The Efficacy of State-Level PrEP Access Programs: A Tale of Two States

Noah Zwiefel, nzwiefel@macalester.edu

Macalester College

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Abstract

Pre-exposure prophylaxis (PrEP) reinvents what we know about HIV prevention by nearly eliminating the risk that an individual will seroconvert after exposure to HIV. Uptake, however, has been slow in many areas where it would be most beneficial. In recent years, several states have introduced programs designed to increase PrEP uptake. Some, as in Washington, focus only on decreasing price; others, such as in New York, focus on addressing other factors, such as a lack of awareness of PrEP among potential patients, and lack of buy-in from providers. In this paper, I use synth and difference-in-differences to examine the efficacy, in terms of increased PrEP prescriptions, of New York and Washington's PrEP access programs. I find relatively weak evidence that Washington's less comprehensive program was associated with at most 700-900 new prescriptions between 2014-2016, and stronger evidence that New York's more sweeping program is associated with an increase of between 5,000-6,000 prescriptions.

1 Introduction

In 2012, the FDA approved Truvada, a patented drug developed by Gilead, as a pre-exposure prophylaxis (PrEP) for HIV infections. This is a single pill, taken daily, that under perfect adherence reduces the risk of contracting HIV by 99% (Anderson, 2012). This drug is posed to recreate what we know about HIV prevention – a new 'wonder-drug' (Charlton, 2014) that could completely eliminate HIV in the United States if taken correctly and by enough people. However, take up of this drug has been slow in many areas. Currently 1.2 million people are classified by the CDC as at high risk of contracting HIV, while only 78,000 Americans – mostly located in coastal, relatively prosperous states, where the risk of contracting HIV is comparatively low – are taking this drug (AIDSVu, 2016).

There are many reasons behind slow PrEP takeup, including cost (Luthra, 2018), given that a 30-day supply has a list price of $1,600 a month. This cost is partially subsidized by the manufacturer, Gilead, however gaps remain, as this program has a cap on benefits. Thus, many states, such as New York, Colorado, Illinois, and Washington, have introduced programs that cover costs associated with this drug. However, these programs vary in what resources are dedicated to addressing the other factors behind slow take up, including a lack of awareness of PrEP, stigma, and a lack of access to willing prescribers.

There has been no research surrounding the effectiveness – in terms of increased PrEP prescriptions – of these state-level programs. Furthermore, there has been no research that compares the relative effectiveness of a more comprehensive program, which covers less of the costs but addresses more of the factors behind slow take up, and a less comprehensive program which covers more of the costs of the drug. Knowing these details is an essential first step in determining where states ought to focus their efforts to increase PrEP takeup.

In this paper, I examine New York and Washington, both states that launched programs designed to increase the uptake of PrEP at the beginning of 2015. These programs vary in comprehensiveness. New York's program consists of several components, including provider outreach and a marketing campaign; meanwhile, Washington's program merely provides free PrEP to individuals certified by a doctor as at high risk of contracting HIV. Using synth and a difference-in-differences analysis, I find evidence that New York's comprehensive program was associated with an increase of 5,000-6,000 prescriptions between 2014-2016, while Washington's program resulted in an increase of at most 700-900 prescriptions over the same time frame, suggesting that New York's more comprehensive program was more effective at increasing PrEP prescriptions.

In this paper, I utilize the term MSM, which refers to men who have sex with men. I also utilize the term risky sexual behavior, which refers to any sexual behavior that increases the risk of contracting HIV, such as condomless sex. This differs from being in a "high risk" group, which refers to an individual that either behaves in risky sexual behavior, or uses IV drugs. I use the term low risk sexual behavior to refer to any sexual behavior that has a relatively lower risk of contracting HIV, such as any form of sex with a condom, or oral sex. Finally, I use the term PrEP to refer to the patented pre-exposure prophylaxis drug Truvada developed by Gilead Sciences, and PrEP-AP (*pr*e-*e*xposure *p*rophylaxis *a*ccess *p*rogram) to refer to any state-health department administered program designed to increase the take up of PrEP.

2 Literature Review

2.1 Reasons Behind Slow PrEP Takeup

Much of the literature surrounding the reasons behind slow PrEP take up is survey based, and can be divided into four general categories.

The first reason is a knowledge gap, which is when individuals are unaware of PrEP and its benefits. Survey data finds this reason is particularly prevalent among those with low income or limited education (Strauss, 2017), those who live outside of major urban centers (Cohen, 2015), and women (Auerbach, 2015) – the exact groups that have the lowest take up rates. Public health centers can address this through education programs (Raifman, 2017). However such programs are not widely implemented, and many individuals are uncomfortable speaking to a care provider about their risky sexual behaviors (Patel, 2018).

Second, stigma is repeatedly cited in the literature as a major factor behind individuals choosing not to take PrEP (Calabrese & Underhill, 2015). AIDS and HIV have long been associated with MSM, promiscuity, and drug use; it is only logical that a drug that prevents HIV would also become associated with those groups. Survey data finds that this stigma is equally prevalent among both low and high risk groups (Golub et al, 2018) including women (Auerbach, 2015) and most MSM (Fisher, 2018), particularly those that are uneducated, poor, or non-white (Golub et al, 2017; Mustanski, 2018) – once again, demographic groups that are prevalent in areas with low PrEP takeup.

Third, assuming an individual overcomes this stigma, they may be unable to find a provider willing to prescribe this drug. PrEP requires regular blood testing and checkups to ensure that rare but significant side effects are not occurring. This is exactly the kind of drug that primary care providers should be prescribing, yet many primary care providers report that they are uncomfortable providing this drug (Turner, 2018; Krakower 2014; Bil, 2018), particularly in the South (Siedman, 2016), an area with relatively few individuals on PrEP. Many providers have concerns about potential side effects (Arnold, 2012), in addition to a fear of risk compensation (Calabrese, 2018; Bil, 2018; Karris, 2014; Puro, 2013; Turner, 2018), a theory that implies that an individual has a prefered risk level, and will perform substitutions to reach this level of risk. In this case, providers fear that individuals will stop using condoms when having sex, given that the risk of contracting HIV is eliminated. This puts them at a much higher risk of other STIs, which in turn reduces the cost effectiveness of PrEP, potentially disincentivizing states and insurance companies from providing this drug (Calabrese & Underhill, 2015).

There is some anecdotal, survey-based data which suggests that PrEP may increase risky sexual behaviors (Strauss, 2017; Brooks, 2012; Golub, 2010). However, many blind laboratory studies and meta-analyses observe no risk compensating behaviors (Fonner, 2016; Freeborn, 2018; Liu, 2013); individuals that were taking part in risky sexual behavior before taking PrEP continued after beginning drug. In other words, in contrast to survey-based studies, blind studies imply that being on PrEP by itself does not increase the likelihood that an individual will take part in risky sexual behavior (Grant, 2014; Grov, 2015; Perez-Figueroa, 2015). This disparity may be caused by the blind nature of laboratory studies, given that the individual is unaware if they're taking PrEP or a placebo: ambiguity may impact their risk compensating behaviors (Myers, 2013). Further, it is possible that individuals could be taking part in risky sexual behavior post-PrEP while taking part in a laboratory study, but not reporting it. These concerns surrounding risk compensation impact prescribing descriptions, with some providers refusing to prescribe PrEP when asked by their patients (Patel, 2018; Puro, 2013), serving as yet another driver of low PrEP take up.

Finally, cost is a major factor (Karris, 2014; King, 2014; Paltiel, 2009). Going to the doctor is expensive, and this drug is expensive (Luthra, 2018). Because it is a patented, brand name drug, many commercial prescription drug insurance plans charge a higher copay. Surveys find that individuals at high-risk of contracting HIV report interest in PrEP, were it provided for free (Fisher, 2018), and when it is provided for free, uptake increases (Grant, 2014). However, at current prices providing the drug for free to all high risk groups would cost governments nearly $85 billion, and this is only for the drug (Vassall, 2013); regular blood work is required for PrEP. It is implied that the cost of these blood tests is a bigger barrier for the uninsured than the costs of the medication, given that manufacturer assistance is available for drug itself (Chan, 2016; Leibowitz, 2011).

2.2 Background of PrEP Assistance and Access Programs

Gilead, manufacturer of Truvada, has an assistance program which has two components: a component that covers drug copays for the privately insured, and a component that provides the drug free of charge to "qualifying" individuals (i.e. the uninsured) (Gilead, 2018). Neither component covers any costs associated with the aforementioned blood tests or doctors visits. Furthermore, the benefits are quite limited, as the copay assistance provided a maximum of $4,800 in benefits a calendar year over the timeframe of my data. This could leave a significant gap, given that actual copay need may be several orders of magnitude higher.

Given the gaps in Gilead's program, several states have launched assistance programs designed to help individuals cover the costs of PrEP. These states include Washington, New York, Colorado, Illinois, and Massachusetts. Both Florida (Straube, 2018) and California (California Department of Public Health, 2018) plan to introduce comprehensive PrEP cost coverage programs in 2018. These programs often provide benefits for both the insured (in the form of deductible and copay assistance) and the uninsured. However, these programs differ in what resources are dedicated to addressing the other factors behind slow take up. In this paper, I focus my analysis on New York and Washington, since these states implemented PrEP-APs at the same time. Each of these PrEP-APs had a different focus and set of programs: I briefly describe these differences below.

2.2.1 New York State

After Andrew Cuomo declared HIV an epidemic in New York state in 2014 (NY State Dept of Health, 2018), a set of programs were implemented with the goal of increasing access to, and awareness around, PrEP. One program utilized provider outreach: the Department of Health sent a packet of information to providers in New York City that included instructions on when and how to provide PrEP, access to workshops, pamphlets, and Medicaid billing codes for PrEP and PrEP services (Daskalakis, 2014). Another program focused on patient outreach, with social media campaigns, poster campaigns (Daskalakis, 2014), and a series of advertisements at bus stations across NYC (Filson, 2016; Bellafante, 2015). Beyond these outreach campaigns, New York state implemented a program which covered the cost of blood work for the un- or underinsured. The costs for the drug itself were not eligible for state reimbursement; providers were required to enroll patients into private insurance, Medicaid, or Gilead's program, depending on their income and need (New York State Dept of Health, 2016). As of March 2016, 360 individuals had requested coverage for blood-work related expenses (Fuller, 2016).

2.2.2 Washington State

Washington's PrEP-AP began in April of 2014. The purpose of this program was to provide free PrEP to those that had been certified by a doctor as likely to contract HIV, based on their self reported behavior (End AIDS Washington, 2016). Individuals are referred first to Gilead and Medicaid for coverage of costs (Aleshire, 2017). Any costs that remain in terms of co-pays from doctors appointments, blood tests, or the drug are fully covered by Washington's program. Once on the program, there are no costs associated with either the drug or the blood work for the participants. As of December 2015, this program had 639 participants (Aleshire, 2016). While more generous than New York, in terms of its financial benefits for participants, Washington's program did not include a coordinated outreach campaign targeted at providers, public health centers, or patients.

There has been no research into whether or not New York and Washington's PrEP programs increased the number of prescriptions relative to comparable states. Furthermore, there has been no research surrounding the respective effectiveness of these programs, given that New York's program was more comprehensive, while Washington's was more generous.

In this paper, I providing evidence of the relative efficacy of these two programs, as evidenced by a synthetic control and a difference-in-differences analysis.

