level models indicate that social capital, contrary to expectations, has a negative and significant relationship with vaccine coverage and a positive and significant relationship with personal belief exemption rates. (The association with medical exemptions is not statistically significant.) Conversely in the state-level models, the estimates comport with the hypothesized direction in states without personal belief exemptions. The state-level social capital index is associated with higher rates of MMR, DTaP, and polio vaccine coverage where PBEs are not allowed. However, the direction of effect is reversed in states with personal belief exemptions.

These mixed results highlight the potential for social capital to generate beneficial or detrimental effects, depending on context. The informal networks that produce social capital can support positive norms and information dissemination in addition to negative ones. States like California, where anti-vaccine sentiment runs high, are more likely to have personal belief exemption policies. In such settings, social capital may serve to promulgate these beliefs. In states where aversion to vaccines is less common, more social capital can highlight the societal benefits of vaccination and promote optimal outcomes.

The results from the state-level models may be considered more valid due to their generalizability (using a nationwide sample) and improvements to the social capital measure based on better availability of key variables at the state-level. These findings provide evidence that higher levels of social capital, representing more connections and trust between individuals, improve vaccination outcomes and help communities move closer to the socially efficient level of coverage under certain conditions. When the messages and values being passed through close community ties are against vaccination, social capital can discourage vaccination. Efforts to improve social cohesion and civic engagement could help produce better public health outcomes where the potential for gains from positive externalities exist.

This paper will proceed as follows—Section 2 summarizes the rationale for public involvement in vaccination and trends in vaccination rates in the U.S., Section 3 discusses theories of social capital and how they apply to public health in general and vaccination policy in particular, Section 4 describes the study methodology—including data sources and econometric models—and presents hypotheses, Section 5 presents and discusses the study findings, and Section 6 concludes the paper with an analysis of the meaning of the results for the understanding of social capital in this policy area.

Vaccination History and Trends

The first modern vaccine—which inoculated against smallpox—was developed in the late-eighteenth century and protected the public from infectious disease even before science developed a coherent germ theory. Over the course of the twentieth century vaccines were discovered for 23 additional diseases, 13 of which are recommended to be universally

administered to children.[4] The ability to immunize against infectious disease emerged as a modern marvel. Diseases that do not exist in the memories of most Americans today were pernicious threats several decades ago (Centers for Disease Control and Prevention, 1999). Both incidence of and deaths from vaccine-preventable diseases plummeted over the course of the 20th century into the present. Since the peaks of their prevalence, cases of polio, diphtheria, measles, mumps, rubella, and tetanus have reduced by more than 90%, with some achieving complete or near-complete elimination (Roush, Murphy, & Vaccine-Preventable Disease Table Working Group, 2007). Mortality from these diseases is essentially unheard of in the United States.

Contrast the present day with earlier decades. In 1920, there were 469,924 cases of measles and more than 7,500 deaths, 147,991 diphtheria cases and more than 13,000 deaths, and 107,473 cases of pertussis and almost 5,100 deaths (Centers for Disease Control and Prevention, 1999). In 2013, there were a mere 187 confirmed cases of measles and no deaths (Hamborsky, Kroger, & Wolfe, 2015). A case can be made that the discovery and widespread administration of immunization was the greatest public health achievement of the previous century.

Discovery alone of effective immunizations was not enough to reduce or eradicate disease. Substantial public health campaigns backed by legal mandates requiring vaccination were necessary to achieve sufficient levels of protection against disease outbreaks. In the United States, Massachusetts passed the first statewide compulsory vaccination law in 1807, requiring all residents to be inoculated against smallpox (Salmon et al., 2006). A legal challenge to the requirement eventually came before the Supreme Court in 1905 in Jacobson v. Massachusetts. The Court decided in favor of the state, providing a broad and lasting precedent that asserted the

[4] Diphtheria, pertussis, tetanus, polio, measles, mumps, rubella, hepatitis B, Haemophilus influenzae type b, hepatitis A, varicella, rotavirus, and pneumococcal disease

rights of the government to infringe on an individual's liberty for the sake of public welfare. In a 7-2 ruling, the Court maintained that, "there are manifold restraints to which every person is necessarily subject for the common good. On any other basis, organized society could not exist with safety to its members" ("Jacobson v. Massachusetts," 1905).

At the time of the Jacobson ruling, 11 states already had compulsory vaccination laws in place. In the latter half of the twentieth century, states began setting vaccine requirements as a prerequisite for school enrollment. (Another Supreme Court decision, Zucht v. King in 1922, upheld the constitutionality of school mandates.) The federal Department of Health and Human Services and the CDC advocated strongly for states to set and enforce immunization school requirements. Not until 1980 had all states had done so (Salmon et al., 2006).

Effective vaccine coverage was not achieved with all sticks and no carrots, however. Public policy has intervened through information sharing and financial incentives as well. The Advisory Committee on Immunization Practices (ACIP) was established in 1963 to make recommendations on establishing and updated an immunization schedule (Roush et al., 2007). By publishing the ACIP schedules, the CDC sets uniform national standards for the numbers and timing of vaccine doses. Finally, in 1993, Congress enacted the Vaccines For Children program to provide free immunizations to uninsured and Medicaid-insured children.

Ironically, these vaccine campaigns have been so effective at eradicating disease, they seem to have become similarly effective at eradicating the perceived threats of disease. Put another way, vaccines may have become victims of their own success. Since many parents cannot remember the very acute dangers that common infectious diseases once posed to small children, they are less likely to be sure to vaccinate their children (Kim-Farley, 2017). American parents are largely unaware that mumps can cause infertility in males; rubella can deafen

children; and diphtheria can cause damage to the heart, nerves, and lungs. As a result, recent trends have shown an increasing number of parents choosing to delay or forego certain doses of vaccine for their children (Gust et al., 2008). Figure 9 displays the distribution of state vaccine coverage rates among kindergarteners over time. For each of the five recommended vaccinations—diphtheria-tetanus-pertussis (DTaP), measles-mumps-rubella (MMR), polio, hepatitis B, and varicella (i.e., chicken pox)—the CDC has set a target of 95% vaccine coverage. In recent years, fewer states are meeting this target, and for all but one vaccine (hepatitis B), more than half of states are failing to achieve 95% coverage.

Surveys of parents show a variety of motivations for their vaccine choices. Many parents have fears that vaccines pose serious dangers to children and can cause the developmental disorder autism (Kennedy, LaVail, et al., 2011). These misperceptions were fueled by a now discredited research study that appeared in the British medical journal *The Lancet* in 1998, which seemed to show a link between the MMR vaccine and autism (Wakefield et al., 1998). However, the journal retracted the research findings in 2010 after discovering that the lead researcher, Andrew Wakefield, had fabricated data (Godlee, Smith, & Marcovitch, 2011). Dr. Wakefield subsequently had his medical license revoked. A number of respected scientific studies have repeatedly failed to find a link between vaccination and autism (DeStefano, Bhasin, Thompson, Yeargin-Allsopp, & Boyle, 2004). The damage has been done; many parents believe that exposure of their children to even a small probability of risk is not acceptable.

Other parents express skepticism that their children are susceptible to the diseases prevented by vaccines, that those diseases entail significant health risks, or that vaccines are effective at preventing those diseases (Smith et al., 2011). Some researchers have suggested that parents find it preferable to risk committing an error of omission (i.e., their unvaccinated child

contracting an infection) versus an error of commission (i.e., their child suffering some harm from receiving a vaccine) (Sadaf, Richards, Glanz, Salmon, & Omer, 2013). Other parents may be responding to the increasing complexity of the recommended vaccine schedule, believing that children are receiving too many vaccines in too short a period of time (Kennedy, Basket, & Sheedy, 2011).

Finally, there is concern that the twin forces of generalized skepticism toward authority along with the expansion of the internet and social media are responsible for creating a dangerous level of doubt in parents regarding the safety and efficacy of vaccines (Kennedy, LaVail, et al., 2011). Parents who choose to delay or refuse vaccines for their children are less likely to report having a good relationship with their child's health care provider and less likely to believe the provider is motivated by the child's best interests (Smith et al., 2011). Parents have vented their skepticism on the internet and found communities of like-minded people to reinforce their beliefs. Additionally, the internet has provided a forum for the wide dissemination of misinformation regarding vaccine safety and facilitated the abilities of individuals to cherry-pick their information sources to fit their preexisting biases (Kim-Farley, 2017).

While vaccination coverage rates have declined in the population overall, the problem is especially acute in small, geographic pockets where immunization coverage may fall to very low levels (Seither et al., 2014).While the median state MMR vaccination rate was 94.6% in 2015, rates ranged from a high of 99.4% in Maryland and Mississippi to a low of only 87.1% in Colorado (Seither et al., 2016). Populations of unvaccinated or undervaccinated children can concentrate even further in local communities. Small, local outbreaks of diseases have caught some public attention. In 2012, 414 children in Colorado were hospitalized for vaccine-preventable diseases (Goodwin, 2015). More recently, a measles outbreak in Disneyland Park in

California received significant press coverage (Zipprich et al., 2015). Public health officials continue to be alarmed at declining rates of childhood immunization.

What these newfound anxieties about immunization reveal is that parents have a cost-benefit analysis to make when it comes to choosing whether or not to have their children vaccinated. In terms of benefits, inoculated children clearly have a protection against a host of dangerous diseases; however, that personal benefit is reduced by the low prevalence of those diseases among the population in the U.S. today. Moreover, parents are likely to weigh the value of the benefit of protection from infectious disease according to today's low level of disease incidence, not by how prevalent those diseases would be should everyone decide to go unvaccinated (Kim-Farley, 2017).

Apart from the private benefits of vaccination, society stands to benefit in a significant way from a parents' decision to vaccinate. First, high levels of vaccination—sometimes referred to as "herd immunity"—form a protective shield for vulnerable individuals who are either too young or too sick to receive vaccines or those whose vaccinations were ineffective. In communities with high numbers of unvaccinated people, even vaccinated individuals are at a higher risk of infection (Salmon et al., 1999). The higher the vaccination coverage, the better the protection for all members of society.

In this way, vaccines are a classic example of a positive externality, in that the decisions of private individuals have positive impacts on the broader population. This wedge between the private and social benefits of vaccination means that vaccines will tend to be underproduced. In other words, the equilibrium level of vaccination will be suboptimal and inefficient. From society's cost-benefit calculation, the answer is clear. Vaccination is well worth it (Zhou et al., 2005). An economic evaluation by Zhou et al. (2014) estimated that the net cost savings

attributable to the recommended vaccine schedule for society (following a cohort of infants from birth through death) were $68.8 billion, with a return on investment of 10.1:1.

This cost-benefit calculation is not so simple for parents. According to the theory of bounded rationality, individuals are not well-suited to weighing all possibilities that might arise from a given decision (Simon, 1947). Instead of maximizing utility, they turn to "satisficing"—that is, making-do with limited information and cognitive ability. Parents might be able to comprehend the direct cost in money, time, and effort that getting their children vaccinated will entail. However, parents will have difficulties imagining the health risks for their children remaining unvaccinated, and they likely have a strong natural reactions against the idea of their children being diagnosed with serious side effects such as autism.

What is more, the extent to which parents will weigh the potential benefits accruing *to society* of their own child being vaccinated is unclear. If a parent is outwardly focused and engaged in her community, these considerations might be important to her. However, a typical problem with goods and services that produce positive externalities is that they are undersupplied because the societal benefits are ignored by individuals making self-interested decisions. The extent to which an individual parent is focused on and associates with the community around her may play a significant role in determining if she has her children immunized. One way of conceiving of the strength of community connections is through the concept of social capital.

Social Capital

Defining Social Capital

Researchers over the past two decades have dedicated substantial attention to the concept of social capital as a way of describing how otherwise similar geographic areas experience variation on a wide range of outcomes. These outcomes include economic prosperity (Fukuyama,

1995; Knack & Keefer, 1997; Putnam, Leonardi, & Nanetti, 1994), international development (Woolcock & Narayan, 2000), intergenerational mobility (Chetty, Hendren, Kline, & Saez, 2014), educational attainment (Coleman, 1988), healthier and longer lives (Folland, 2007), and more. Generally, social capital refers to shared norms and values in addition to informal interpersonal networks that exist in some communities—those communities ranging from nations to city blocks. Higher degrees of social capital are hypothesized to enable greater cooperation between actors and facilitate beneficial transactions, activities, and behaviors that would otherwise not occur. These positive outcomes that result from cooperative behaviors are hypothesized to radiate out beyond the individuals directly involved in the behaviors. As such, social capital is often believed to be associated with positive externalities for the community at large.

While many pages have been devoted to the concept of social capital and its purported effects, this literature is still troubled by problems related to a lack of consensus on the basic definition and measurement of social capital. One of the concept's earliest proponents, James Coleman (1988), conceived of social capital as an input into the human capital production process. He sought to explain how differences in social contexts—related to social norms, communication channels, and expectations—had an impact on an individual's efforts to achieve their economic self-interest through educational attainment. Coleman's work was an attempt to unite concepts from sociology (e.g., values and norms) with the utility maximizing predictions of economics.

Subsequent definitions have homed in on some aspect of trust and other mutual values, personal connections and networks, or both. Fukuyama (1997) asserts that the concept of social capital derives exclusively from norms such as expectations that individuals will meet

obligations, fulfill promises, be truthful, and return goodwill with goodwill (i.e., reciprocity). These norms and values usher in cooperation between individuals. Similarly, Bowles and Gintis (2002) suggest that social capital pertains to "a willingness to live by the norms of one's community and to punish those who do not" (p. 2). In contrast, Lin (2001) stresses the networks side of social capital. She defines social capital as the "resources embedded in social networks and accessed and used by actors" (p. 25) and that social capital is created through "investment in social relations with expected returns in the marketplace" (p. 19). Likewise, Portes (1998) maintains that the consensus view on social capital is "the ability of actors to secure benefits by virtue of membership in social networks or other social structures" (p. 6).

The sociologist Robert Putnam has been one of the most influential researchers advancing a conception of social capital. His early research explored the differences between Northern and Southern Italy that he maintained helped explain the relative economic advantage enjoyed in the north (Putnam et al., 1994). His later work, *Bowling Alone*, popularized the concept of social capital and purported to document the secular decline of social capital in American communities since World War II. Putnam's definition of social capital is the "connections among individuals - social networks and the norms of reciprocity and trustworthiness that arise from them" (2000, p. 19). Notably, he includes both aspects of social capital, values-based (trust) and networks-based (connections).

Most recent operationalizations of the concept attempt to include both norms and networks. The mechanism of influence for social capital on social outcomes is presumed to occur as follows. Trust and other shared values produce externalities for society (Durlauf & Fafchamps, 2004). When they are present, they enable interactions and transactions to occur that would either fail to take place in absence such norms and values or would occur less efficiently.

Trust is the lubricant for generating and improving cooperation between actors (Glaeser, Laibson, & Sacerdote, 2002). When an individual's decision to cooperate would be dependent upon the actions of others but those actions are unknowable to the individual *a priori*, trust can give the individual confidence to decide to cooperate under the assumption that others will do the same (Dasgupta, 2003).

These shared norms and values that generate externalities arise from and are spread through informal networks. Networks can build trust by reinforcing rules and providing a forum for repeated contacts between individuals, much like repeated games in game theory (Dasgupta, 2003). For example, the interpersonal ties inherent to social capital can help overcome collective action problems by "greasing the wheels" to produce cooperation between parties and enables an optimal result. Values related to trust and community-mindedness can help address free-rider problems (Durlauf & Fafchamps, 2004). Such consideration of one's neighbors can also combat the underinvestment in behaviors that produce positive externalities (or discourage the overinvestment in behaviors that entail negative externalities).

There are a number of ways in which social capital, operating through networks, is viewed as facilitating social interactions and improving outcomes. First, it can improve information flows, thus correcting information asymmetries or misinformation (Lin, 2001). Second, it affirms group identity, shifting focus toward more community-focused values. Altruism may be the most prominent of such values, encouraging actions that aid the group over the individual, but group identity could also spur people to act out of guilt or a desire to emulate or mimic other members of the group. An important caveat is that mimicry, unlike altruism, can produce negative behaviors as well as positive ones (Durlauf & Fafchamps, 2004).

Several scholars have pointed out that social capital is not necessarily a force for good. Portes (2014) describes the potential downsides of social capital, such as the deprivation of resources by the in-group for those in the out-group. Network participation can prove to be overly burdensome for individuals (Hawe & Shiell, 2000). In the extreme, Berman (1997) emphasizes that levels of social capital in 1920-30s Weimer Germany were high, and these networks enabled rather than inhibited the rise of Nazism.

Finally, as mentioned earlier, social capital can encourage coordination and cooperation thanks to repeated interactions. Importantly, the benefits of these networks can accrue to those participating in the network in addition to community members not participating in the network (Scheffler & Brown, 2008). For example, children whose parents do not contribute to PTA activities still benefit from the higher quality schools that an active PTA may help produce.

A major difficulty in studying social capital is in observing and capturing the concept, which is undeniably intangible, in a valid quantifiable measure that can be compared across geographic areas. Putnam (2001) developed a measure called the Social Capital Community Benchmark Survey using data from the General Social Survey (GSS) and other datasets on trust and group participation. Other measures have relied on factor analyses of variables thought to be indicators of social capital. For example, the Petris Social Capital Index uses information on local employment in social organizations from the U.S. Census Bureau's County Business Patterns (CBP) data. This study will build upon these efforts by using data on community organizations, nonprofit resources, voter turnout and other measures at the county- and state-levels.

Social Capital and Health

Building on this general framework of social capital and its potential to generate positive externalities, many researchers have examined the relationships between social capital and health outcomes. There are a variety of hypothesized channels through which social capital could influence health. Scheffler and Brown (2008) suggest that social capital can help spread information about healthy lifestyles and behaviors, strengthen a sense of community to encourage the actions that improve public health (such as receiving vaccines), provide a support network that can help alleviate psychosocial stress, and encourage collective action to help build better health care infrastructure and systems.

Other authors add to this list. Kawachi and Kennedy (1997) propose that social capital helps individuals avoid isolation, which has been shown to damage health. Rocco, Fumagalli, and Suhrcke (2014) suggest that the networks that are a part of social capital can be important for the provision of informal care or financial support to community members in need. Trust reassures the delivery of such support by reinforcing an expectation of reciprocity; people help others with the understanding that they would be helped if the need should arise. Finally, Folland (2006) argues that greater social capital increases the expected value of life and health by increasing an individual's sense that they are living for others in addition to for themselves. Raising the value of life incentivizes individuals to invest more in health-promoting behaviors (e.g., exercise and good nutrition) and to avoid risky behaviors (e.g., cigarette or drug use). Hawe and Shiell (2000) observe that social capital can lead to greater empowerment of individuals and strengthen local health promotion efforts.

The literature shows many positive correlations between measures of social capital and improved health outcomes. A study by d'Hombres, Rocco, Suhrcke, and McKee (2010) finds better self-reported health status among individuals in eight post-Soviet republics in areas with

great social capital. Another study found significant negative relationships between social capital in U.S. communities and overall mortality and mortality from cancer, accidents, and suicide (Folland, 2007). Kim, Subramanian, Gortmaker, and Kawachi (2006) observe lower rates of obesity and higher rates of physical activity associated with greater social capital. Finally, a recent study shows decreased cigarette consumption in areas with higher religiously-associated social capital (Brown, Scheffler, Seo, & Reed, 2006).

No study to date has examined the relationship between social capital and vaccination rates. There is good reason to suspect that vaccinations would be positively associated with social capital. First, vaccines are a public good; they produce both private (individual immunity) and public benefits (community immunity). Social capital is thought to facilitate the production of public goods by encouraging altruism and acting ways that support community wellbeing. Second, social capital could reinforce a norm of vaccination. In other words, vaccinating one's child may be "just what you do" and anti-vaccination movements may be subjected to more skepticism. Third, social capital is expected to strengthen expectations of reciprocity. Parents may be more likely to vaccinate their own children if they believe other parents will do the same. Fourth, communities with more social capital might be more likely to have philanthropic programs in place to provide free or reduced-cost vaccines for needy families. Finally, social capital is thought to facilitate information exchange, which could allow the exchange of more knowledge about the benefits of vaccines.

However, this last hypothesis could work in the opposite direction. Networks that allow for information flows about the benefits of vaccines could just as easily serve as conduits for misinformation about the dangers of vaccines. Such a case would be an example of the "dark

side" of social capital and is a reminder that social capital can generate negative as well as positive outcomes under certain conditions.

Methodology

Data

The vaccination data for the California, school-level analyses are publicly available through the California Department of Public Health (CDPH). For each school year, both public and private schools report the percent of their enrolled kindergarten students who have met the state requirements for five vaccines—five doses of DTaP vaccine, two doses of MMR vaccine, four doses of polio vaccine, three doses of hepatitis B vaccine, and 1 dose of varicella vaccine. (These recommendations follow the schedule published by the CDC.) Schools also report the percent of enrolled kindergarteners who have filed either medical or personal belief exemptions. I use data from all California schools from the 2010-11 to the 2015-16 school years.

The vaccination data for the state-level estimates are similar. They are collected by the CDC each year from states and published as the Annual School Assessment Reports. For each of the five vaccines, states provide estimates of the percent of kindergarteners that are up-to-date. Most states collect this information, like California, as a census of all enrolled kindergarteners in all schools. Some states conduct stratified surveys of a sample of schools and students each year to generate statewide estimates. In most years, there is at least one state that did not report to the CDC. For the MMR, DTaP, and polio vaccines, the average number of states reporting each year was greater than 47. For hepatitis B, 43 states reported on average and for varicella, the number was lower, with an average of 40.5. I rely on eleven years of CDC data, from the 2005-06 to the 2015-16 school years.

Policy variables indicating if a state allowed religious or philosophical exemptions were taken from the CDC's SchoolVaxView website. Previous studies have found that that the details of school exemption policies matter and that some exemption policies impose a tighter constraint on parents than others (Blank, Caplan, & Constable, 2013; Bradford & Mandich, 2015). For example, Oregon recently began requiring parents to receive a vaccine education certificate by meeting with a health care provider or watching an online module before receiving an exemption. However, for this study, I will treat exemption policies as simple dichotomous variables because an up-to-date, comprehensive list of these policy details is not currently available.

In both the California and state-level models, I control for a number of variables that have been shown to be related to vaccination status. I use demographic and socioeconomic information from the Census Bureau's American Community Survey (ACS). For the California models, these data are collected at the school district level. In order to get estimates for these relatively small areas, I use the ACS 5-year estimates. For the state-level models, I use the more precise 1-year estimates, which are available every year for all 50 states. These variables are median family income (adjusted to 2015$), percent of families with children with married heads of household, and the percent of the population 25 years and older with different levels of educational attainment (not a high school graduate, high school graduate, some college, and college graduate).

For the California models, I use additional school-level data from the state's Department of Education to control for other demographic characteristics. I control for the racial and ethnic composition of the kindergarten population (percents that are Hispanic and non-Hispanic white, black, Asian, and other races). I calculate a Herfindahl-Hirschman Index (HHI) of racial

diversity as the sum of the squared percentages of each of these categories. These HHI values range from 0 to 1, with higher values indicating less diversity. While the value of the HHI is variant depending on the racial categories included in the measure, this version of the HHI is consistent across years since the same categorization schema is maintained over the entire study period (and for both the California schools- and state-level models). I also include the percent of students receiving free or reduced price meals, which is a common measure of poverty and low-income. I control for whether the school is private and whether it is located in a Metropolitan Statistical Area (MSA).

To control for access to health care, in both the California (at the county-level) and the state-level models, I include the percent of the below 18-year-old population that is uninsured. These data come from the Census's Small Area Health Insurance Estimates. I also include the number of primary care physicians practicing in the area per 100,000 of the population. These measures come from the Area Health Resource Files released by the Agency for Healthcare Research and Quality (AHRQ).

I also include a measure of economic inequality, known as a Gini Index, that ranges from 0 for populations where income is equally distributed among the population to 1 where all income is concentrated in a single individual. This is also measured at the county-level in the California models. Together, the Herfindahl-Hirschman Index and the Gini Index identify areas that are more homogenous, either racially (HHI) or socioeconomically (Gini). This is important, since individuals may be more likely to be outwardly focused in their decision-making if they are in communities where more people resemble themselves (Putnam, 2007).

My key explanatory variable is an index of social capital. I used factor analysis to generate this index based on multiple indicators that the literature on social capital suggests are

related to the concept. These variables, for both the county- and state-level indices—are listed in Table 11. Broadly, these variables cover the number and financial resources of nonprofit organizations per capita and the number and employment in civic, recreational, religious, and charitable organizations per capita[5]. Because social capital may be built between members of a community over time, it includes the percent of residents who moved from outside the county in the past year and the percent of homes that are owner-occupied.

Another variable is an index of dissimilarity that represents a measure of housing segregation. It is created by comparing the distributions of white to nonwhite residents from a larger jurisdiction (here, county or state) to a smaller jurisdiction (census tract or county). Higher numbers indicate more segregation—that is, a large proportion of members of one group would have to move in order to make the small-area racial distributions match the larger-area distribution. Finally, the social capital index includes both the violent and property crime rates in addition to the percent of eligible voters who voted in the most recent presidential election.

A number of other variables were available at the state- but not county-level and were included in the state-level index. These are the percent of state residents who report volunteering and the annual number of volunteer hours per capita. Finally, there are survey responses for the percent of people who report trusting most of their neighbors, talking often with their neighbors, doing and receiving favors from neighbors often, always voting in local elections, being members of a local committee, and participating in civic groups.