3 Theory

The marketplace for PrEP can be described as a simple demand and supply market. Generalizing broadly, let the supply of PrEP in a state be perfectly elastic, given that any amount can be provided at the list price. If all else is held constant, let these state assistance programs reduce the price of the drug from current equilibrium price P_1 to new equilibrium price P_0. This causes a shift in the supply curve, which leads to a movement along the demand curve, increasing the quantity demanded (or, in other words, prescriptions) of PrEP, as illustrated in Figure 1.

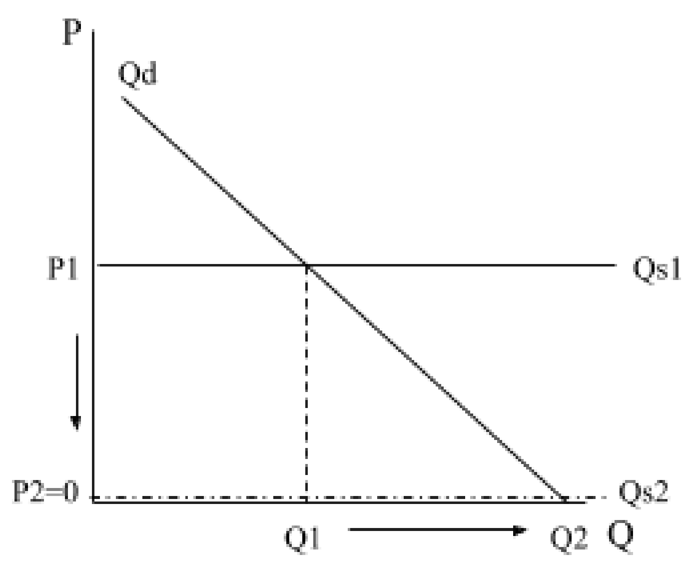
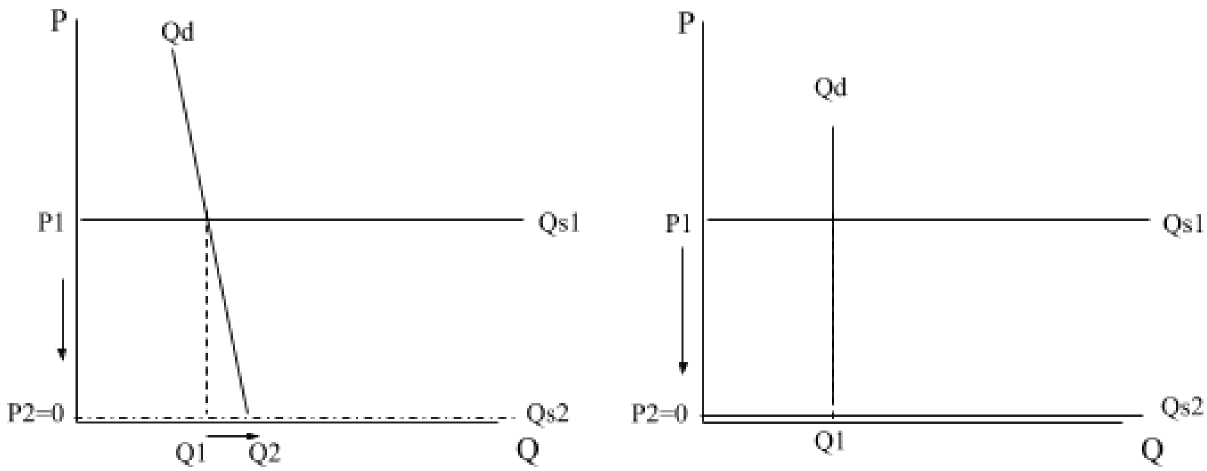


Figure 1: Theoretical change in quantity when price falls from P_1 to $P_2 = 0$

However, because of the knowledge gap, stigma, and lack of providers in some areas, the demand curve among groups at high risk of contracting HIV may be more inelastic. This implies that the quantity demanded



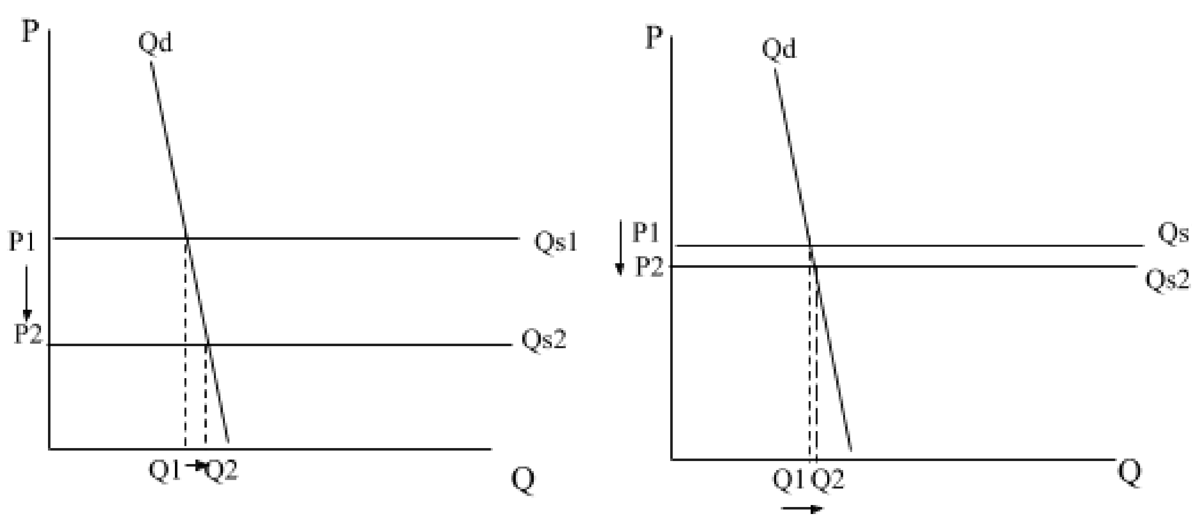
(a) Slightly Elastic Demand

(b) Perfectly Inelastic Demand

Figure 2: The change in PrEP prescriptions after PrEP-AP depends on the elasticity of the demand curves.

might not increase as much as one might expect, or in the extreme, by none at all. This situation is displayed in Figure 2.

Furthermore, there are costs associated with the regular blood tests needed for this drug that and costs associated with the amount of time needed to enroll in these programs. These costs may not be reimbursed under a state's assistance programs. Given these details, the true price for Truvada may not actually become zero, as illustrated in Figure 3. This results in a situation where the equilibrium quantity may increase by only a slight amount, even if demand is somewhat elastic.

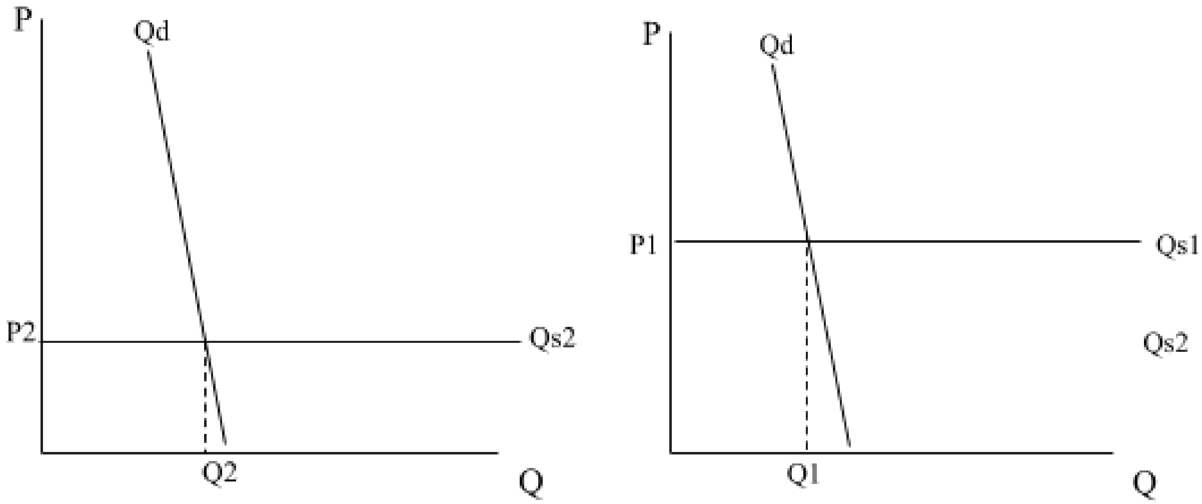


(a)

(b)

Figure 3: The true 'price' of PrEP after the introduction of a free PrEP program may not be zero, depending on what other costs are associated with acquiring this drug.

Given these underlying factors, it seems possible that any change to the prescription patterns could be nearly imperceptible or non-existent, depending on the states market, as illustrated in Figure 4.

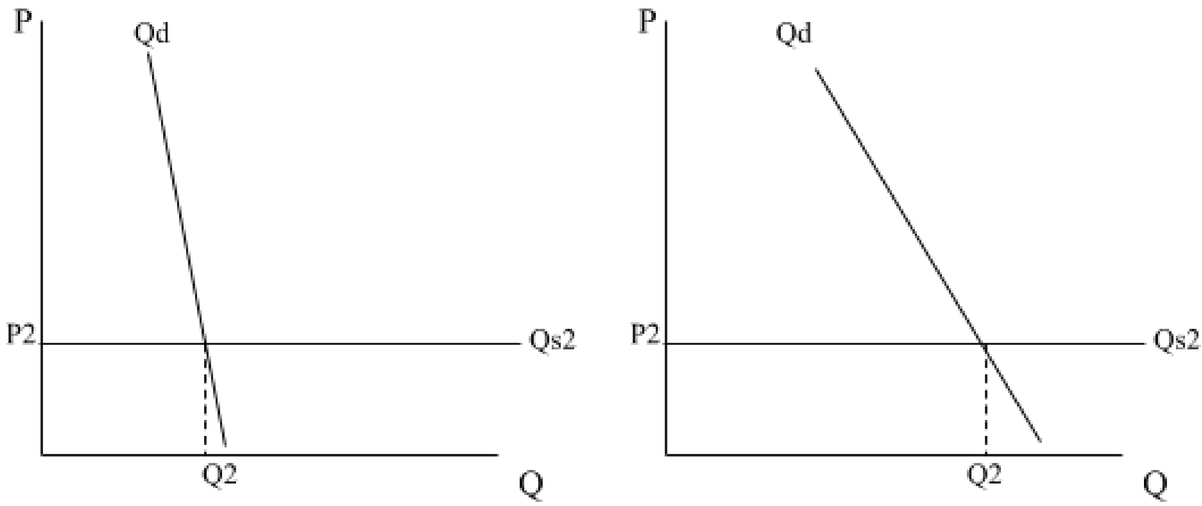


(a) State With PrEP-AP

(b) State Without PrEP-AP

Figure 4: The impact of the PrEP-AP may be rather small if only the list price of the drug is considered when developing a PrEP-AP.

Components that are included in these programs which address other factors, beyond cost – such as provider outreach, or advertising PrEP to the general public – may cause the demand curve to both shift out and become more elastic. More individuals become aware of PrEP and its benefits, and thus more individuals are willing to purchase PrEP at any price. As a result of this shift, the equilibrium quantity could be much larger at the same equilibrium price, as demonstrated in Figure 5.