These social capital indices are designed to capture the latent level of community cohesion and civic-mindedness in California's 58 counties and in the 50 U.S. states. The indices

[5] Data on civic organizations come from the Census Bureau's County Business Patterns dataset and are defined by the following North American Industry Classification System (NAICS) numbers: 818321- (Grantmaking Foundations), 713990 (All Other Amusement and Recreation Industries), 813110 (Religious Organizations), and 813410 (Civic and Social Organizations).

are longitudinal, such that each jurisdiction's social capital score varies over time. For the county-level factor analysis, the social capital index is the factor with the largest eigenvalue. At 2.76, this factor's eigenvalue exceeds the commonly accepted threshold of 1 and is substantially larger than the eigenvalue of the next highest factor (1.75). The variables contributing most to the index are the number of nonprofits, the number of civic groups, voter turnout, and the percent of owner-occupied housing. Figure 10 displays the average social capital values for each county. For the county-level measure, the values of the index spanned a low value of -1.6 (Kings County in 2012) to a high value of 3.5 (Alpine County in 2013).

For the state-level factor analysis, the social capital index is again created from the factor with the largest eigenvalue. In this case, the eigenvalue is 5.73 and more than twice as high as the value of the next largest factor (2.09). The variables providing the most variance in the index are volunteerism and volunteer hours, trust of neighbors, committee membership, civic group participation, voter turnout, the number of nonprofits, the number of civic groups, and the percent of owner-occupied housing. It is important to note that some of the most influential variables in this measure were not available at the county-level—variables related to connections and trust between neighbors and volunteer and civic group participation. For this reason, the state-level social capital index likely has more validity than the county-level index. The state-level index ranges from a low value of -2.0 (Louisiana in 2013) to a high of 4.1 (Utah in 2012). Figure 11 displays the average social capital values for each state.

Variable means and standard deviations for the California schools models are presented in Table 12. During the study period, schools have an average of 3.3% of kindergarten students with a personal belief exemption on file and 0.20% of students with medical exemptions. The average number of kindergarten students with up-to-date vaccine coverage is 89.6% for all five

vaccines. The lowest coverage levels are for MMR (91.9%), DTaP (91.8%), and polio (92.0%). Coverage is 94.4% for hepatitis B and 94.7% for varicella. It is useful to note that all of these average coverage rates fall below the CDC target of 95%. Private schools make up 20.1% of the full sample.

Summary statistics for the state-level models are displayed in Table 13. The values are given for the full sample and then broken out by states with and without personal belief exemptions. The average state-level vaccine coverages are 94.5% for MMR, 94.9% for DTaP, 95.2% for polio, 95.7% for hepatitis B, and 93.1% for varicella. Comparing states that allow PBEs with states that do not, those with PBE policies have lower average coverage rates across all five vaccines. Scores on the state social capital index are also higher on average for states with PBEs than states without such policies. For this reason, I will interact a state's PBE status with its social capital score in the state-level regression models in order to distinguish between the effects of social capital in states that have PBEs and those that do not.

Econometric Models

To estimate the relationship between county-level social capital values and school-level vaccination and exemption rates, I rely on a series of eight ordinary least squares (OLS) regression models. The dependent variable in each model is the percent of enrolled kindergarteners who were up-to-date (UTD) (i.e., received all required doses) on all five of the mandated vaccines, percent of kindergarteners UTD on each of the five vaccines individually (MMR, DTaP, polio, hepatitis B, and varicella), and the percent of kindergarteners with medical exemptions and personal belief exemptions. I regress the dependent variables on the county's score in the social capital index in addition to a number of school-, school district-, and county-level variables that predict vaccination rates. The social capital scores have been standardized to

indicate the number of standard deviations from the mean score, such that regression coefficients will be interpreted as the change in the outcome from a one standard deviation increase in the social capital index. I also use year fixed effects to control for secular time trends in vaccination during the study period, 2010-2015. I do not include county (for the California schools models) or state (for the state-level) models fixed effects because, although the social capital indices vary over time, the variation within geographic area over time is not large. Therefore, including fixed effects introduces significant multicollinearity problems.

Because all of my dependent variables are continuous, I proceed with the following OLS models:

$$(1)\ VAX_{sdct} = \beta_0 + \beta_1 SC_{ct} + \beta_2 X_{sdct} + \beta_3 Z_{dct} + \beta_4 W_{ct} + \tau_t + \varepsilon_{sdct}$$

where VAX_{sdct} is the vaccination outcome variable in the *s*th school, the *d*th school district, and the *c*th county in year *t*. SC_{ct} represents the county's standardized value on the social capital index. X_{sdct} is a vector of school-level covariates including a dichotomous indicator for identifying private schools, the proportion of enrolled kindergarten students by racial and ethnic background (Hispanic and non-Hispanic white, black, Asian, and other races), the Herfindahl-Hirschman Index of racial diversity, and the percent of enrolled students receiving free or reduced-price meals. A vector of district-level variables, Z_{dct}, contains median family income (in 2015$), percent of families with children headed by married couples, and educational attainment of the population 25 years and older (no high school degree, high school degree, some college, and college graduate). W_{ct} is a vector of county-level covariates—a dummy variable for metropolitan status, the Gini Index of socioeconomic equality, the percent of children without health insurance, and the number of primary care physicians per 100,000 of the population. The year dummies are represented by τ_t, and the error term is captured in ε_{sdct}.

The models estimating the correlation between state vaccine coverage rates and social capital contain many of the same variables in (1) and also employ OLS regression. The dependent variables are the percent of kindergarteners in a state that have received all required doses of the MMR, DTaP, polio, hepatitis B, and varicella vaccines. The principal difference is that the state-level models contain an interaction term between a state allowing personal belief exemptions and the social capital variable. These specifications can be defined as:

$$(2)\ VAX_{st} = \beta_0 + \beta_1 SC_{st} + \beta_2 SC_{st} \times PBE_{st} + \beta_3 PBE_{st} + \beta_4 X_{st} + \tau_t + \varepsilon_{st}$$

where again, VAX_{st} is the vaccine outcome and SC_{st} is the standardized value on the social capital index. This time, both of these are measured in state s in time t. PBE_{st} is a dummy variable indicating if a state allows personal belief exemptions, and $SC_{st} \times PBE_{st}$ is the interaction between this dummy and the state's social capital score. The vector of state-year characteristics, X_{st}, consists of the following covariates—a dummy indicating if the state allows religious exemptions, median family income (in 2015$), the poverty rate among families with children, the Gini Index, the percent of families with children with married heads of household, the number of primary care physicians per 100,000 of the population, the percent of children without health insurance coverage, the HHI of racial diversity, the racial and ethnic composition of the population (Hispanic and non-Hispanic white, black, Asian, and other races), and the educational attainment of the population 25 years and older (no high school degree, high school degree, some college, and college graduate). The year fixed effects are represented by τ_t, and the error term is captured in ε_{st}.

Hypotheses

As reviewed above, there is an extensive literature predicting that social capital can encourage activities that produce positive externalities. Social capital is believed to promote

behaviors that serve the public interest in addition to the private interest by encouraging cooperation and engendering trust and norms of reciprocity. More social capital can also help overcome collective action problems and information asymmetries to arrive at more socially efficient outcomes. In addition, social capital is expected to encourage health-enhancing behaviors by increasing the value of statistical life and spreading information about healthy behaviors. Because of this, I arrive at the following predictions with respect to vaccination outcomes.

For the California schools models:

H1: Schools located in counties with higher social capital values will have a higher percentage of kindergarteners that are up-to-date on the full series of vaccines in addition to each of the five vaccines individually (MMR, DTaP, polio, hepatitis B, and varicella).

H2: Schools located in counties with higher social capital values will have a lower percentage of kindergarteners with personal belief exemptions.

H3: Social capital will not be significantly related to a school's medical exemption rate.

For the state-level models:

H4: States that score higher in the social capital index will have higher vaccination coverage rates for each of the five recommended vaccines—MMR, DTaP, polio, hepatitis B, and varicella.

H5: For states that allow personal belief exemptions, the effect of social capital on vaccination coverage rates will be even larger, as parents have more discretion in these states and more ability to act on their preferences.

H6: States allowing personal belief exemptions will have lower vaccination coverage rates.

Research Findings

Results

Table 14 displays the regression results for the California school specifications estimating the relationships between social capital and medical exemption rates, personal belief exemption rates, and percent of students up-to-date on all five vaccines. Due to the large sample size (41,800 school-year observations), statistical significance is reported at the 95% (*) and 99% (**) confidence levels.

As expected, social capital is not significantly related to medical exemptions. This makes intuitive sense because social capital would not be expected to have an impact on the small number of children who are deemed medically ineligible to receive vaccines. Contrary to Hypothesis 2, higher social capital scores are associated with more students submitting personal belief exemptions. A standard deviation increase in the social capital score is related to a 0.75 percentage point increase in the percent of students with PBEs. While the effect on being UTD on all five vaccines is not statistically significant, its direction is also against expectations. There is a negative relationship between social capital and the overall level of vaccination coverage in a school.

This last relationship holds when examining the regression results for the coverage rates of the five individual vaccines, as shown in Table 15. In each of the five specifications, the results show a significant and negative relationship between social capital and vaccination rates. These range from a low for MMR vaccines with a 0.49 percentage point decrease related to a one standard deviation increase in social capital to a high of 1.06 percentage points for varicella coverage.

Other covariates operate primarily according to expectations. Students in private schools are more likely to file a PBE and less likely to be fully vaccinated for each of the five vaccines. These effects are quite large. Controlling for other factors, private schools have coverage rates for the MMR vaccine that are more than three percentage points below those of public schools. Students in private schools are less likely to be vaccinated for a number of reasons. Many private schools are religiously affiliated, increasing the probability of students have religious objections to vaccines. Even without religious motivations, many attending private schools may show a general skepticism toward the strictures of traditional public education, which is likely related to less trust in authority and vaccine skepticism as well.

Vaccine coverage is generally higher for schools in metropolitan areas and for schools in areas with higher median incomes, more socioeconomic equality, and more racial diversity. Interestingly, schools with more students receiving free or reduced-price meals also had higher vaccination rates. While schools with greater numbers of students in poverty or in low-income families would seem likely to have lower vaccination coverage, this result may have an alternate explanation. Schools with many poor students receiving meal assistance may be better adept at providing all kinds assistance to needy children, including public health assistance. Because of this, students in these schools might be more likely to be up-to-date on their vaccinations because they are Medicaid (the joint federal state program providing health insurance for low-income families) recipients or participants in the Vaccines For Children program.

If social capital is unexpectedly *negatively* related to vaccine coverage in California schools, does it operate similarly at the state-level for a national sample of kindergarteners? The state-level findings for these models are found in Table 16. Due to the much smaller sample sizes (438 to 521 state-year observations, depending on the specification), confidence levels are shown

at the 90% (*), 95% (**), and 99% (***) levels. As is clear from Figure 11, the state of Utah is an outlier for in the state social capital index. A sensitivity analysis reveals that the Utah observations in the sample were highly influential on the regression results; therefore, Utah is excluded from the final regressions.

Unlike the California schools models, social capital generally shows a positive effect on vaccination rates. Vaccine coverage is higher for the MMR, DTaP, and polio vaccines in states with higher social capital scores. There is not a statistically significant relationship between social capital and hepatitis B vaccination rates; however, social capital is negatively related to varicella vaccine coverage.

These coefficients cannot be considered in isolation because of the inclusion of the interaction term between the standardized social capital scores and the personal belief exemption policy dummies. In fact, the positive relationships just referenced should be interpreted to apply only to states without personal belief exemptions. The coefficients for the interaction terms tell a different story about states where PBEs are allowed. The effect of social capital in PBE states is—like in California, a state that allowed PBEs during the study period—generally negative and statistically significant for the MMR and DTaP vaccines. This provides evidence that the relationship between vaccine coverage and social capital is nuanced depending on other characteristics of the state.

As expected, both religious and personal belief (or philosophical) exemption policies were strongly negatively related to vaccine coverage. This result is consistent with previous research (Omer et al., 2012; Safi et al., 2012; Thompson et al., 2007). Like in the California models, higher median income was associated with higher vaccination rates. Additionally, in some specifications, higher poverty rates among families with children was related to increased

vaccination coverage. While the mechanism is unclear, this may again relate to availability to assistance through programs like Medicaid, the State Children's Health Insurance Program (CHIP), and Vaccines For Children. More availability to primary care physicians also had a positive effect on vaccination coverage.

Discussion

These results do not lend themselves to simple explanations or clear interpretation. Seemingly, differences between the findings among California schools and state-level vaccine rates present conflicting conclusions. However, there may be an underlying explanation that unites these results.

The tendency among social capital scholars is to expound on the benefits or untapped positive potential of social capital for community wellbeing; however, the literature also makes occasional references to the possible downsides of social capital (Portes, 2014). In this way of thinking, social capital can be a conduit for information, behaviors, values, and norms that lead to desirable outcomes. But certain norms and values can lead to socially undesirable outcomes. Similarly, networks of people can disseminate valid and helpful or invalid and harmful information.