(a) State without Consumer Outreach (b) State with Consumer Outreach

Figure 5: The impacts of the PrEP-AP may be greater if other factors behind low PrEP takeup (such as lack of consumer knowledge) are addressed.

4 Empirical Approach

Because of the large heterogeneity between states, no single state will have the characteristics ideal for a meaningful control group. Thus, I utilize a method used by Abdie (2010) and thoroughly described by the Urban Institute (McClelland, 2017), which builds a weighted average "non-treated" control version of the state. I use this approach to generate synthetic versions of New York and Washington with no PrEP-AP.

To do this, I utilize the synth module in STATA. This module calculates the weighted-average of PrEP prescriptions in a group of states that are theoretically comparable to the treated state, aside from their treatment status (McClelland, 2017). These states are picked via a mathematical algorithm that matches states based on how closely they match the pre-treatment trends, in addition to a set of control variables (McClelland, 2017).This provides an insight into the counterfactual "but-for" number of prescriptions – that is, how many PrEP prescriptions would have been filled in New York and Washington between 2014-2016 but-for their PrEP-AP.

As an additional robustness check on my Synth results, I utilize an Ordinary Least Squares regression, with a difference-in-differences estimation strategy. My regression is defined below for New York:

$$Y_{it} = \beta_0 + \beta_1 \text{Is New York}_i + \beta_2 \text{Post2014}_t + \beta_3 \text{Post2014}_t * \text{Is New York}_i + \beta_4 X_{it} + \varepsilon_{it}$$

and Washington:

$$Y_{it} = \beta_0 + \beta_1 \text{Is Washington}_i + \beta_2 \text{Post2014}_t + \beta_3 \text{Post2014}_t * \text{Is Washington}_i + \beta_4 X_{it} + \varepsilon_{it}$$

where Y_{it} is the PrEP prescription rate per 100,000 residents in state i during year t, β_1 is the coefficient on a dummy variable indicating whether or not it is a state of interest (i.e. New York or Washington, depending on the regression), β_2 is the coefficient on a dummy variable indicating whether or not we are the post-program implementation timeframe, β_3 is the coefficient on the interaction term between these two terms, β_4 is a vector of coefficients on a group of control variables for a state, and ε_{it} is an error term for state i in year t. The interaction term – β_3 – will provide insight into whether or not these programs are associated with an increase in prescriptions.

5 Data

Ideally I would have a complete and accurate monthly census of PrEP prescriptions pre- and post- implementation of the PrEP-AP, as synth performs best when significant amounts of data are available pre-treatment (McClelland, 2017). To ensure that my synthetic control is composed of states that are roughly comparable in terms of their PrEP policies, I would have data on how much each state spent promoting PrEP, a measure of access to prescribers, some measure of how aware individuals are of PrEP, and a measure of how often individuals visit a public health center. Each of these serves as an important indicator of how homogenous states are in their public health policies towards PrEP, thus enabling synth's donor-state matching algorithm to select appropriate states for my synthetic control. Unfortunately, much of my ideal data is inaccessible, given the time and budget constraints of my paper.

Instead I have state level data on PrEP prescriptions from AidsVU (2018). To build my weighted-average synthetic counterfactual, I use percent of the population 25 years of age and older with a bachelor's degree as a proxy of the knowledge of PrEP, since more highly educated people are more likely to know about PrEP. I use a count of clinics which received Ryan White HIV/AIDS grants per 100,000 residents in a state (Health Resources & Services Administration, 2017) as a rough proxy for how accessible PrEP is within a region, as well as a measure of how much each state spent promoting PrEP. As a measure of how accessible healthcare in general is, I use the number of licensed doctors per 100,000 residents, as reported by the Association of American Medical Colleges odd-year State Physician Workforce Data Report (2017), with a midpoint between the two values assigned for each even year.

As a measure of how often individuals visit a public health center, and thus how likely they are to have access to PrEP, I utilize Chlamydia infections per 100,000 residents as reported by the CDC (2017). Such a measure may be problematic given that individuals on PrEP are theoretically more at risk for Chlamydia, given that risky sexual behaviors might increase post-prescription. However, it is the best proxy given my data constraints – I would prefer to use some form of survey based data, but such data does not exist.

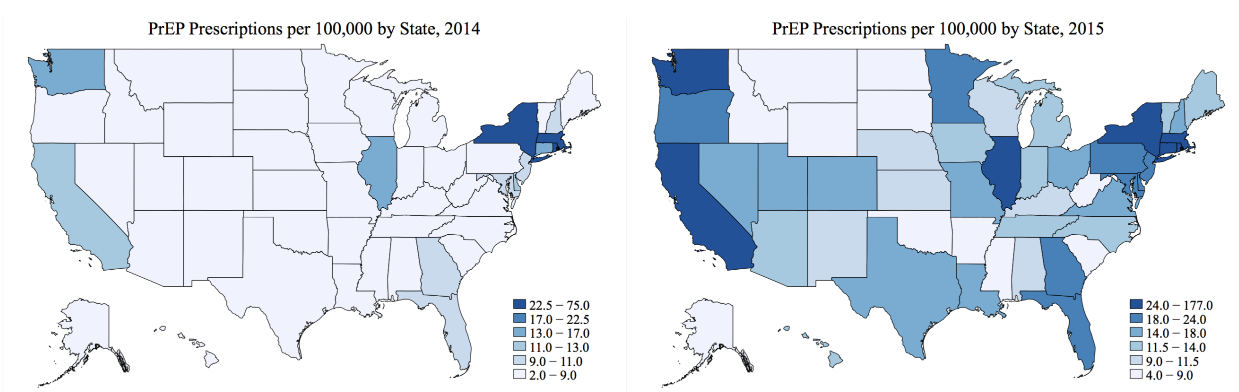
As demographic controls, I utilize the unemployment rate, median income, the population of an area, and racial characteristics, all retrieved from GeoFRED (St Louis Federal Reserve, 2018). Unfortunately, given Washington D.C's relatively small sample size, I was unable to acquire a consistent, accurate, annual estimate of the racial characteristics of Washington D.C. Instead, I assume that it remained constant, and use the 2010 Census data on race.

My summary statistics are presented in Table 1.

VARIABLES	N	mean	sd	min	max
# of Ryan White AIDS Grant Recipients per 100,000	240	3.123	3.252	0.831	20.51
% of population with Bachelor Degree	240	29.57	6.125	18.6	56.8
Unemployment Rate	240	5.9	1.682	2.683	11.17
Median Income	240	55,151	9,320	32,338	76,260
Chlamydia Cases per 100,000	240	465.4	229.7	138.7	1,310
PrEP Prescriptions per 100,000	240	12.43	22.86	0	268
Providers per 100,000	336	268.8	101.9	176.4	879.1
Population	336	6.06E+06	7.14E+06	547,637	3.93E+07
% of population that is black	287	0.0818	0.106	0.00197	0.415
% of population that is hispanic	287	0.0853	0.0926	0.00955	0.481
% of population that is white	287	0.786	0.147	0.43	0.968

Table 1: Summary statistics

Figure 6 shows PrEP prescription rates by state, before and after these PrEP-APs were implemented. Prescriptions grow nationwide over this period, and thus it is difficult to say whether or not these programs had a measurable impact.



(a) Pre- PrEP-AP Implementation

(b) Post- PrEP-AP Implementation

Figure 6: PrEP prescriptions per 100,000 before and after implementation of PrEP-AP in New York and Washington.

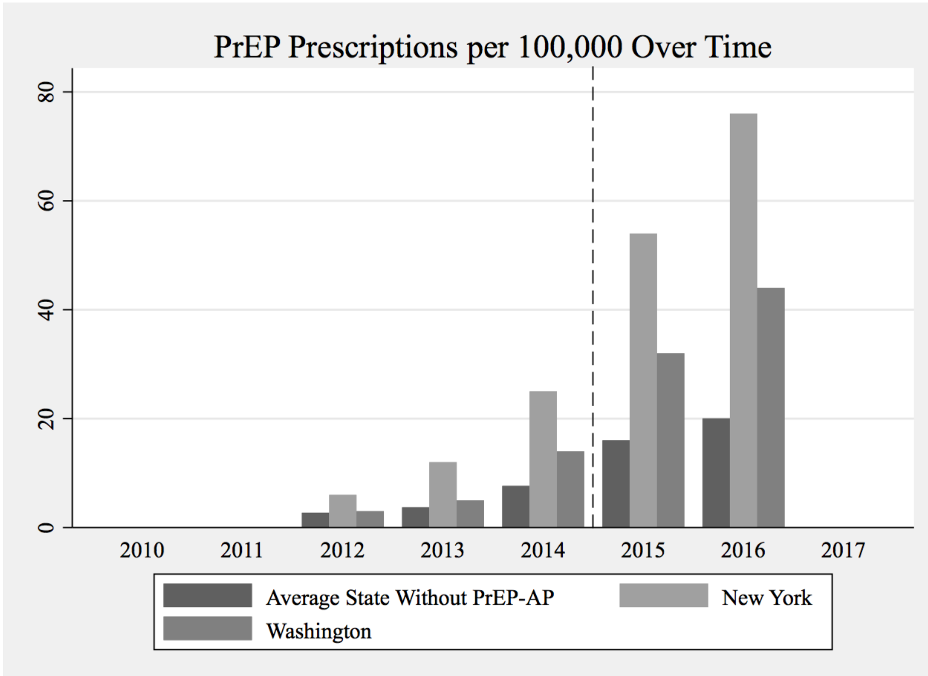


Figure 7: PrEP prescription trends over time.

As we see in Figure 7, post PrEP-AP implementation in New York and Washington, prescriptions increased overall, but particularly when compared states that had no formal PrEP-AP. Assuming all else was held constant, this implies that the PrEP-AP program increased PrEP prescriptions. However, any conclusions that can be drawn are limited. It is likely that there are fundamental differences in how each state approaches sexual health in general. Such differences limit our conclusions about the impact of each state's PrEP-AP, unless we use a set of comparable states, or an appropriate set of control variables. In other words, a visual inspection ignores the fact that many of these states are not comparable to New York or Washington, given the heterogeneity among states.

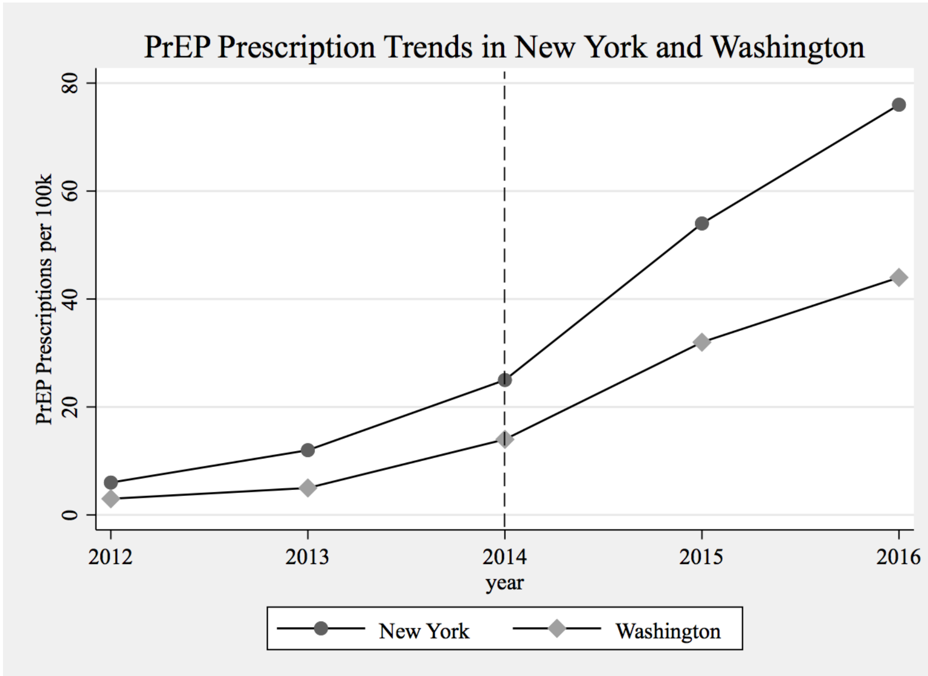


Figure 8: PrEP prescription trends over time in Washington and New York.

In terms of which PrEP-AP was more efficacious, it appears in Figure 8 as if New York had a greater increase in PrEP prescriptions per 100,000 post-program implementation when compared with Washington. Of course, this approach is a rather naive approach, given that we are controlling for nothing; thus a more thorough Econometric analysis is needed.

6 Results

6.1 New York

6.1.1 Synth

I first estimate synthetic New York as a function of the PrEP prescription rate in New York in 2014, the number of cases of Chlamydia, the number of prescribers and Ryan White AIDS grant receiving public health organizations per 100,000 residents, the raw population, the percent of the population with a bachelor's degree, the median income, the unemployment rate, and the percents of the population which are white, black, and hispanic. I exclude Washington, Illinois, and Colorado as potential donor states, given that these states all had PrEP-APs which were introduced over the timeframe of my data. The results of this estimation are displayed in Figure 9.

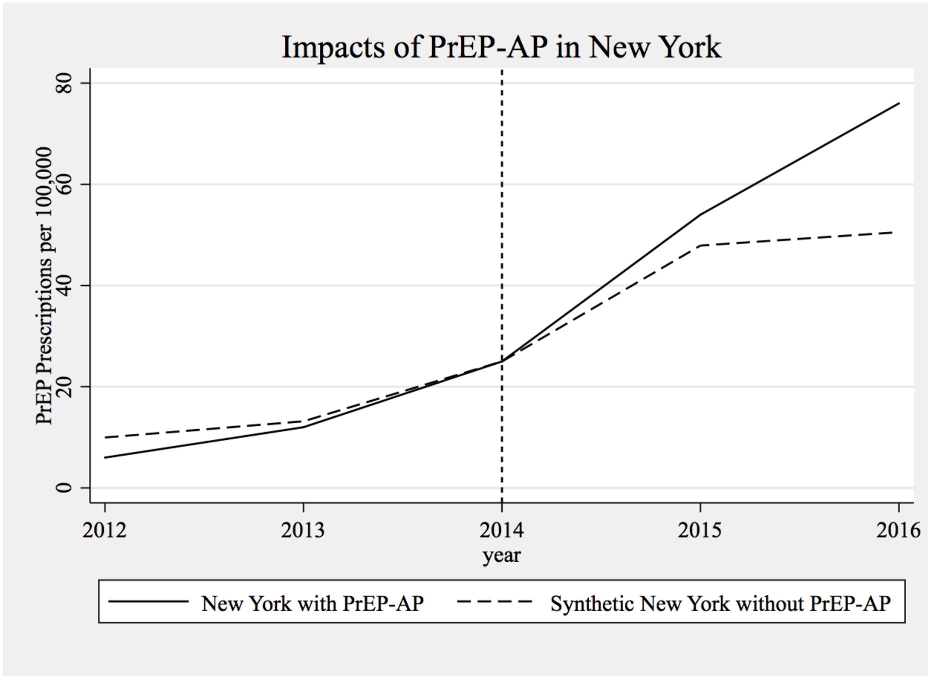


Figure 9: Comparing counterfactual New York with no PrEP-AP to actual New York with PrEP-AP.

As we see, treated New York had more prescriptions relative to synthetic New York. Based on these results, New York's program did, in fact, increase prescriptions more than comparable states. The balance of this predictor is displayed in Table 2. We observe in this instance that our synthetic control's pre-treatment PrEP prescription rate in 2014 and demographic break downs closely matches actual New York. However, pre-treatment synthetic New York tended to have fewer cases of Chlamydia, a higher median income, and a significantly smaller population.

Variable	Treated	Synthetic
Chlamydia Cases per 100,000	332.85	321.2005
Median Income	48823	58340.15
Unemployment Rate	8.116667	8.30965
% of population with bachelor's degree	33.75	34.9251
# of Ryan White Grant Recipients per 100,000	2.447364	3.143804
# of doctors per 100,000	348.2	358.006
% of the population that is black	0.0586113	0.0645415
% of the population that is white	0.8410713	0.829006
% of the population that is hispanic	0.0705602	0.0777392
Population	1.96E+07	5140195
PrEP Prescriptions per 100,000 (2014)	25	24.991

Table 2: Balance of synthetic New York.

My synthetic control is built from the states in Table 3. The two donor states with the most weight – Rhode Island and Massachusetts – are both geographically and culturally comparable to New York, lending credence to this counterfactual. Unfortunately, the inclusion of Georgia in synthetic New York seems rather arbitrary: however, it is important to note that it is assigned a weight of less than 10%.

To test the robustness of these results, I first re-estimated synth with varying combinations of lags: the results are presented in Figure 10. The weight that synth has assigned to the predictors is listed in Table 4. Regardless of the number of lags I use, the majority of the weight used to pick donor states is placed on states with similar pre-treatment PrEP prescription rates.

State	0 lags + all predictors	1 lag	2 lags	3 lags	3 lags + no predictors
Alabama	0	0	0	0	0
Alaska	0	0	0	0	0
Arizona	0	0	0	0	0
Arkansas	0	0.005	0	0	0
California	0	0.012	0.235	0	0.081
Connecticut	0	0	0	0	0
Delaware	0	0	0	0	0
District of Columbia	0.142	0.003	0.177	0.142	0.078
Florida	0	0	0	0	0.05
Georgia	0	0.089	0	0	0
Hawaii	0	0	0	0	0
Idaho	0	0	0	0	0
Indiana	0	0	0	0	0
Iowa	0	0	0	0	0
Kansas	0	0	0	0	0
Kentucky	0	0	0	0	0
Louisiana	0	0	0	0	0
Maine	0	0	0	0	0
Maryland	0	0	0	0	0
Massachusetts	0.348	0.431	0	0.348	0.215
Michigan	0	0	0	0	0
Minnesota	0	0	0	0	0
Mississippi	0	0	0	0	0
Missouri	0	0	0	0	0
Montana	0	0	0	0	0.082
Nebraska	0	0	0	0	0
Nevada	0	0	0	0	0
New Hampshire	0	0	0	0	0
New Jersey	0	0	0	0	0
New Mexico	0	0	0	0	0
North Carolina	0	0	0	0	0.118
North Dakota	0	0	0	0	0
Ohio	0	0	0	0	0.236
Oklahoma	0	0	0	0	0
Oregon	0	0	0	0	0
Pennsylvania	0	0	0	0	0
Rhode Island	0	0.443	0.296	0	0.139
South Carolina	0	0	0	0	0
South Dakota	0	0	0	0	0
Tennessee	0	0	0	0	0
Texas	0	0.018	0	0	0
Utah	0.51	0	0.292	0.51	0
Vermont	0	0	0	0	0
Virginia	0	0	0	0	0
West Virginia	0	0	0	0	0
Wisconsin	0	0	0	0	0
Wyoming	0	0	0	0	0

Table 3: Donor states for synthetic New York.

Variable	0-lags	1-lag	2-lags	3-lags
Chlamydia Infections per 100,000	0.006	0.002	0.001	0
Median Income	0.008	0	0	0
Unemployment Rate	0.017	0.001	0	0
% with Bachelor Degree	0.041	0.003	0	0
Number of Ryan White Grant Recipients	0.005	0	0	0
Doctors per 100,000	0.883	0.02	0.006	0
% of population that is black	0.009	0.002	0.001	0
% of population that is hispanic	0.011	0.003	0	0
% of population that is white	0.02	0.005	0.001	0
Population	0.002	0	0	0
PrEP Prescription per 100,000 in 2014	-	0.964	0.885	0.848
PrEP Prescription per 100,000 in 2012	-	-	0.106	0.055
PrEP Prescription per 100,000 in 2013	-	-	-	0.097

Table 4: Weights used to pick donor states for synthetic New York.

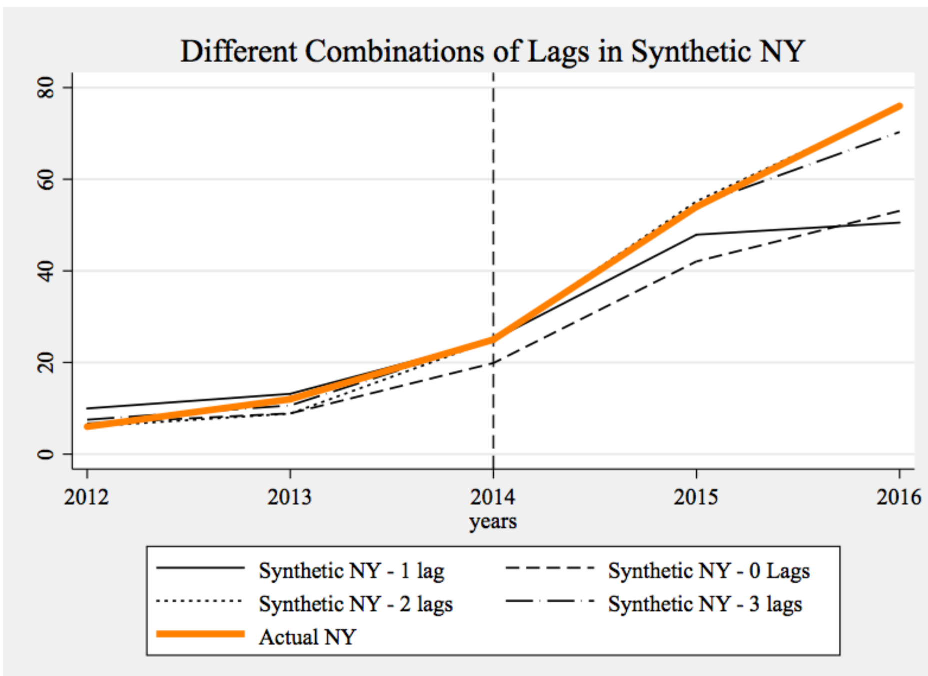
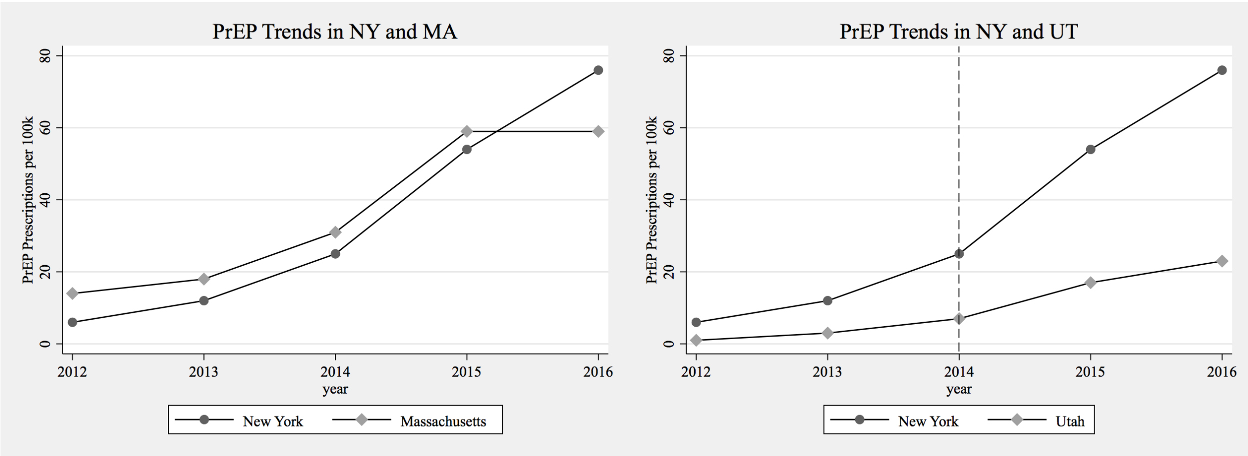


Figure 10: Comparing synthetic New Yorks calculated with different combinations of lags.