These distinctions can apply with respect to vaccination decisions as well. If networks of people are robust in a community with a strong sense of reciprocity and advancing the public interest, social capital could help encourage people to place more value in the public benefits of vaccination and increase vaccination coverage. Conversely, if networks are robust but they tend to channel information doubting the effectiveness or safety of vaccines or if they foster distrust of medical and educational authorities, they could deter vaccination.

In the models studying variation in vaccination and exemption rates in California schools, social capital appears to have a detrimental effect on vaccine coverage. The three-quarter percentage point increase in exemptions associated with a standard deviation increase in social capital represents a substantial 22.4% increase over the average school exemption rate, which is only 3.3%. The decrease of 0.49 percentage points in MMR vaccination rates is a 6.0% decrease in the number of undervaccinated children. The declines for other vaccines are 8.7% for DTaP, 10.0% for polio, 15.7% for hepatitis B, and 20.8% for varicella. At least in California, the relationship between social capital and vaccination rates is not one that favors better vaccine coverage.

Turning to the national results, states that that do not have personal belief exemption policies display different tendencies. Among these states, a one standard deviation increase in the state's social capital score is associated with an 11.1% improvement in the rate of MMR vaccines, an 11.3% improvement in the rate of DTaP vaccines, and a 17.1% improvement in the rate of polio vaccines. It is important to note that these vaccines that are positively and significantly related to social capital (MMR, DTaP, and polio) are also the ones that have shown the most precipitous declines in coverage in recent years (see Figure 9). Because these are the vaccines that parents are increasingly likely to forego, it is not surprising that these vaccines were the ones that covaried most with social capital.

These seemingly beneficial effects from social capital are flipped for states that allow personal belief exemptions. Combining the baseline social capital coefficient with the interaction coefficient, the results indicate that the overall effect of social capital in PBE states is negative for MMR and DTaP vaccines—0.71 percentage points less coverage for MMR and 0.2

percentage points less coverage for DTaP for a one standard deviation increase in a state's social capital score.

One way to approach these findings is to consider that a state's personal belief exemption policy is not randomly assigned. Like most policies, it is the result of public decision-making and likely reflects the preferences of a state's residents. In other words, states have exemption policies because more citizens demand their children have the option of being exempt. It is probably a fair assumption that, in states allowing PBEs, parents have a higher baseline level of doubt about vaccine efficacy and safety. Some number of these parents also probably subscribes to exaggerated or dubious claims about dangers and side effects of vaccines.

Therefore, by interacting the PBE policy with social capital, these state-level models could be picking up the yin and yang of social capital. Social capital operates as originally hypothesized—by increasing vaccine compliance—in states without strong preferences for vaccine exemption. Higher degrees of social capital lead to more socially efficient outcomes when the ideas and values being encouraged are not anti-vaccine. This result provides evidence for social capital as typically conceived—that is, a force for positive outcomes emerging from norms of trust and reciprocity.

However, the darker side of social capital is also evident in these findings. In states that value the option to forego vaccines (presumably due to negative opinions of vaccines), increased social capital leads to worse vaccination outcomes. This conclusion supports the notion that more social capital can spread misinformation and a propensity to question medical recommendations and conventions. In this context, where vaccine skepticism is already high, the networks of social capital can exacerbate that skepticism, with the effect being fewer parents deciding to fully vaccinate their children.

California is one such state where suspicion of vaccines and personal belief exemptions coexist. In 2014, California ranked 34th and 37th among states for its vaccination coverage for MMR and DTaP, respectively. Smith, Chu, and Barker (2004) find that California had more geographic pockets of completely unvaccinated (as opposed to the more common situation of a child being undervaccinated) children than any other state. Clearly, California is a state with an undercurrent of strong vaccine skepticism. In this light, the results from the California schools models are less surprising. It is quite possible under those conditions that social capital exacerbates low vaccination rates rather than improving them.

Finally, there are also direct implications for state policymakers found in these results. Lenient vaccine exemption policies decrease state vaccination coverage. Policymakers wanting to expand immunization coverage should consider abandoning or tightening personal belief exemptions and possibly religious exemptions as well.

Limitations

This study has several limitations that should be considered when interpreting its results. First, while there were statistically significant relationships estimated between social capital and vaccination outcomes, these cannot be determined as causal under the current econometric models. Specifically, the social capital variable is potentially endogenous. People choose the types of communities they live in and they themselves help to produce social capital through their actions and connections with others. People also decide whether to vaccinate their children according to CDC and state recommendations. It is possible that some unobserved, omitted variable is related to both social capital and the error term and is biasing the results. Establishing a firm causal relationship between social capital and vaccination decisions would require another

approach to isolate the direct effect of social capital, such as a natural experiment or an instrumental variable, neither of which were immediately available for the present study.

A second limitation is the use of a state-level measure of social capital to study a concept that is more appropriately applied to a local context. The California schools models are able to leverage more local-level variation with a county-level social capital index; however, as previously discussed, these conclusions are specific to California and may lack generalizability. In very recent years, more states have begun to publish county-, district-, or school-level vaccination rates. When more of these data are readily available, it may be possible to expand the analysis to a wider number of states at a local-level.

Finally, while the county-level social capital index has the advantage of adapting to local variations in community characteristics, the state-level index is potentially more valid for other reasons. Key variables used in the factor analysis that generated these indices were only available at the state-level. These included measures of trust, contact with neighbors, and civic participation. Another explanation for why divergent results were obtained from the California models and the state-level models is that the state-level social capital index has more construct validity and captures more important aspects of social capital.

Conclusions

All states have established vaccination standards as a precondition for school enrollment; however, states also have a range of exemptions that provide ways for parents to avoid getting their children in full compliance with recommended vaccine doses. As vaccination rates continue to dip below target levels, exposing vulnerable individuals to dangerous diseases, the ability to depend on parents to vaccinate their children becomes more imperative.

A parent's vaccination decision process is sometimes complicated by fears that they might be putting their child in danger by immunizing her. Conversely the perceived benefits of vaccination may seem small in comparison. Most of the diseases prevented by today's vaccines are not a part of parents' lived experiences. They have never known individuals to die of tetanus or become paralyzed by polio. Additionally, society's broader immunity provides significant (though not complete) protection for an unvaccinated child. In short, vaccination is not a foregone conclusion for many of today's parents; they seem to be weighing the pros and cons of vaccination more carefully than in the past. In the cost-benefit analysis of vaccinating a child, one of the benefits is strengthening a community's "herd immunity" and protecting others from infectious disease.

However, this public benefit may be undervalued from a societal perspective in a parent's decision-making process if the parent is lives in a community with weak social ties between people, low trust, or few shared norms. These characteristics—networks, trust, and shared norms—are the hallmarks of what researchers refer to as social capital. Communities that rank high on social capital are hypothesized to be able to engender cooperation in ways that can overcome collective action problems and help produce activities that generate positive externalities. Vaccination is a classic example of a behavior with clear positive externalities; therefore, this study has examined the relationship between vaccination rates and community social capital.

The results do not present a clear-cut conclusion. While expectations may be that higher social capital consistently improves vaccination outcomes, the actual results were more nuanced. Looking at school-level kindergarten vaccination rates from California, schools in counties with

higher scores on a social capital index have uniformly worse vaccination rates. They also have significantly higher use of personal belief exemptions.

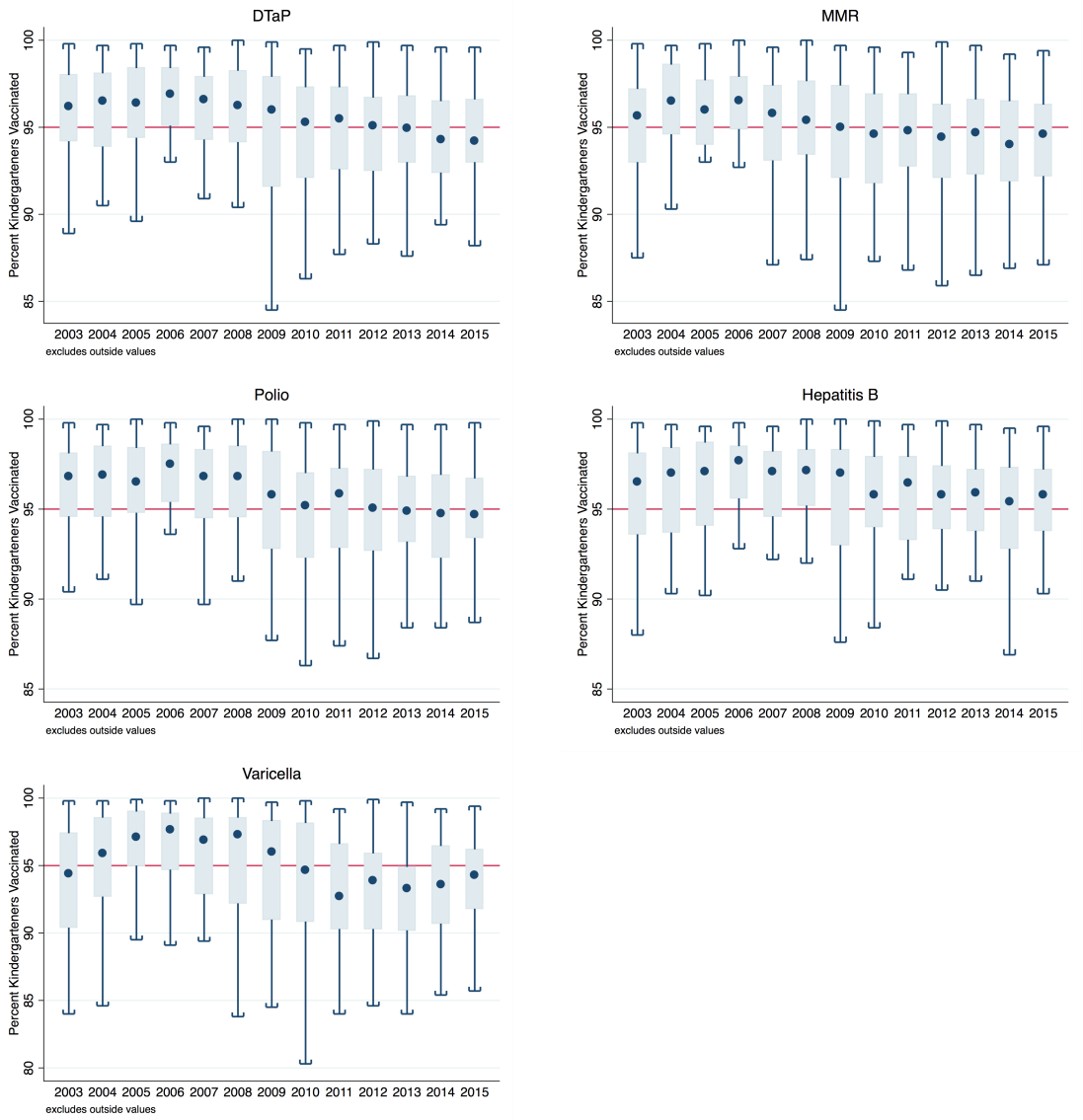
Conversely, analyses using state-level vaccination coverage data from the CDC show that in states without personal belief exemption policies, more social capital is associated with higher vaccination rates for MMR, DTaP, and polio vaccines. Indeed, these vaccines are the ones that have shown declines in recent years as parents opt out of the recommended vaccine schedule. Therefore, these positive results suggest that social capital can be beneficial for improving vaccine coverage. However, in states that allow personal belief exemptions (of which California was one of 20 during this study period), social capital was correlated with decreased vaccine coverage.

Together, these findings suggest that social capital can play a positive or negative role with respect to vaccinations. States with personal belief exemption policies are likely to have stronger underlying preferences for refusing certain vaccines, and those preferences are likely motivated in part by perceived dangers related to vaccine safety. This study supports the idea that, in places where suspicion about vaccines thrives, social capital can serve to magnify the beliefs and norms that discourage vaccination. In places where such fears and misinformation have less purchase, social capital can increase vaccination coverage by affording more value to the public benefits of vaccination.

These conclusions point to a need for public health officials to engage with informal networks, especially in communities with low vaccination rates. Efforts to contradict misinformation and impress upon people the public health imperative of a sufficiently immunized population may be more effective if they are channeled through these networks rather than through school or medical officials.

This study is not without limitations. Future research will be able to analyze social capital at a more local-level across many states as more states release data on vaccine coverage rates. Also, social capital is a potentially endogenous variable; therefore, it is not possible to make a definitive causal claim that social capital directly has an impact on parent's vaccination decisions. However, this initial look suggests that community characteristics such as the degree of interconnectedness and trust are related to vaccination decisions. When government mandates are not enough to address declining vaccine coverage, it is important to recognize other avenues that may help influence choices so that communities are sufficiently protected against preventable infectious diseases.