It appears as if the number of lags does impact the results slightly; however, it is essential to note that there is only one synthetic New York which predicts no change post treatment – synthetic New York with 2 lags. We can discredit this portrayal of counterfactual New York, given the fact that Massachusetts is excluded as a donor state. The exclusion of Massachusetts seems peculiar, given Massachusetts' cultural similarities to New York and its nearly parallel trends in PrEP prescriptions pre-treatment. Further weakening this model is the inclusion of Utah, which seems to be an inappropriate choice of donor state, given New York and Utah's cultural and behavioral heterogeneity. The contrast between Massachusetts and Utah in terms of PrEP prescriptions is illustrated in Figure 11. I thus believe that counterfactual New York with 2 lags is an inaccurate representation, and ought to be discounted.



(a) MA and NY PrEP Trends

(b) UT and NY PrEP Trends

Figure 11: Comparing the trends of PrEP prescriptions in NY, MA and UT.

I next examined how my synthetic control model was impacted by removing predictors from my 1 lag model. The results are presented in Figure 12 below. The number of predictors do slightly change my results, however, all synthetic New York's still imply that this program increased prescriptions.

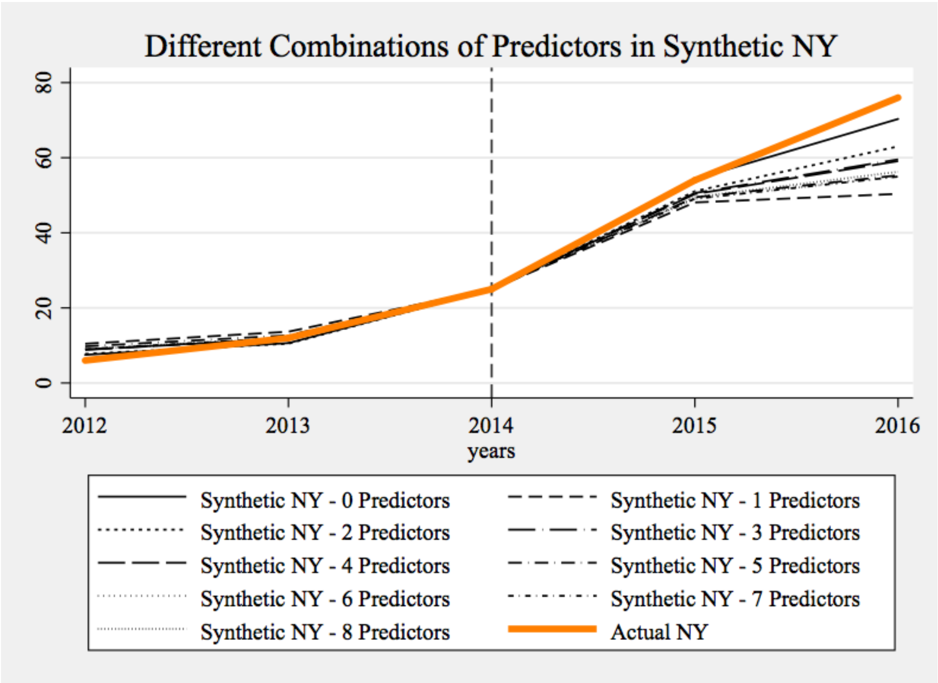
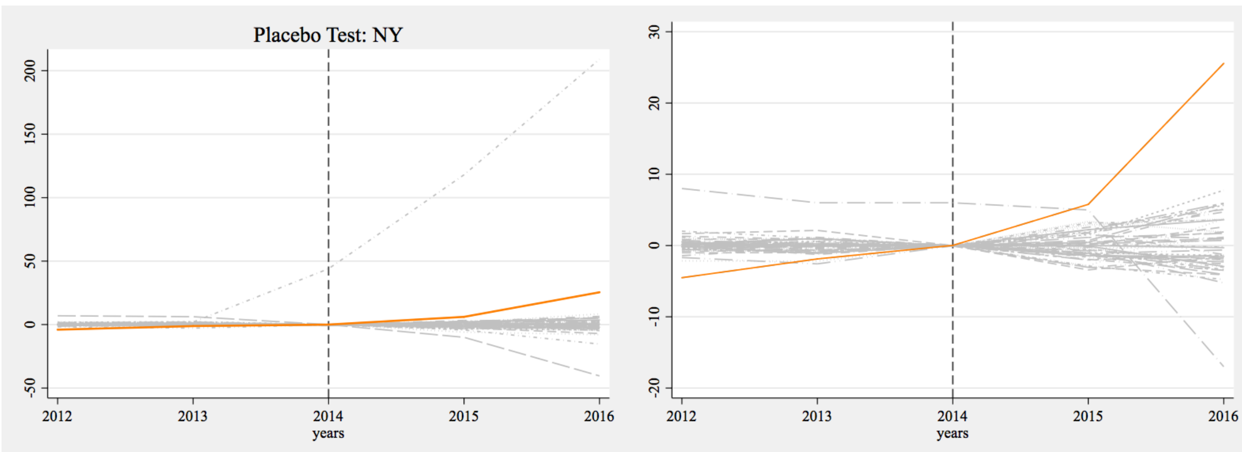


Figure 12: Synthetic New York created with 1-lag and differing numbers of predictors.

I present the root-mean squared prediction error (RMSPE) for each model, as a measure of how well the synthetic control fit prior to this program's implementation in Table 5. The RMSPE remains relatively constant, regardless of the number of lags or predictors I use.

I next perform a placebo test, by building a synthetic control for each state with no PrEP-AP, using the same inputs as in synthetic New York. I then plot the treatment effect – that is, the difference between the actual state and its synthetic counterpart – for each placebo in Figure 13. New York is highlighted.



(a) Placebo Test

(b) Placebo Test: Washington D.C. Suppressed

Figure 13: Placebo test of synthetic New York.

As we see (when suppressing Washington D.C., as we do on the right), New York by far has the largest treatment effect of all the states included in my placebo test. Thus, my results appear not to be the product of a calculation anomaly when building synthetic New York, but are instead the product of a program which actually had an impact.

As a final robustness check, I performed leave-one-out testing, by removing the donor states that synth used to build untreated New York, one at a time. The results are displayed Figure 14. With the exception of Massachusetts, my synthetic control remains relatively unchanged when I remove the donor states. These results imply that Massachusetts has an outsized influence on synthetic New York. Given the parallel trends before the treatment we observe in Figure 11, I believe these results weaken the case that this synthetic control is any more accurate than a difference-in-differences would have been.

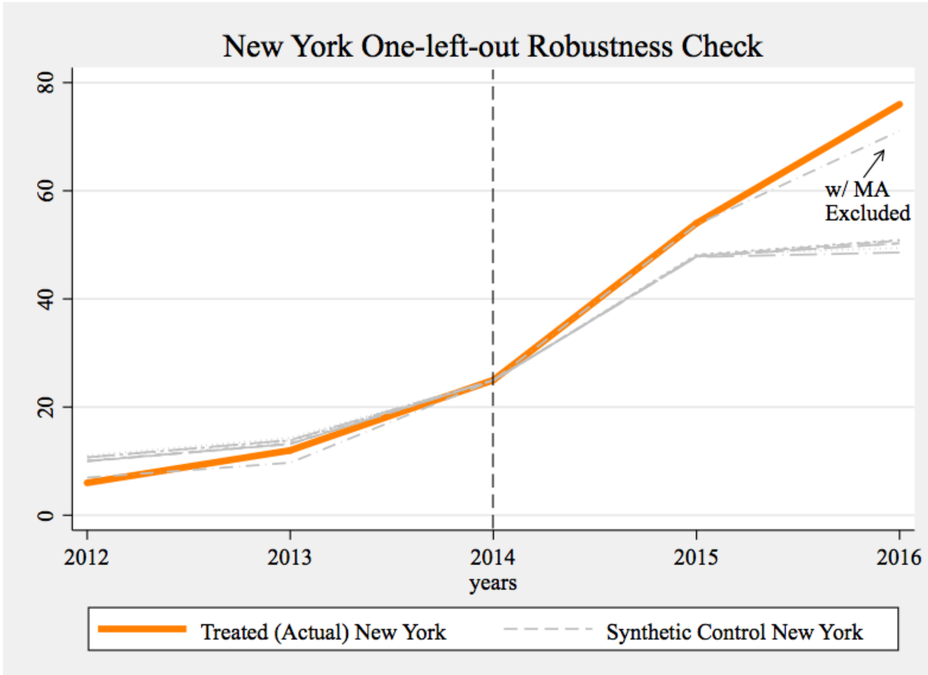


Figure 14: New York one-left-out robustness check. Massachusetts seems to have an outsized influence on my synth results.

Given these results, I conclude that the PrEP-AP in New York did in fact increase the number of prescriptions; however the true impact is ambiguous, and varies depending on what combination of predictors and lags I utilize.

Model	RMSPE
0 lags, all predictors	2.585
1 Lag, All Predictors	2.388
2 Lags, all predictors	1.82
3 Lags, all predictors	1.176
3 Lags, no predictors	1.176
2 Lags and:	
1 predictor	2.717
2 predictors	1.338
3 predictors	1.848
4 predictors	1.629
5 predictors	2.155
6 predictors	2.089
7 predictors	2.089
8 predictors	2.407
9 predictors	1.925
10 predictors	2.082
11 predictors	2.577

Table 5: Root Mean Squared Prediction Error (RMSPE) for pre-treatment synthetic New York.

6.1.2 Difference-in-Differences

To further validate the results I found using synth, I utilize a difference-in-differences approach. I exclude Colorado, Washington, and Illinois from my dataset for this analysis, since these states launched formal PrEP-APs over the timeframe of my data. My results are presented in Table 6. Residual analysis indicated that Washington D.C. appeared to be having an outsized influence on my model, so I additionally estimated this regression without Washington D.C. The results remain relatively unchanged, and both are consistent with the results from my synthetic control approach. Both my synthetic control and difference-in-differences find an increase by 2016 of between 27-31 prescriptions per 100,000 residents associated with this program.