Tables and Figures



Notes: Red line at 95% indicates the target coverage rate set by the Centers for Disease Control and Prevention. DTaP = diphtheria-tetanus-pertussis; MMR = measles-mumps-rubella
Source: Centers for Disease Control and Prevention Annual School Assessment Reports

Figure 9: Distribution of State Kindergarten Vaccination Rates, 2003-2015

Table 11: Variables Used in Factor Analysis for Social Capital Indices

Measure	County-Level Source	State-Level Source
Percent of Population that Volunteered	N/A	CPS Volunteer Supplement
Hours Volunteered Per Capita	N/A	CPS Volunteer Supplement
Percent Who Report Trusting Most Neighbors	N/A	CPS Civic Engagement Supplement
Percent Who Report Talking to Neighbors At Least a Few Times Per Week	N/A	CPS Civic Engagement Supplement
Percent Who Report that Neighbors Do Favors At Least a Few Times Per Week	N/A	CPS Civic Engagement Supplement
Percent Who Report Always Voting in Local Elections	N/A	CPS Civic Engagement Supplement
Percent Who Served on Local Committees	N/A	CPS Civic Engagement Supplement
Percent Who Participated in a Civic Group	N/A	CPS Civic Engagement Supplement
Number of Nonprofit Organizations Per Capita	National Center for Charitable Statistics	National Center for Charitable Statistics
Reported Nonprofit Revenue Per Capita (adjusted to 2015$)	National Center for Charitable Statistics	National Center for Charitable Statistics
Number of Civic Groups Per Capita (defined as NAICS codes 81321, 713990, 813110, and 813410	Census County Business Patterns	Census County Business Patterns
Employment by Civic Groups Per Capita (defined as NAICS codes 81321, 713990, 813110, and 813410	Census County Business Patterns	Census County Business Patterns
Percent of Population with Commute > 45 min.	ACS 5-year estimates	ACS 1-year estimates
Percent of Population that Moved from Outside the County in the Past Year	ACS 5-year estimates	ACS 1-year estimates
Percent of Occupied Homes that are Owner-Occupied	ACS 5-year estimates	ACS 1-year estimates
Violent Crime Rate	California Department of Justice	Federal Bureau of Investigation Uniform Crime Reporting (UCR)
Property Crime Rate	California Department of Justice	Federal Bureau of Investigation Uniform Crime Reporting (UCR)
Voter Turnout in Most Recent Presidential Election	California Secretary of State plus eligible voter data from Census Redistricting Data Program	United States Election Project
Dissimilarity Index	ACS 5-year estimates (Census Tract- and County-Level)	ACS 5-year estimates (County- and State-Level)

Notes: ACS = American Community Survey; CPS = Current Population Survey

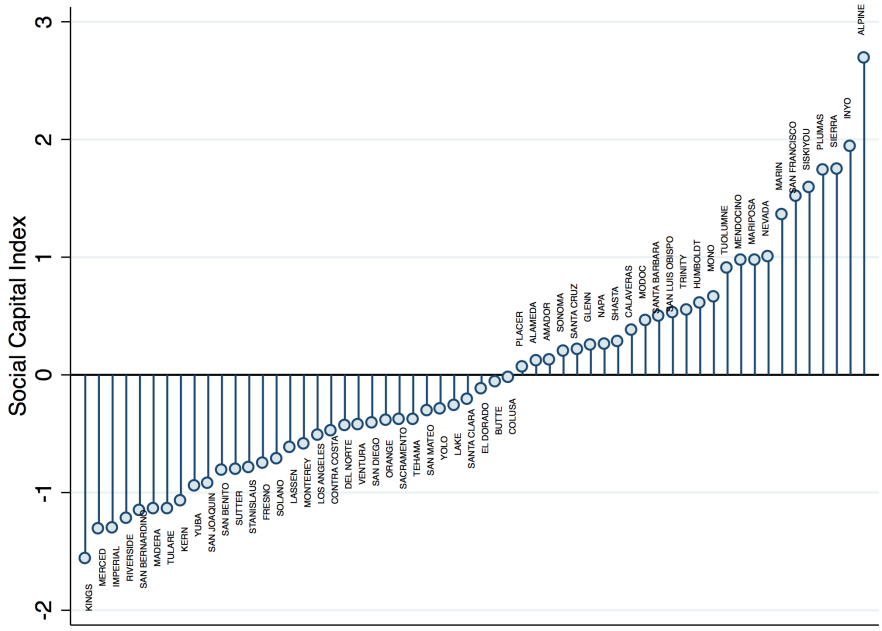


Figure 10: Average Social Capital Values by California Counties, 2010-2015

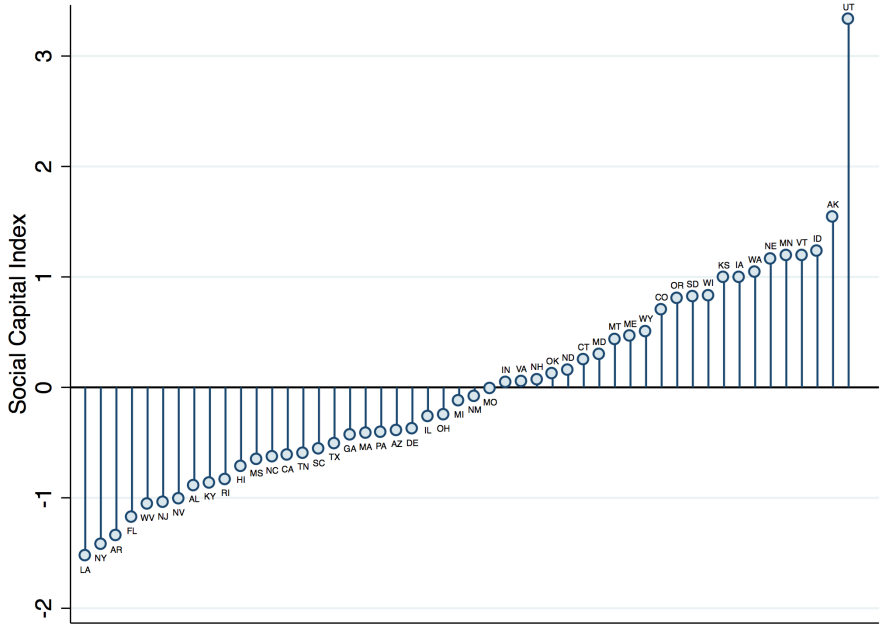


Figure 11: Average Social Capital Values by States, 2005-2015

Table 12: Summary Statistics for California Schools

	Variable Mean	
% with Medical Exemption	0.195	(1.014)
% with Philosophical Belief Exemption	3.342	(7.576)
% UTD on 5-Vaccine Series	89.64	(13.51)
% UTD on MMR	91.89	(11.64)
% UTD on DTaP	91.82	(11.57)
% UTD on Polio	92.03	(11.45)
% UTD on Varicella	94.87	(9.313)
% UTD on Hepatitis B	94.43	(9.419)
Social Capital Index	-0.503	(0.566)
Private School	0.201	(0.401)
Metropolitan Area	0.971	(0.167)
Racial Diversity (HHI)	0.516	(0.216)
Gini Index	0.464	(0.0237)
Median Family Income (2015$)	7.556	(2.823)
% Free/Reduced Meals	0.532	(0.319)
% Uninsured Children	7.547	(1.965)
Primary Care Physicians (per 100,000)	78.17	(22.93)
% Married Families	69.98	(8.885)
% White	25.92	(23.94)
% Black	5.373	(9.190)
% Hispanic	51.42	(28.95)
% Asian	8.094	(12.73)
% Other Race	6.634	(6.835)
% Less Than HS Diploma	19.29	(11.18)
% HS Graduate	21.14	(5.733)
% with Some College	29.74	(6.425)
% College Graduate	29.83	(15.48)
Observations	41822	

Note: Standard deviations in parentheses. UTD = up-to-date; MMR = measles-mumps-rubella; DTaP = diphtheria-tetanus-pertussis; HS = high school; HHI = Herfindahl-Hirschman Index

Table 13: Summary Statistics for State Models, Full Sample and by Personal Belief Exemption Policies

	Full Sample		No PBE		Allows PBE	
Percent Kindergarteners with MMR Vaccine	94.46	(3.538)	95.23	(2.943)	93.16	(4.053)
Percent Kindergarteners with DTaP Vaccine	94.86	(3.657)	95.50	(3.282)	93.74	(4.000)
Percent Kindergarteners with Polio Vaccine	95.18	(3.580)	95.77	(3.132)	94.17	(4.047)
Percent Kindergarteners with Hepatitis B Vaccine	95.67	(5.281)	95.73	(6.212)	95.56	(3.236)
Percent Kindergarteners with Varicella Vaccine	93.14	(10.72)	93.45	(12.32)	92.57	(6.863)
Social Capital Index	0.00	(0.969)	-0.165	(0.824)	0.291	(1.127)
Personal Belief Exemption	0.355	(0.479)	0	(0)	1	(0)
Religious Exemption	0.882	(0.322)	0.909	(0.288)	0.834	(0.373)
Median Family Income (2015$)	6.796	(1.061)	6.904	(1.196)	6.599	(0.718)
Poverty Rate for Families with Children	16.30	(4.422)	16.30	(4.743)	16.31	(3.782)
Gini Index	0.452	(0.0232)	0.454	(0.0257)	0.448	(0.0172)
% Families with Children That are Married	67.55	(5.083)	66.84	(5.271)	68.83	(4.454)
% without HS Diploma	12.85	(3.480)	13.06	(3.329)	12.45	(3.716)
% with HS Diploma	29.63	(4.214)	29.71	(3.771)	29.48	(4.925)
% with Some College	29.32	(4.093)	28.67	(4.131)	30.50	(3.754)
% with College Degree	28.21	(5.832)	28.56	(6.472)	27.56	(4.380)
Primary Care Physicians (per 100,000)	86.71	(20.97)	87.31	(22.90)	85.62	(16.89)
Uninsured Rate, 18 and Under	8.030	(3.632)	7.886	(3.657)	8.291	(3.581)
% White	71.01	(16.07)	69.01	(16.46)	74.63	(14.71)
% Black	10.87	(10.94)	12.75	(12.01)	7.452	(7.572)
% Asian	3.629	(5.365)	3.994	(6.319)	2.965	(2.817)
% Hispanic	8.258	(9.353)	7.959	(8.571)	8.804	(10.63)
% Other Race	6.273	(7.626)	6.296	(7.648)	6.231	(7.603)
Racial Diversity (HHI)	0.583	(0.159)	0.563	(0.156)	0.620	(0.157)
Observations	561		362		199	

Notes: Standard deviations in parentheses. PBE = Personal Belief (or, Philosophical) Exemption; MMR = measles-mumps-rubella; DTaP = diphtheria-tetanus-pertussis; HS = high school; HHI = Herfindahl-Hirschman Index

Table 14: OLS Coefficients Predicting School Rates of Personal Belief and Medical Exemptions and Being Up-to-Date on All Vaccines, Year Fixed Effects

	(1) **Medical Exemptions**	(2) **Personal Belief Exemptions**	(3) **UTD All Vaccines**
Standardized Social Capital Index	-0.028	0.75**	-0.36
	(-1.52)	(6.01)	(-1.57)
Private School	0.0052	1.48**	-2.93**
	(0.31)	(13.00)	(-14.14)
Metropolitan Area	0.0013	-1.84**	4.06**
	(0.03)	(-6.73)	(8.13)
Racial Diversity (HHI)	-0.19**	4.66**	-7.26**
	(-4.68)	(17.14)	(-14.63)
Gini Index	-0.67*	-8.04**	-38.3**
	(-2.41)	(-4.25)	(-11.08)
Median Family Income (in 10,000 2015$)	0.014**	-0.42**	1.35**
	(2.87)	(-12.84)	(22.50)
% Free/Reduced Meals	-0.087**	-1.52**	0.31
	(-3.12)	(-8.07)	(0.91)
% Uninsured Children	0.018**	0.22**	-0.057
	(3.55)	(6.44)	(-0.90)
Primary Care Physicians (per 100,000)	0.00052	0.0014	-0.0093
	(0.96)	(0.38)	(-1.40)
% Married Families	-0.0024**	0.011	0.033**
	(-2.60)	(1.80)	(2.93)
Constant	0.74**	19.8**	67.7**
	(4.15)	(16.40)	(30.66)
Race/Ethnicity Controls	Yes	Yes	Yes
Educational Attainment Controls	Yes	Yes	Yes
Year Dummies	Yes	Yes	Yes
F-Statistics	17	445	338
Observations	41800	41800	41800

Notes: Required vaccines for kindergarten enrollment in California are 5 doses of diphtheria-tetanus-acellular pertussis (DTaP) vaccine, 2 doses of measles-mumps-rubella (MMR) vaccine, 4 doses of polio vaccine, 3 doses of Hepatitis B vaccine, and 1 dose of varicella vaccine. All specifications also include the following controls: percents of population over 25 years old with less than high school degree, high school graduates, and some college; percents of enrolled kindergarteners that are Hispanic and non-Hispanic black, Asian, and other races; and year dummies. UTD = up-to-date; HHI = Herfindahl-Hirschman Index

* $p<0.05$, ** $p<0.01$

Table 15: OLS Coefficients Predicting School Rates of Being Up-to-Date on Individual Vaccines, Year Fixed Effects

	(1) **MMR**	(2) **DTaP**	(3) **Polio**	(4) **Hepatitis B**	(5) **Varicella**
Standardized Social Capital Index	-0.49*	-0.71**	-0.80**	-0.88**	-1.06**
	(-2.50)	(-3.64)	(-4.13)	(-5.59)	(-6.80)
Private School	-3.15**	-2.45**	-2.58**	-1.24**	-1.71**
	(-17.65)	(-13.78)	(-14.70)	(-8.66)	(-12.09)
Metropolitan Area	3.54**	3.17**	3.17**	2.70**	2.80**
	(8.24)	(7.39)	(7.52)	(7.86)	(8.24)
Racial Diversity (HHI)	-6.67**	-6.69**	-6.89**	-5.52**	-5.75**
	(-15.65)	(-15.71)	(-16.43)	(-16.19)	(-17.00)
Gini Index	-22.1**	-19.6**	-19.6**	-6.65**	-7.53**
	(-7.44)	(-6.62)	(-6.70)	(-2.80)	(-3.20)
Median Family Income (in 10,000 2015$)	1.11**	1.09**	1.10**	0.81**	0.77**
	(21.56)	(21.10)	(21.66)	(19.50)	(18.77)
% Free/Reduced Meals	0.75*	0.22	0.58*	1.73**	1.56**
	(2.53)	(0.74)	(2.01)	(7.32)	(6.63)
% Uninsured Children	-0.095	-0.041	-0.062	-0.18**	-0.13**
	(-1.75)	(-0.76)	(-1.15)	(-4.13)	(-3.10)
Primary Care Physicians (per 100,000)	-0.0051	-0.0045	-0.0053	-0.0075	-0.0018
	(-0.89)	(-0.80)	(-0.95)	(-1.66)	(-0.40)
% Married Families	0.018	0.025*	0.020*	0.0033	-0.0032
	(1.88)	(2.53)	(2.03)	(0.43)	(-0.42)
Constant	70.7**	69.2**	69.9**	72.8**	75.4**
	(37.27)	(36.53)	(37.48)	(47.94)	(50.10)
Race/Ethnicity Controls	Yes	Yes	Yes	Yes	Yes
Educational Attainment Controls	Yes	Yes	Yes	Yes	Yes
Year Dummies	Yes	Yes	Yes	Yes	Yes
F-Statistics	348	328	348	400	387
Observations	41800	41800	41800	41800	41800

Notes: Required vaccines for kindergarten enrollment in California are 5 doses of diphtheria-tetanus-acellular pertussis (DTaP) vaccine, 2 doses of measles-mumps-rubella (MMR) vaccine, 4 doses of polio vaccine, 3 doses of Hepatitis B vaccine, and 1 dose of varicella vaccine. All specifications also include the following controls: percents of population over 25 years old with less than high school degree, high school graduates, and some college; percents of enrolled kindergarteners that are Hispanic and non-Hispanic black, Asian, and other races; and year dummies. HHI = Herfindahl-Hirschman Index
* p<0.05, ** p<0.01

Table 16: OLS Coefficients Predicting State Kindergarten Vaccination Coverage Excluding Utah, Year Fixed Effects

	(1) **MMR**	(2) **DTaP**	(3) **Polio**	(4) **Hepatitis B**	(5) **Varicella**
Standardized Social Capital Index	0.62*	0.59*	0.84**	0.19	-3.22**
	(1.94)	(1.71)	(2.45)	(0.32)	(-2.52)
Personal Belief Exemption	-2.30***	-1.89***	-1.78***	0.21	-0.035
	(-7.80)	(-5.87)	(-5.60)	(0.37)	(-0.03)
Personal Belief Exemption X Standardized Social Capital Index	-1.33***	-0.76**	-0.57	0.43	0.36
	(-3.93)	(-2.07)	(-1.56)	(0.81)	(0.27)
Religious Exemption	-2.73***	-2.05***	-1.72***	-2.04**	-3.37**
	(-6.15)	(-4.26)	(-3.60)	(-2.50)	(-1.99)
Median Family Income (in 10,000 2015$)	1.20***	1.20**	1.44***	1.86**	1.76
	(2.68)	(2.48)	(2.97)	(2.27)	(1.02)
Poverty Rate for Families with Children	0.20*	0.16	0.18	0.077	0.83*
	(1.69)	(1.19)	(1.40)	(0.34)	(1.71)
Gini Index	22.4	20.0	33.2**	-2.01	-125.1**
	(1.46)	(1.20)	(2.01)	(-0.07)	(-2.05)
% Families with Children That are Married	-0.15*	-0.18**	-0.11	-0.012	0.20
	(-1.87)	(-2.03)	(-1.25)	(-0.08)	(0.60)
Primary Care Physicians (per 100,000)	0.045**	0.054**	0.053**	0.0069	-0.032
	(2.20)	(2.41)	(2.41)	(0.17)	(-0.38)
Uninsured Rate, 18 and Under	-0.0081	0.11	0.11	-0.26	-0.54*
	(-0.11)	(1.31)	(1.32)	(-1.63)	(-1.75)
Racial Diversity (HHI)	3.60	9.57**	9.91**	-12.6	-12.1
	(0.88)	(2.15)	(2.24)	(-1.54)	(-0.71)
Constant	64.0***	65.2***	43.2***	72.1***	155.9***
	(4.24)	(3.99)	(2.66)	(2.62)	(2.66)
Race/Ethnicity Controls	Yes	Yes	Yes	Yes	Yes
Educational Attainment Controls	Yes	Yes	Yes	Yes	Yes
Year Dummies	Yes	Yes	Yes	Yes	Yes
F-Statistics	10	7	7	2	2
Observations	510	505	510	472	431

Notes: Recommended vaccines for kindergarten enrollment are 5 doses of diphtheria-tetanus-pertussis (DTaP) vaccine, 2 doses of measles-mumps-rubella (MMR) vaccine, 4 doses of polio vaccine, 3 doses of Hepatitis B vaccine, and 1 dose of varicella vaccine. All specifications also include the following controls: percents of population over 25 years old with less than high school degree, high school graduates, and some college; percents of population that are Hispanic and non-Hispanic black, Asian, and other races; and year dummies. Observations from Utah are excluded. HHI = Herfindahl-Hirschman Index

* p<0.1, ** p<0.05, *** p<0.01

CHAPTER 5

CONCLUSION

The policy questions in these three essays will not soon be obsolete. If anything, pharmaceutical policies have gained more public attention and scrutiny in recent years. This is certainly the case for drug pricing. A series of drug pricing "scandals" have gained widespread attention, including issues concerning the $84,000 hepatitis C drug Sovaldi (Armstrong, 2014), the steep price increases for the allergy rescue injection EpiPen (Willingham, 2016), and the public chastising of "Pharma Bro" Martin Shkreli (Sanneh, 2016). The Kaiser Family Foundation conducts surveys to track public opinion on a wide range of issues related to health care. In a recent poll, 77% of Americans answered that they believed drug prices were "unreasonable," an increase of 72% over responses from the previous year (Kirzinger, Wu, & Brodie, 2016).

When more than three-quarters of Americans believe something, politicians will not be far behind. Indeed, then-President-elect Donald J. Trump said during a press conference on January 11, 2017, that drug companies were "getting away with murder," and he promised that the government would "start bidding" on drugs (Humer & Campos, 2017). Presumably, he was advocating against the noninterference clause in Medicare Part D and implying that CMS should have the ability to negotiate directly with pharmaceutical manufacturers on drug prices.

The findings in the essay on protected classes, however, support the idea that the current system, when it pits private insurers and drug manufacturers against each other in competitive negotiations, is effective at holding down drug prices. Other studies reach the same conclusion

(Frank & Newhouse, 2008). Rather than upending a system that has functioned successfully for over a decade, policymakers would be better served to look at the instances where competitive negotiations do not lead to competitive pricing. As the current experience with Sovaldi illustrates, one such instance is when expensive and innovator drugs enter the market without any competition. The other primary instance is in the case of protected classes, where Medicare policies shield the drugs from the full force of competition.

I find that the protected class policy substantially increases total expenditures for the drugs in these six classes. If lawmakers maintain their focus on drug prices and attempt to make changes to Medicare pricing policies, changes to the protected class policy is one of the key ways to have "bang for the buck" and yield big results. However, what will be interesting to see is if U.S. policymakers have the fortitude to make difficult decisions. For example, will they uphold a commitment to cost containment by refusing access to expensive drugs that are demanded by patients? While such actions are more common in Western Europe and Canada, the U.S.—the country that spent the summer of 2009 arguing about "death panels"—has a long tradition prioritizing unfettered access to health care interventions over affordability concerns (Sorenson, 2010). As in many areas of health policy, and indeed, public policy more generally, any significant change entails the kinds of trade-offs and changes to the status quo that make lawmakers uncomfortable. Whether or not real policy shifts occur will depend in large part on lawmakers' tolerance for this type of discomfort.

Drug pricing is not the only issue in this work that is leading headlines. Another recent Kaiser poll indicates that 66% of Americans believe that prescription opioid abuse is a very serious issue, putting opioid drug abuse on approximately the same level of concern as diabetes

and heart disease and more serious than obesity (Kaiser Family Foundation, 2016). The same poll finds that 49% of respondents say they know someone addicted to prescription painkillers.

At the end of 2016, Congress passed the 21st Century Cures Act, a large law relating to many aspects of health care that devoted $1 billion for state grants over two years to combat opioid abuse and addiction ("21st Century Cures Act," 2016). While this is an impressive commitment to addressing the opioid crisis, it remains to be seen how states will utilize the funds in effective ways. Multiple studies have found that current policies have had little or no effect on opioid use and abuse (Meara et al., 2016). My essay on prescription drug monitoring programs has similar findings. The only clear-cut impact of PDMPs on prescribing I observe is in relation to drugs containing oxycodone, and this effect size is quite small when compared with the scale of current opioid use. Meanwhile, as opioid addiction continues to expand, many prescription abusers have shifted to cheaper and easier-to-find heroin (Muhuri et al., 2013; Rudd, Aleshire, et al., 2016). Clearly, new solutions are needed.

When policymakers encounter a problem as seemingly intractable as the opioid epidemic, one avenue they may neglect to consider is community engagement. Nevertheless, some policy objectives are not achievable without buy-in and even active participation from policy targets (Alford & O'Flynn, 2012). The need for cooperation from opioid prescribers is on example of this. Low utilization of PDMPs is an indication that physicians are still not convinced of their role to play in reducing opioid abuse (Kreiner et al., 2013). Vaccines are another example of health policy where public participation—in this case, by parents—is necessary for successful outcomes.

The final essay of this work explored the role that community social capital has to play in public health. Social capital has been billed by some researchers as a panacea for overcoming

many kinds of difficult social problems (Portes, 2014). My results suggest caution in heralding social capital as universal force for positive change. Social capital in this context was only positively related to vaccine coverage rates in states without personal belief exemptions.

Operating on the assumption that these are states that have lower baseline opposition to vaccines, I argue that social capital promotes the salience of the public value of vaccines and improves vaccination rates. However, in states with person belief exemption policies, social capital may work in the opposite direction by disseminating anti-vaccination norms and information. While further studies will be needed to bolster these conclusions, some lessons emerge. First, public health officials should not rely solely on school and medical authorities to spread information about the importance of vaccines and their safety and efficacy. Informal networks are influential, especially in an environment of increased skepticism toward experts and officials (Kim-Farley, 2017). Secondly, the benefits of social capital depend upon context. Under certain circumstances, robust community networks and norms can support adverse outcomes in lieu of positive ones.

In conclusion, the results found in these three essays support the notion that there are few silver bullets when it comes to complex policy choices. The policy arena is fraught with unintended consequences, public opposition, and underwhelming results. However, these barriers are not a reason for retrenchment in the scope of public action. In effect, they magnify the need for objective policy analysis to uncover the policy approaches that are successful and to identify and weight the trade-offs they entail.

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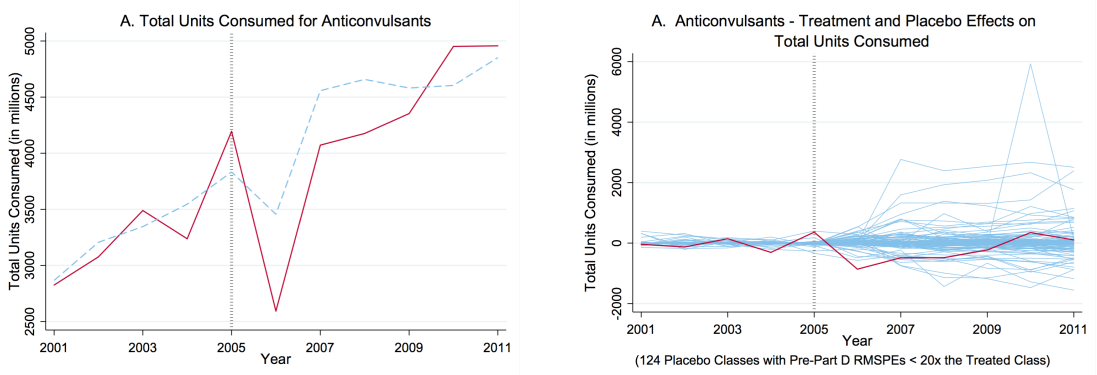
Zucht v. King, No. No. 84, 260 174 (Supreme Court 1922).