VARIABLES	(1)	(2) D.C. Excluded
isNY	-4.121	-5.308*
	(5.022)	(2.839)
Post2014	10.03***	7.109***
	(2.452)	(0.986)
isNY*Post2014	27.01**	31.65***
	(11.66)	(10.22)
Percent with Bachelor Degree	-0.171	0.0765
	(0.295)	(0.165)
Unemployment Rate	-1.597*	-0.908***
	(0.831)	(0.327)
Median Income	7.40e-05	0.000121
	(0.000178)	(9.17e-05)
Gonorrhea Cases per 100k	0.0102	0.0531***
	(0.0444)	(0.0117)
Public Health Centers	0.00104	0.00276
	(0.00513)	(0.00282)
Providers per 100k	0.146**	0.0918***
	(0.0627)	(0.0197)
% of the population that is black	40.55***	21.04***
	(14.22)	(6.190)
% of the population that is hispanic	49.69***	38.18***
	(17.67)	(7.370)
% of the population that is white	20.07**	21.84***
	(9.513)	(4.384)
Constant	-47.25***	-49.22***
	(17.11)	(7.293)
Observations	240	235
R-squared	0.555	0.687
Adjusted R-squared	0.531	0.67
F	11.15	26.15
rss	55589	8609
Robust standard errors in parentheses		
*** p < 0.01, ** p < 0.05, * p < 0.1		

Table 6: Predicting PrEP prescriptions per 100,000 that is associated with being in New York post-program implementation.

VARIABLES	(1)
isNY	-0.564
	-1.699
Post2013	3.146***
	-0.808
isNY*Post2013	8.173*
	-4.399
Percent with Bachelor Degree	-0.0801
	-0.195
Unemployment Rate	-0.175
	-0.266
Median Income	1.72E-05
	-8.55E-05
Gonorrhea Cases per 100k	-0.0212
	-0.0177
Public Health Centers	0.00146
	-0.00245
Providers per 100k	0.0568**
	-0.0259
% of the population that is black	19.38***
	-7.162
% of the population that is hispanic	15.88**
	-7.826
% of the population that is white	5.319
	-4.307
Constant	-14.49**
	-6.446
Observations	144
R-squared	0.6
Adjusted R-squared	0.563
F	.
rss	3229
Robust standard errors in parentheses	
*** p<0.01, ** p<0.05, * p<0.1	

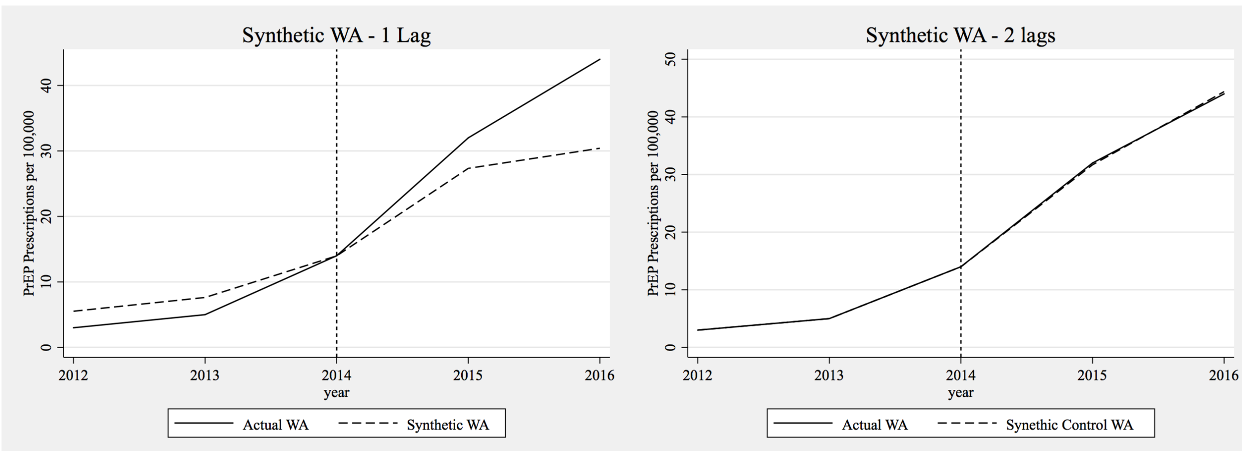
Table 7: Placebo difference-in-differences with arbitrary treatment date of 2013, and data between 2012-2014. Predicting PrEP prescriptions per 100,000.

To test this difference-in-differences model, I perform a placebo test by assigning an arbitrary treatment date of 2013, and restricting the timeframe of my data to 2012-2014. As we observe in Table 7, there is not a statistically significant relationship between being post-arbitrary treatment and in New York. This is what we would expect if this change in prescriptions was actually a result of New York's PrEP-AP. Thus, difference-in-differences provides further evidence that New York's comprehensive program did, in fact, increase prescriptions.

6.2 Washington

6.2.1 Synth

To compare New York's more comprehensive program to Washington's less comprehensive program, I perform the same analysis on Washington's program. For this synthetic control, I use a two lags of PrEP prescriptions per 100,000: one in 2014, and one in 2012. I do this because there is a great decrease in root mean squared prediction error when using the two lags versus just one lag, as we observe visually in Figure 9 and numerically in Table 9. Based on this specification, it seems as if Washington's program had very little to no impact.



(a) Two-Lag

(b) One-Lags

Figure 15: Synthetic Washington.

The balance of synthetic and actual Washington is displayed in Table 8. Synthetic Washington and actual Washington are quite similar – more similar than synthetic and actual New York were. Synth has built an ideal control in this instance, thus lending more credence to these results.

Variable	Treated	Synthetic
Chlamydia Cases per 100,000	499.8	496.9055
Median Income	63054.5	56478.53
Unemployment Rate	7.583333	7.047046
% of population with bachelor's degree	32.2	32.15085
# of Ryan White Grant Recipients per 100,000	2.936541	1.740486
# of doctors per 100,000	265.25	269.8519
% of the population that is black	0.0123335	0.0324792
% of the population that is hispanic	0.1306227	0.1247186
% of the population that is white	0.8099318	0.8011333
Population	6821606	7050404
PrEP Prescriptions per 100,000 (2014)	14	14.029
PrEP Prescriptions per 100,000 (2012)	3	3.009

Table 8: Balance of synthetic Washington.

The weights synth is assigning to each variable when picking control states is displayed in Table 10 below. Once again, much of the weight is placed on lagged values of the dependent variable. The donor states are displayed in Table 11 – the states picked seem rather odd, particularly the fact that Wyoming and Utah are assigned so much weight, given that to the casual observer, these states seem culturally orthogonal to Washington.

Model	RMSPE
0 lags, all predictors	2.775
1 Lag, All Predictors	2.099
2 Lags, all predictors	0.005
3 Lags, all predictors	0
3 Lags, no predictors	0
2 Lags and:	
1 predictor	0.215
2 predictors	0.204
3 predictors	0.111
4 predictors	0.206
5 predictors	0.1
6 predictors	0.091
7 predictors	0.091
8 predictors	0.091
9 predictors	0.015
10 predictors	0.003
11 predictors	0.008

Table 9: Root Mean Squared Prediction Error(RMSPE) for pre-treatment synthetic and treated Washington.

Variable	0-lags	1-lag	2-lags	3-lags
Chlamydia Infections per 100,000	0.006	0.003	0	0
Median Income	0.008	0.001	0.001	0
Unemployment Rate	0.017	0.001	0	0
% with Bachelor Degree	0.041	0.003	0.001	0
Number of Ryan White Grant Recipients	0.005	0.001	0	0
Doctors per 100,000	0.883	0.016	0.002	0
% of population that is black	0.008	0.002	0	0
% of population that is hispanic	0.019	0.006	0	0
% of population that is white	0.011	0.004	0	0
Population	0.002	0	0	0
PrEP Prescriptions per 100,000 in 2014		0.966	0.879	0.851
PrEP Prescriptions per 100,000 in 2012			0.117	0.057
PrEP Prescriptions per 100,000 in 2013				0.092

Table 10: Weights on variables used to pick donor states (Washington).

State	0 lags + all predictors	1 lag	2 lags	3 lags	3 lags + no predictors
Alabama	0	0	0	0.007	0.007
Alaska	0	0	0	0.008	0.008
Arizona	0.077	0.072	0	0.007	0.007
Arkansas	0	0	0	0.005	0.005
California	0.216	0.158	0.183	0.012	0.012
Connecticut	0.093	0	0	0.007	0.007
Delaware	0	0	0	0.005	0.005
DC	0.008	0.004	0.101	0.098	0.098
Florida	0	0	0	0.007	0.007
Georgia	0	0	0	0.007	0.007
Hawaii	0	0	0	0.005	0.005
Idaho	0	0.119	0	0.008	0.008
Indiana	0.067	0.104	0	0.007	0.007
Iowa	0	0	0	0.007	0.007
Kansas	0	0	0	0.005	0.005
Kentucky	0	0	0	0.008	0.008
Louisiana	0	0	0	0.007	0.007
Maine	0	0	0	0.007	0.007
Maryland	0	0	0	0.007	0.007
Massachusetts	0	0.312	0.04	0.01	0.01
Michigan	0	0	0	0.007	0.007
Minnesota	0.23	0	0	0.017	0.017
Mississippi	0	0	0	0.005	0.005
Missouri	0	0	0	0.007	0.007
Montana	0.162	0	0	0.008	0.008
Nebraska	0	0	0	0.007	0.007
Nevada	0	0	0	0.007	0.007
New Hampshire	0	0	0	0.011	0.011
New Jersey	0	0	0	0.009	0.009
New Mexico	0	0	0	0.007	0.007
North Carolina	0	0	0	0.008	0.008
North Dakota	0	0	0	0.008	0.008
Ohio	0	0	0	0.005	0.005
Oregon	0.148	0	0	0.007	0.007
Pennsylvania	0	0	0	0.007	0.007
Rhode Island	0	0	0	0.011	0.011
South Carolina	0	0	0	0.005	0.005
South Dakota	0	0	0	0.008	0.008
Tennessee	0	0	0	0.005	0.005
Texas	0	0	0	0.008	0.008
Utah	0	0.011	0.303	0.566	0.566
Vermont	0	0	0	0.003	0.003
Virginia	0	0.016	0.019	0.005	0.005
West Virginia	0	0	0	0.008	0.008
Wisconsin	0	0	0	0.005	0.005
Wyoming	0	0.204	0.355	0.011	0.011

Table 11: Weights on states used to build synthetic Washington.

I tried varying the number of predictors and lags, the results of which are presented in Figures 16 and 17. The RMSPE for each specification I utilized is displayed in Table 9. The majority of specifications have similar RMSPEs, thus pre-treatment fit is not overly influenced by the number of predictors or lags I use. Unlike in New York, there is only one combination of lags and predictors which predicts that Washington's PrEP-AP resulted in a measurable increase in prescriptions. Thus, it seems more likely than not that Washington's program had little impact on the prescription rate.

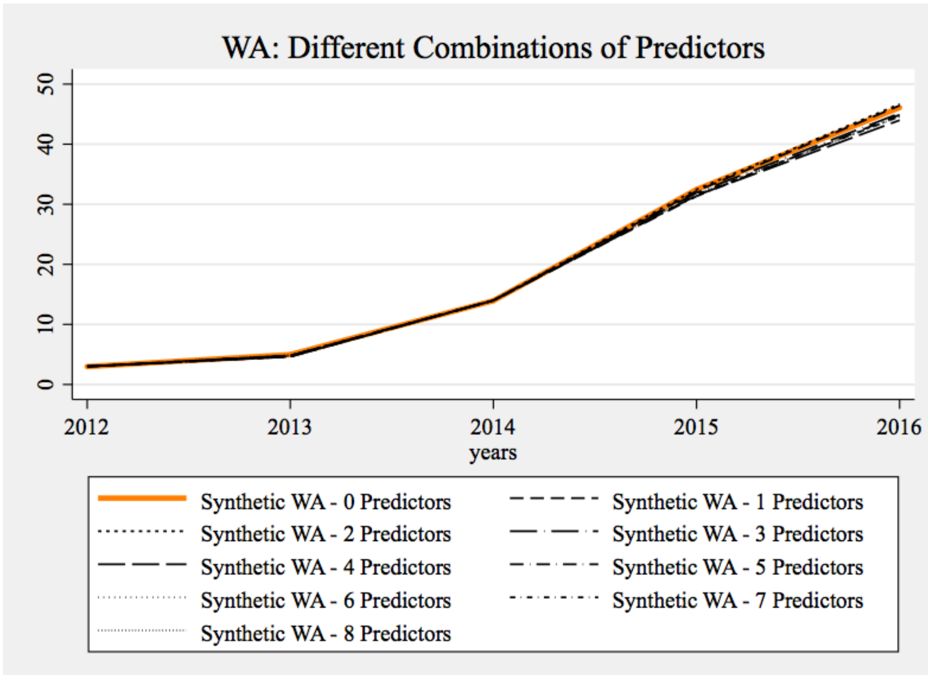


Figure 16: Synthetic Washington created with 2-lags and differing numbers of predictors.

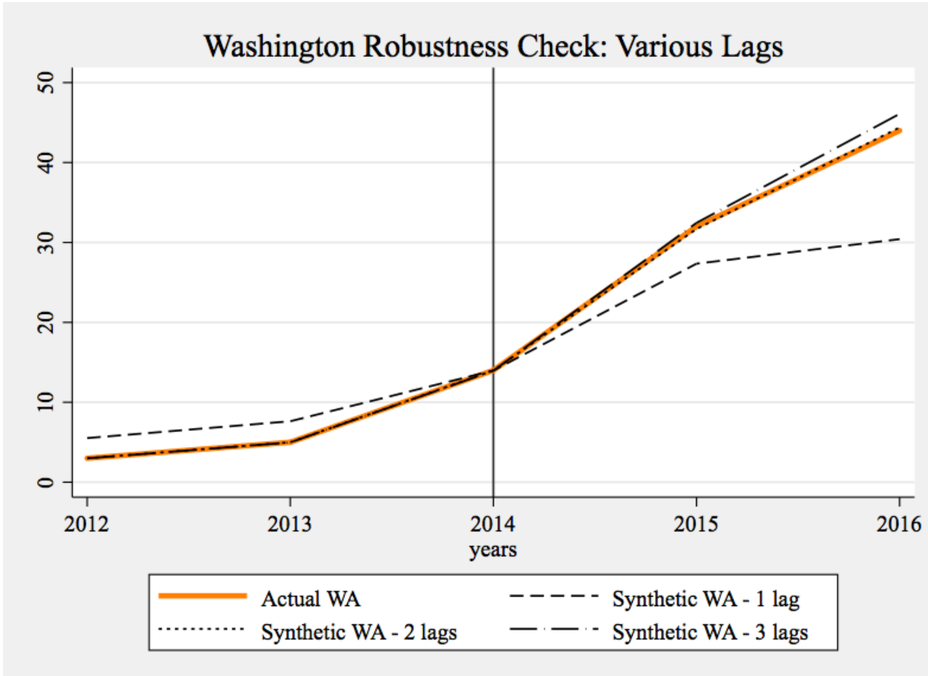


Figure 17: Synthetic Washington created with all predictors and different combinations of lags.

To validate this finding, I next performed a placebo test, the results of which are displayed in Figure 18. In this case, we observe that the treatment effect – the difference between actual Washington and synthetic Washington – is approximately 0. These results strongly imply that Washington's program had very little impact on the PrEP prescription rate.

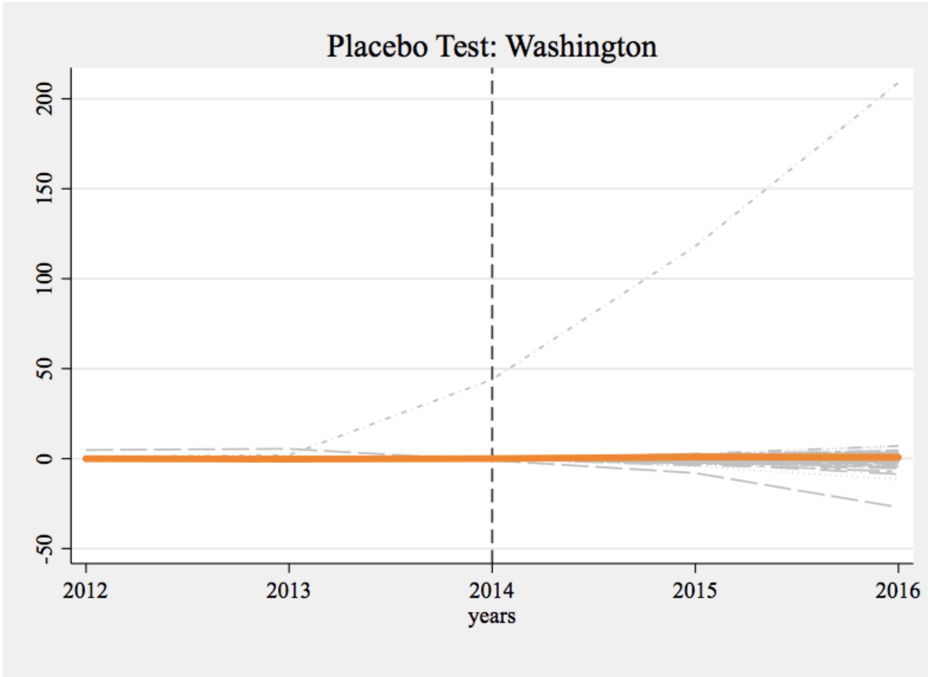


Figure 18: Placebo test of synthetic Washington.

Finally, I performed leave-one-out testing in Figure 19. As we see, Washington D.C. seems to be driving these results; thus, it is possible that there was an impact from Washington state's program. However, even if we accept these results, and exclude Washington D.C. as a donor, this robustness check suggests that PrEP prescriptions increased by merely 10 prescriptions per 100,000 residents. This is a much smaller impact than New York's program, and when calculating the real increase in prescriptions, this number becomes an increase of 750 PrEP prescriptions, which is roughly the number of the number of individuals enrolled in Washington's free PrEP program as of late 2015 (Aleshire, 2016)

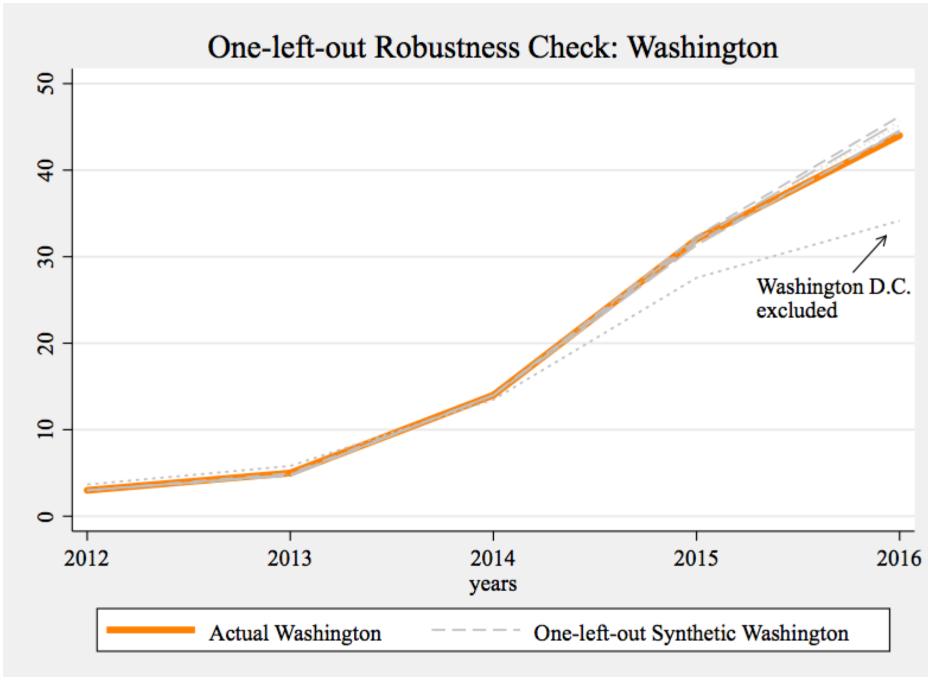


Figure 19: One-state-left-out robustness check of synthetic Washington created with 1-lag and all predictors.

6.2.2 Difference-in-Differences

To validate these synthetic control results, I next utilize a difference-in-differences approach to examine Washington's PrEP program. I exclude Colorado, Illinois, and New York, which, again, had similar PrEP-APs launched over this timeframe. The results of this analysis are displayed in Table 12. As with New York, residual analysis again indicated that Washington D.C. appeared to be having an outsized influence on my model, so I re-estimated this model without Washington D.C. Based on these results, the impact of Washington's program, compared with the nation at large, was rather limited. Being in Washington post-implementation is associated with a slight increase in prescriptions, but this increase is not nearly as large as that which occured in New York.

As a further robustness check, I performed a placebo test, the results of which are in Table 13. I utilized an arbitrary treatment date of 2013, and restricted my data to between 2012-2014. As we observe, there is not a statistically significant relationship between being post-2013 and in Washington, which, in the context of my prior results, implies that this program did increase prescriptions slightly.

VARIABLES	(1) PrEP Prescriptions per 100k	(2) Removed D.C.
isWA	1.25	-0.367
	-1.993	-0.806
post2014	10.26***	7.388***
	-2.45	-0.948
isWA*post2014	12.11*	13.55**
	-6.871	-5.977
Percent with Bachelor Degree	-0.183	0.0705
	-0.297	-0.164
Unemployment Rate	-1.524*	-0.824**
	-0.83	-0.32
Median Income	7.30E-05	0.000123
	-0.000177	-9.12E-05
Gonorrhea Cases per 100k	0.00539	0.0475***
	-0.0445	-0.0103
Public Health Centers	0.000913	0.00285
	-0.00517	-0.00286
Providers per 100k	0.147**	0.0901***
	-0.0626	-0.0198
% black	41.36***	21.71***
	-14.29	-6.1
% hispanic	49.50***	37.37***
	-17.71	-7.234
% white	19.59**	21.16***
	-9.532	-4.257
Constant	-46.84***	-48.29***
	-17.12	-7.118
Observations	240	235
R-squared	0.544	0.646
Adjusted R-squared	0.52	0.627
F	24.46	34.62
rss	54890	8028

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Table 12: Difference-in-differences estimate of impact of Washington's PrEP-AP.