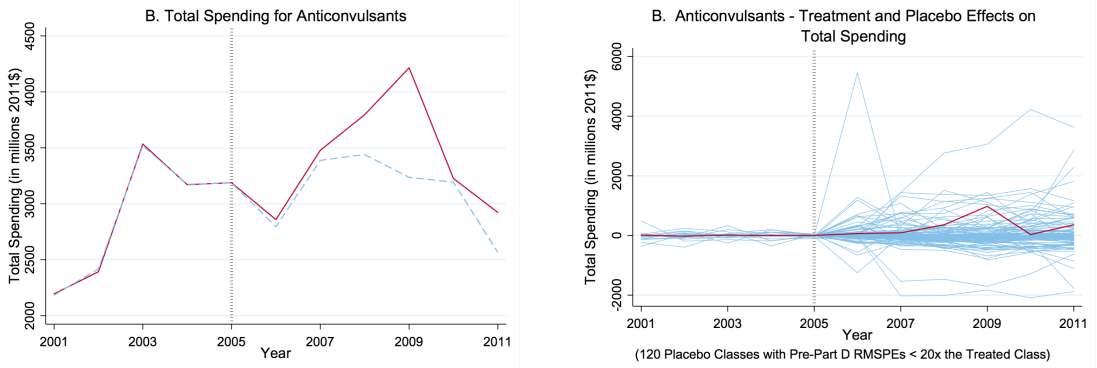
APPENDIX A

EFFECTS OF PROTECTION FOR THE ANTICONVULSANT CLASS AND PLACEBO EFFECTS



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 12: Effects of Protection on Drug Utilization for Anticonvulsants and Placebo Effects

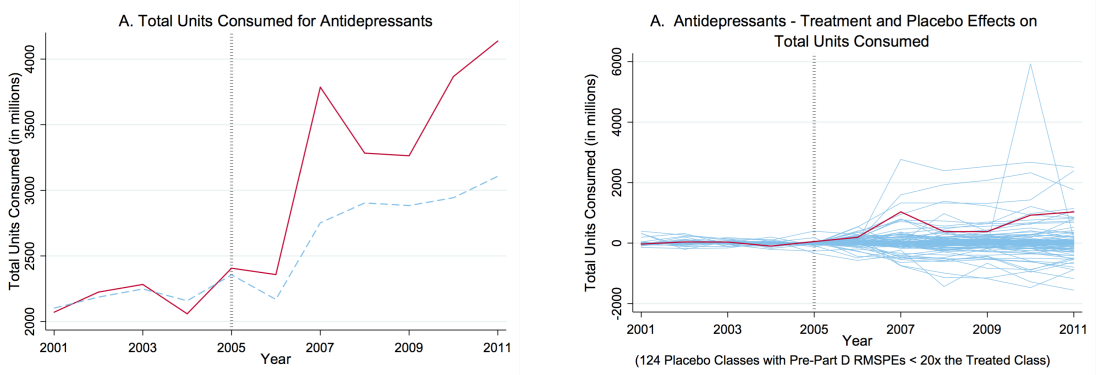


Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 13: Effects of Protection on Drug Expenditures for Anticonvulsants and Placebo Effects

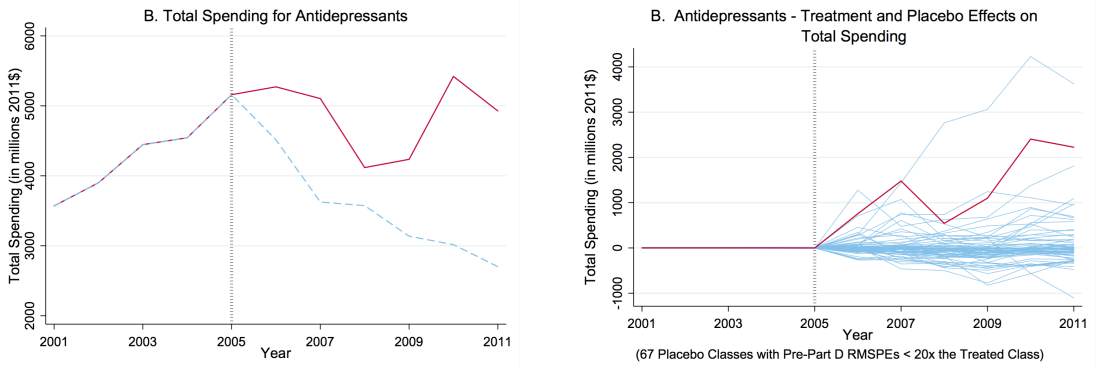
APPENDIX B

EFFECTS OF PROTECTION FOR THE ANTIDEPRESSANT CLASS AND PLACEBO EFFECTS



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 14: Effects of Protection on Drug Utilization for Antidepressants and Placebo Effects

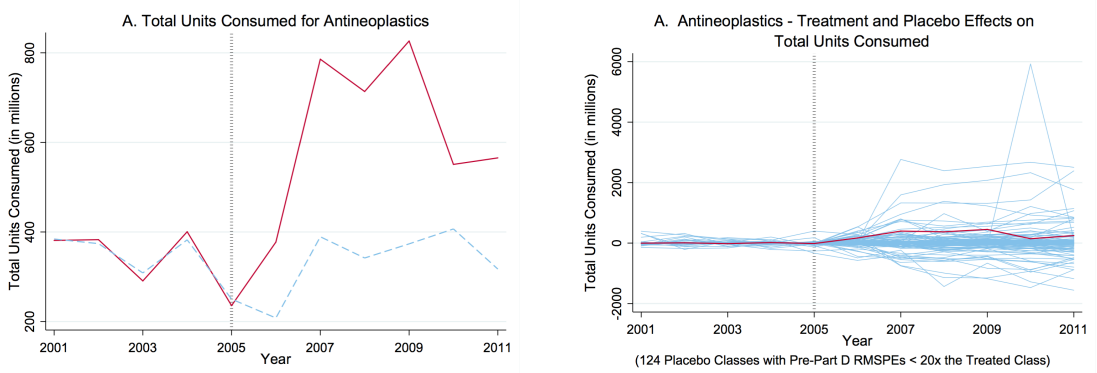


Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 15: Effects of Protection on Drug Expenditures for Antidepressants and Placebo Effects

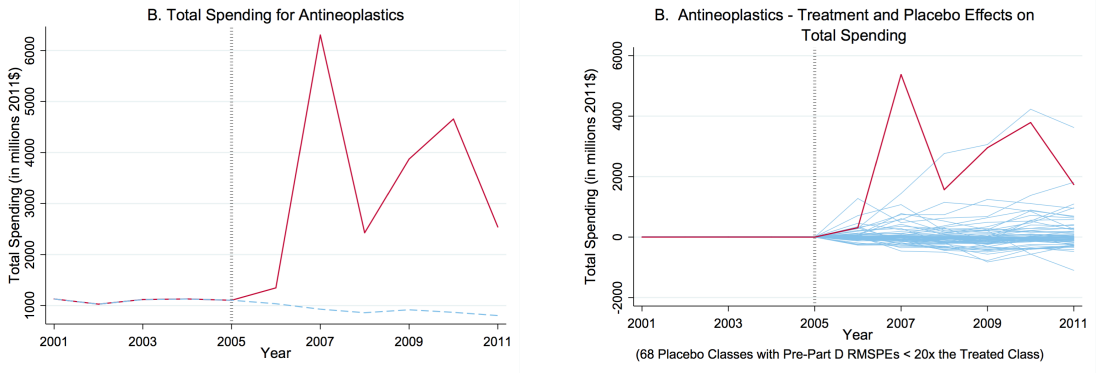
APPENDIX C

EFFECTS OF PROTECTION FOR THE ANTINEOPLASTIC CLASS AND PLACEBO EFFECTS



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 16: Effects of Protection on Drug Utilization for Antineoplastics and Placebo Effects

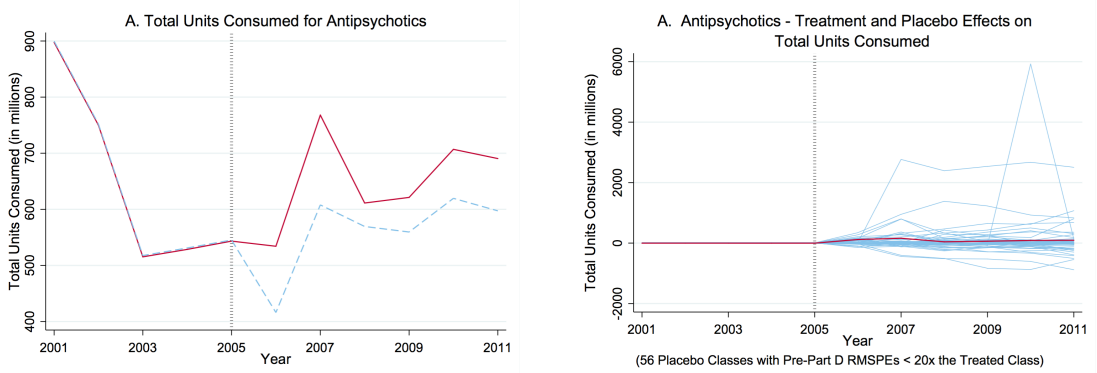


Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 17: Effects of Protection on Drug Expenditures for Antineoplastics and Placebo Effects

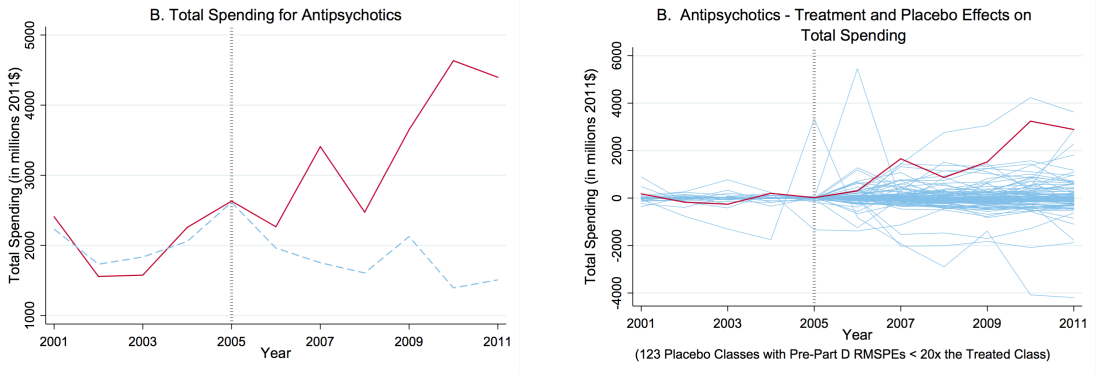
APPENDIX D

EFFECTS OF PROTECTION FOR THE ANTIPSYCHOTIC CLASS AND PLACEBO EFFECTS



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 18: Effects of Protection on Drug Utilization for Antipsychotics and Placebo Effects

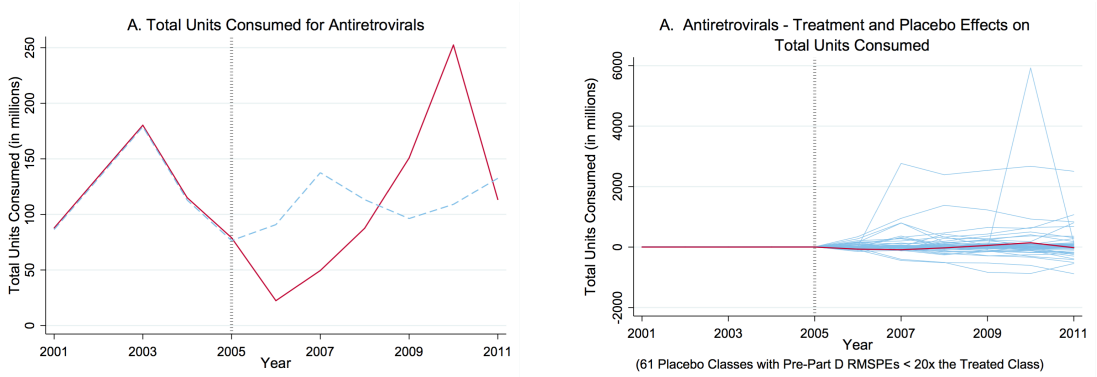


Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 19: Effects of Protection on Drug Expenditures for Antipsychotics and Placebo Effects