VARIABLES	(1)
isWA	-0.731
	-0.82
post2013	3.185***
	-0.807
isWA*post2013	3.376
	-3.487
Percent with Bachelor Degree	-0.0377
	-0.194
Unemployment Rate	-0.157
	-0.266
Median Income	2.13E-06
	-8.49E-05
Gonorrhea Cases per 100k	-0.0191
	-0.0179
Public Health Centers	0.00146
	-0.00246
Providers per 100k	0.0550**
	-0.026
% of the population that is black	18.07**
	-7.122
% of the population that is hispanic	15.05*
	-7.8
% of the population that is white	5.073
	-4.257
Constant	-14.40**
	-6.449
Observations	144
R-squared	0.585
Adjusted R-squared	0.547
F	.
rss	3206

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Table 13: Placebo test on difference-in-differences model for Washington using an arbitrary treatment date of 2013 and data from 2012-2014.

7 Discussion

I present a comparison of my synthetic control and difference-in-differences results in Washington and New York in Figures 20 and 21. I plotted the difference-in-differences estimate of each state's prescribing patterns – had there been no PrEP-AP – by using the actual values of my controls in each year, and the appropriate dummy variable for being in Washington, and for being post-2014, but not the interaction term between the two.

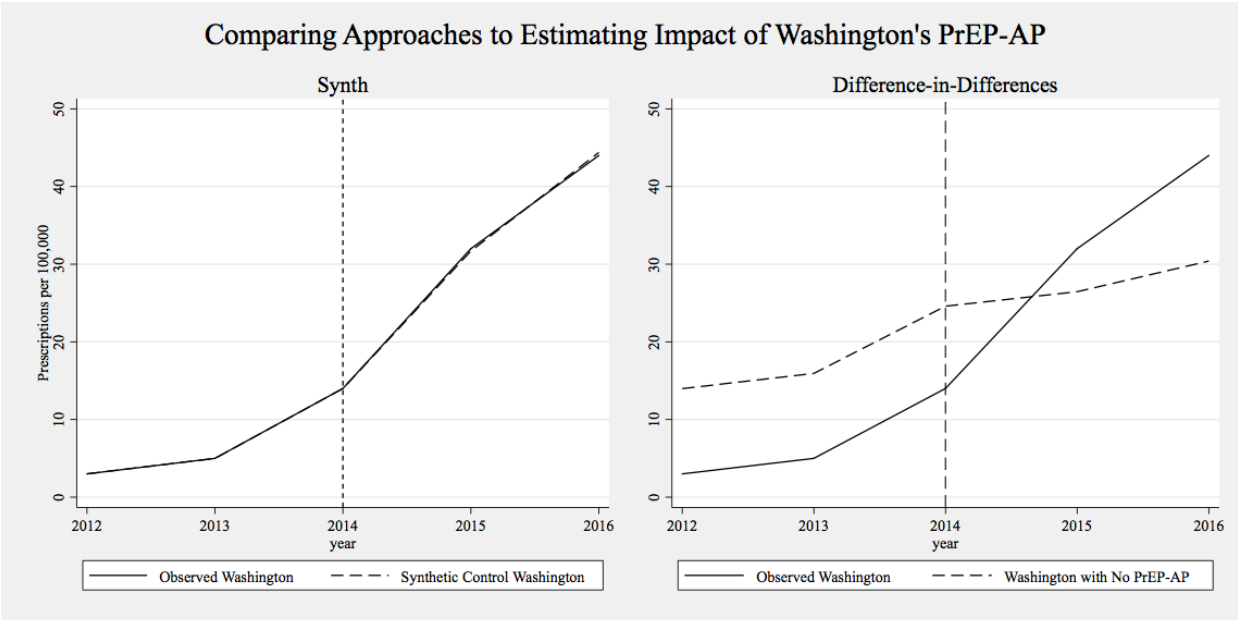


Figure 20

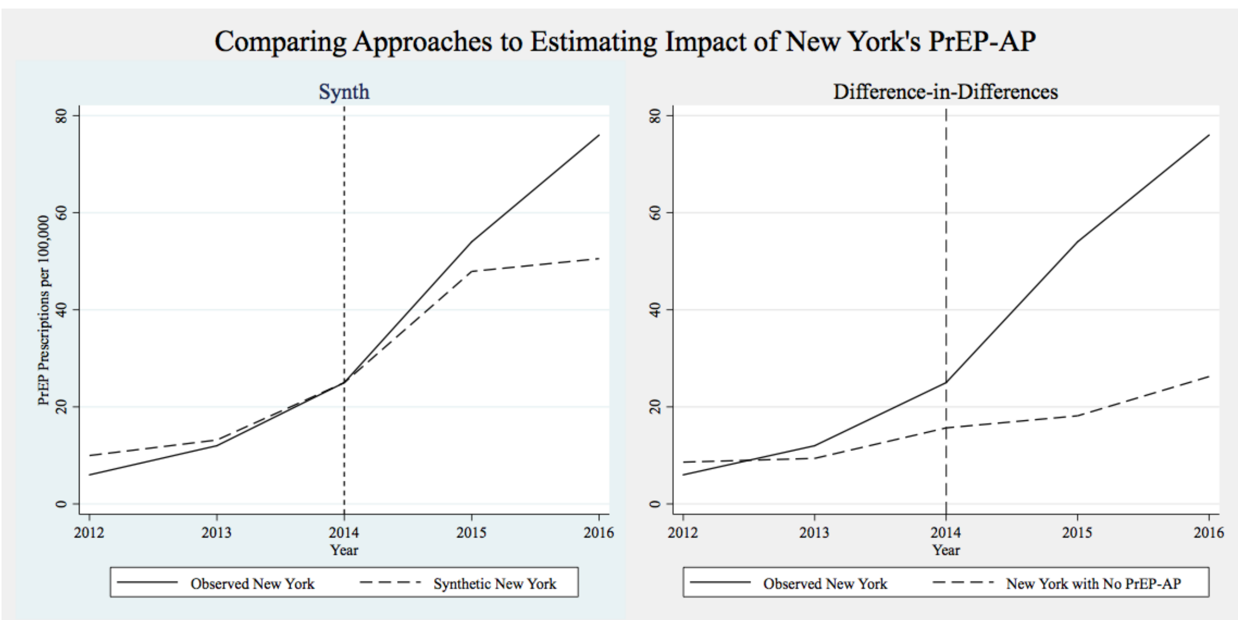


Figure 21

In New York, the difference-in-differences and synth estimation for the impact of this program are quite similar. The difference-in-differences estimation implies that an increase of 31.65 additional prescriptions per 100,000 is associated with the timeframe post-program implementation in New York. Similarly, synth estimates that this program is responsible for an increase of approximately 27 PrEP prescriptions per 100,000 over the synthetic control. When translated into real terms, this implies that this PrEP-AP resulted in an increase of between 5,000-6,000 additional PrEP prescriptions in New York. Assuming that each of these prescriptions resulted in an HIV infection averted, and given the CDC's lifetime treatment estimate for an HIV infection of $379,668 in 2010 dollars (Centers for Disease Control and Prevention, 2017), this means that between $1,898,340,000 - $2,278,008,000 in HIV treatment costs over the lifetime of these individuals may have been averted.

This figure is very likely an overstatement of the costs averted. First, it is reliant on each patient having perfect adherence, and remaining on PrEP for as long as they were partaking in behavior which puts them at risk of HIV. Next, it assumes that had each of these individuals not been on PrEP, they would have become infected with HIV, which is most certainly not the case. Thus the actual impact, in terms of number of HIV cases prevented and costs averted, is likely much lower. However, even if one utilizes a much lower estimate of 600 HIV infections prevented by this program, this still translates into $227,800,800 in lifetime HIV treatment costs averted.

Washington's program, on the other hand, appears to have had little impact. If we take the results of the difference-in-differences analysis at face value, and disregard the synth results, I estimate that this program was associated with between a 700-900 increase in PrEP prescriptions, which is quite similar to the number reported as receiving benefits from Washington's PrEP-AP in late 2015 (Aleshire, 2016). In other words, the benefits of Washington's PrEP-AP were very limited. When calculating the cost savings from lifetime treatment cost averted, if we assume that this program resulted in 900 HIV infections averted, I estimate that the maximum costs averted in terms of HIV treatment is $341,701,200. If instead we assume that 70 HIV infections were averted, I find a benefit of $26,576,760.

8 Limitations

I am first limited by the sensitivity of synth to different combinations of lags and predictors. I believe that my robustness checks, in addition to the difference-in-differences approach, strengthen these results; however, on its own, synth seems to be offer somewhat ambiguous results.

I am next limited by my definition of "effective". I define an effective PrEP-AP as one which increases prescriptions per 100,000, and ignore other important factors of how effective a program is – namely whether or not it increased prescriptions among those in high risk groups. I conclude that Washington's program did not increase prescriptions by as much as New York's, but this is irrelevant if New York had a large increase in prescriptions among the "worried well", but none among those actually in a high risk group. In such a scenario, the number of HIV cases prevented would likely be zero, and thus this program would be entirely ineffective, under a traditional definition. I further do not consider the cost-effectiveness of these programs, given that I do not have the data to support such an analysis.

I am also limited in that I cannot break down New York's program into each individual component, to determine which component had the most impact. This limits conclusions that other public health departments can draw from this study. Rather than being able to determine which portion of New York's PrEP-AP was most efficacious, we have only the vague conclusion that a more comprehensive programs translates into a greater increase in prescriptions.

Finally, I am limited by my data. First, I do not have an ideal amount of data pre-treatment to use synth effectively. This drug was approved in 2012, and I only have annual data from AIDSvu. Second, I only have data at a state level, which misses many local community factors, and doesn't allow localized analyses on specific metro areas, such as New York City and Seattle. Finally, my proxy variables may be inappropriate choices to use as criteria for an ideal synthetic control.

9 Conclusion

New York's program seems to have increased PrEP prescriptions by more than Washington's. This is what we would logically expect, given the comprehensiveness of New York's program. There are a variety of reasons behind slow PrEP takeup, all of which must be addressed for takeup to meet its full potential.

My results imply that state health departments in areas with low PrEP take up and high HIV incidence – such as the South – ought to focus their efforts in multiple areas, rather than just on subsidizing cost. A program which just provides free PrEP, as in Washington, will likely be less successful than a comprehensive program which addresses the multiple factors behind low PrEP take up. Perhaps to address the stigma and lack of access to prescribers, state health departments in regions with low PrEP takeup could introduce "prescribe by mail" services, where individuals are able to complete the required pre-requisite and continued tests by mail, and be prescribed this drug from the comfort of their home. This, combined with an ad campaign and highly subsidized (or free) PrEP would likely increase prescriptions greatly, particularly in the South.

Finally, these results reveal the unreliability of using synth naively, without solid theory and a strong ethical binding. Despite the Urban Institute's claims that synth is "not a black box" (2017), the complexity of the background computations and mathematics make it appear that way to the casual observer. In the hands of the clever but unscrupulous, this tool could almost certainly be used to twist data into saying almost anything, or supporting any policy.

Future research should focus on recent developments in the PrEP access and marketing landscape, including evaluating the impact of Gilead's recent nationwide television advertising campaign, which began running during the nightly news between June 2018-August 2018 (Gorman, 2018). Such a campaign provides an excellent opportunity for a natural experiment, assuming appropriate data is available, given the fact that such ads may not air in certain markets. Further research should additionally focus on evaluating the impact and efficacy of California and Florida's recently launched PrEP programs. Finally, future research should also examine who is actually taking Truvada as a result of these programs, to determine if takeup is actually increasing among those who need it, or if it is instead increasing among the worried well. Knowing these will help state public health departments develop appropriate, evidence-based policies.

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