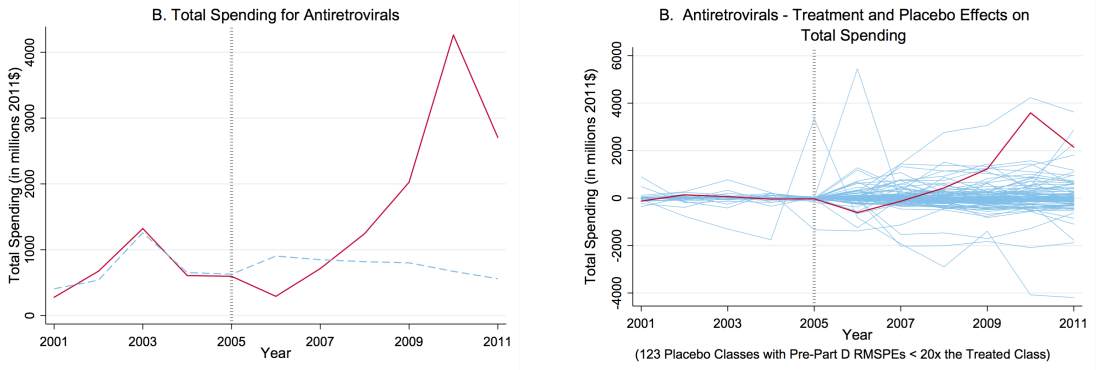
APPENDIX E

EFFECTS OF PROTECTION FOR THE ANTIRETROVIRAL CLASS AND PLACEBO EFFECTS



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 20: Effects of Protection on Drug Utilization for Antiretrovirals and Placebo Effects

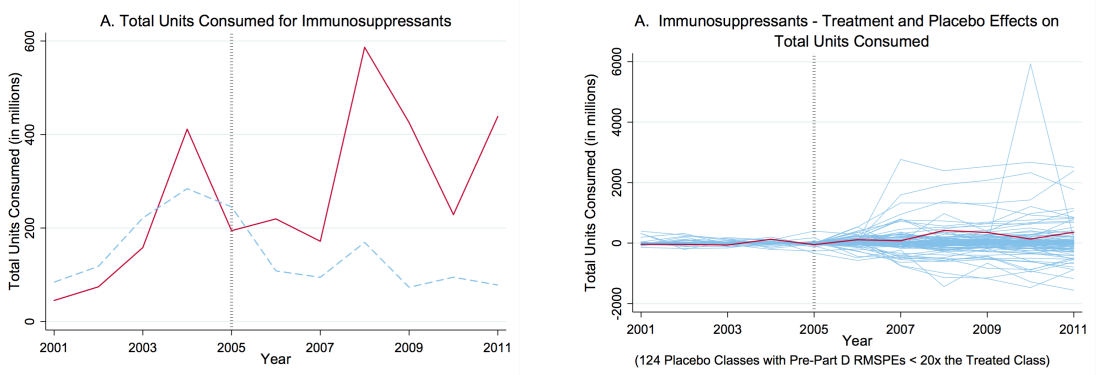


Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 21: Effects of Protection on Drug Expenditures for Antiretrovirals and Placebo Effects

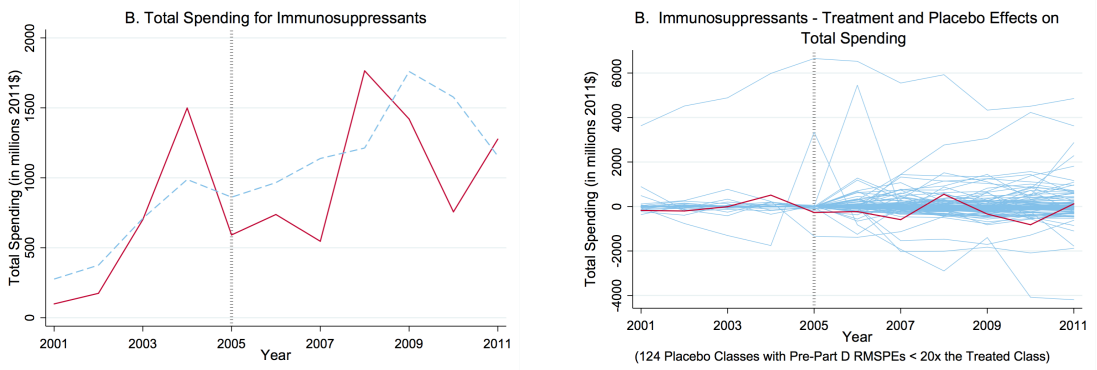
APPENDIX F

EFFECTS OF PROTECTION FOR THE IMMUNOSUPPRESSANT CLASS AND PLACEBO EFFECTS



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 22: Effects of Protection on Drug Utilization for Immunosuppressants and Placebo Effects



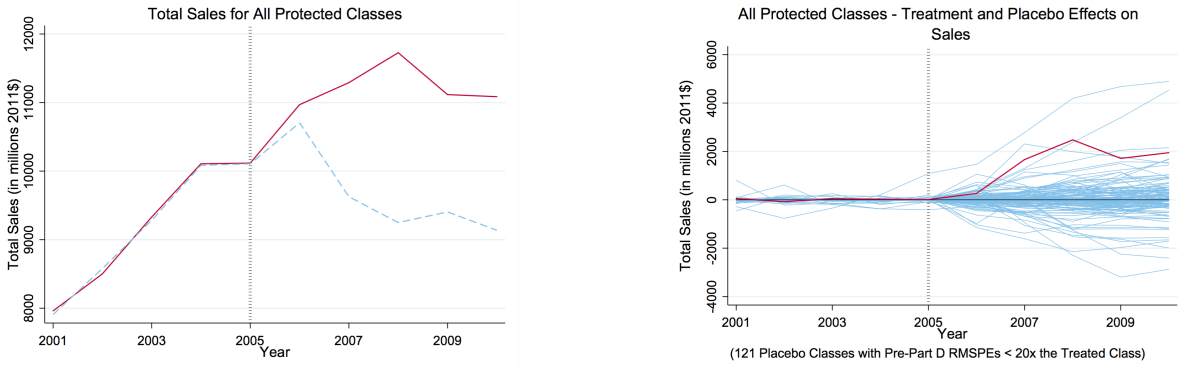
Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 23: Effects of Protection on Drug Expenditures for Immunosuppressants and Placebo Effects

APPENDIX G

EFFECTS OF PROTECTION FOR THE AGGREGATE PROTECTED CLASS AND

PLACEBO EFFECTS USING IMS HEALTH DATA



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 24: Effects of Protection on Drug Sales for the Aggregate Protected Class and Placebo Effects Using IMS Health Data

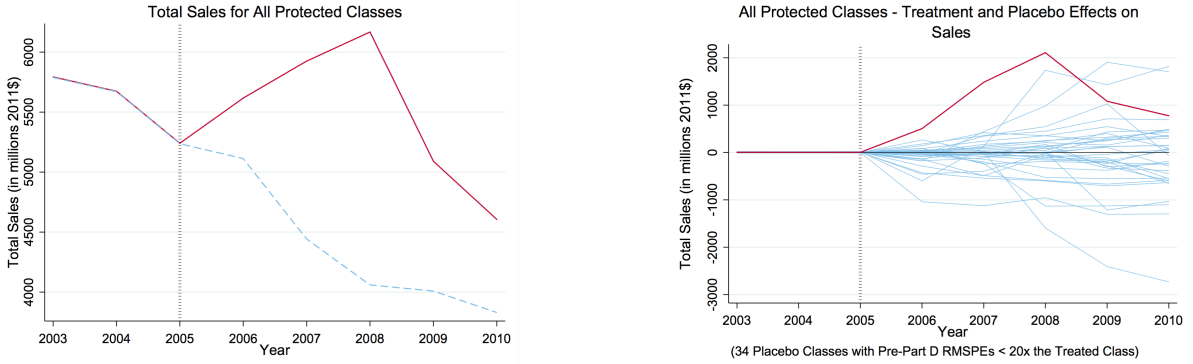
Table 17: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Drug Sales for the Aggregate Protected Class Using IMS Health Data

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2006-2010**
Tx Value	10969.42	11290.5	11727.03	11115.84	11085.55	11237.67
S.C. Value	10703.07	9626.51	9249.1	9404.37	9136.86	9623.98
Effect Size	**266.35**	**1663.99****	**2477.93*****	**1711.47***	**1948.69****	**1613.69****
P-Value	**(.189)**	**(.016)**	**(.008)**	**(.066)**	**(.049)**	**(.033)**
% Change	2.5%	17.3%	26.8%	18.2%	21.3%	16.8%

* p<0.10, ** p<0.05, *** p<0.01

APPENDIX H

EFFECTS OF PROTECTION FOR THE AGGREGATE PROTECTED CLASS AND PLACEBO EFFECTS USING VERISPAN VOTA DATA



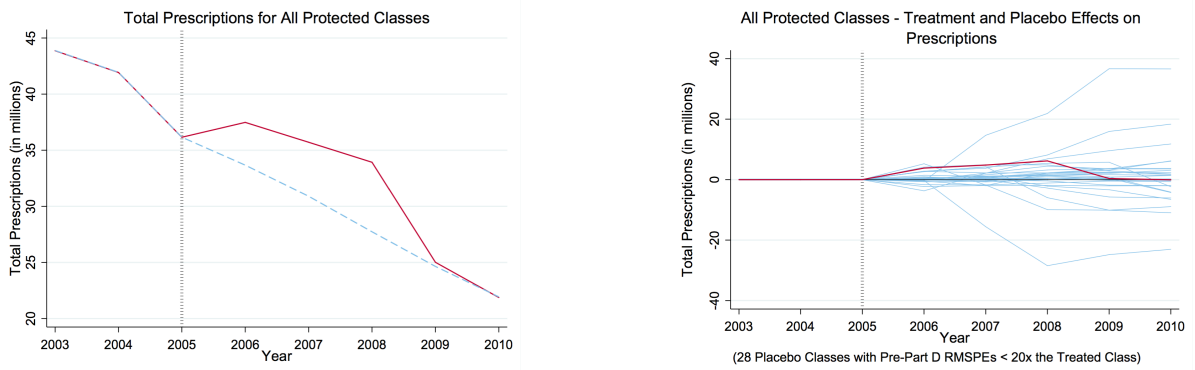
Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 25: Effects of Protection on Drug Sales for the Aggregate Protected Class and Placebo Effects Using Verispan VOTA Data

Table 18: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Drug Sales for the Aggregate Protected Class Using Verispan VOTA Data

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2006-2010**
Tx Value	5617.03	5925.15	6167.67	5090.14	4605.76	5481.15
S.C. Value	5112.74	4442.46	4059.7	4008.63	3829.5	4290.61
Effect Size	**504.28***	**1482.69*****	**2107.98*****	**1081.52**	**776.26**	**1190.54****
P-Value	**(.057)**	**(0)**	**(0)**	**(.171)**	**(.171)**	**(.029)**
% Change	9.9%	33.4%	51.9%	27%	20.3%	27.7%

* p<0.10, ** p<0.05, *** p<0.01



Left: The solid red lines are the protected classes and the dashed blue lines are the synthetic protected classes. Right: The red lines are the protected class effects and the blue lines are the placebo effects. All: The vertical black dotted line represents the last year of data collected in 2005 before Part D and protected class implementation in 2006.

Figure 26: Effects of Protection on Drug Utilization for the Aggregate Protected Class and Placebo Effects Using Verispan VOTA Data

Table 19: Effect Sizes and P-Values from Synthetic Control Models by Year and Post-Treatment Average: Drug Utilization for the Aggregate Protected Class Using Verispan VOTA Data

	Lead 1	Lead 2	Lead 3	Lead 4	Lead 5	Post-Tx Average
Year	**2006**	**2007**	**2008**	**2009**	**2010**	**2006-2010**
Tx Value	37.48	35.71	33.93	25.01	21.88	30.8
S.C. Value	33.67	30.9	27.73	24.64	21.93	27.78
Effect Size	**3.81***	**4.81**	**6.19**	**.37**	**-.06**	**3.03**
P-Value	**(.069)**	**(.103)**	**(.172)**	**(.862)**	**(.931)**	**(.31)**
% Change	11.3%	15.6%	22.3%	1.5%	-.3%	10.9%

* p<0.10, ** p<0.05, *** p<0.01

APPENDIX I

EFFECTS OF PROTECTION ON DRUG EXPENDITURES AND UTILIZATION USING DIFFERENCE-IN-DIFFERENCES REGRESSION

Table 20: Difference-in-Differences Coefficients for Drug Spending and Utilization for the Aggregate Protected Class, Class and Year Fixed Effects

	(1) **Total Spending (in millions 2011$)**	(2) **Quantity (in millions)**
Protected Class	992.8**	317.5**
	(8.49)	(4.16)
Avg. Risk Adjustment Score	-65.0*	-17.6
	(-1.08)	(-0.45)
Percent Dual Eligibles	81.0	-45.4
	(0.58)	(-0.50)
Constant	153.2*	-7.80
	(0.92)	(-0.07)
Class Dummies	Yes	Yes
Year Dummies	Yes	Yes
F-Statistics	84	82
Observations	1452	1452

* p<0.5, ** p<0.01