

# PrEP and Moral Hazard\*

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## Abstract

Approved nationally in 2012, Pre-exposure prophylaxis (PrEP), a drug that effectively prevents HIV infections, has the potential to save lives but also carries a risk of moral hazard if people engage in riskier sex practices after taking the drug due to lower HIV risk. We document the first evidence of PrEP on aggregate STI and HIV infections, showing there is an increase in STIs and a decrease in HIV infections in high PrEP states. Using the pre-treatment variation in gay male and HIV and AIDS prevalence, we show that STI rates were parallel in high and low PrEP states before the introduction of PrEP and begin to diverge afterwards. However, HIV infections were consistently downwardly trending in high PrEP states before PrEP with no break at the introduction of PrEP, making inference of the effect of PrEP on HIV infections difficult. Specifically, we show that one additional male PrEP user increases chlamydia infections by 0.73 cases and gonorrhea infections by 0.83 cases. However, the relative cost of treating these STIs is smaller than that of HIV. To break even on cost, the 88,151 male PrEP users in 2017 would need to prevent only 31 male cases of HIV, a prevention rate of 0.04%.

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# 1 Introduction

HIV and AIDS have devastated lives by cutting them short, hitting the gay community hardest. At the start of AIDS epidemic in the early 1980s, an HIV or AIDS infection sentenced one to death, but as investment in medical interventions and treatments improved, so did health outcomes. One potential concern with new medical treatments is the potential of unintended consequences of people adjusting their behavior to new medications, attenuating the effect of an intervention. Researchers have shown significant moral hazard responses to HIV medical breakthrough, wherein people adjust their behavior and engage in riskier sex practices if the consequence of that behavior becomes less dangerous (Lakdawalla, Sood and Goldman (2006); Chan, Hamilton and Papageorge (2015)).

We examine the effect of a new HIV treatment, Pre-exposure prophylaxis (PrEP), a drug that effectively prevents HIV infections, on aggregate STIs and HIV infections. Approved nationally in 2012, PrEP has the potential to save lives but also carries a potential risk of moral hazard with it. PrEP has been clinically shown to be effective at preventing new HIV infections in the medical literature, and it has steadily gained use and popularity among men who have sex with men (MSM). Users of PrEP may rationally adjust their sexual behavior and may have sex with more partners and may stop wearing condoms given the drastically decreased likelihood of contracting HIV. PrEP may reduce the number of HIV infections but may give a trade off of increased STIs. However, PrEP could possibly have no effect on HIV infections if all PrEP users used condoms and safer sex practices before PrEP, underlying the importance of examining the effect of PrEP on STIs and HIV.

We are the first to examine the relationship between the roll out of PrEP and aggregate STI and HIV levels. We contribute to the medical literature that has examined PrEP, but they have not viewed the drug in the context of aggregate STI levels, focusing on the people that actively take PrEP. However, this approach could underestimate the effect that PrEP has on aggregate level since STIs can spread to people who are not taking PrEP. We also add to the literature on moral hazard as well as contributing to an open question on increasing

STI rates.

We obtained data on state level PrEP usage per 100,000 for 2012 to 2017 from AidsVU, an organization created by Emory University’s Rollins School of Public Health and Gilead Sciences Inc., the company that manufactures PrEP. We paired that data on STI rates from the Center for Disease Control (CDC) from 2008 to 2017 for chlamydia, gonorrhea, syphilis and HIV infections. PrEP usage and STI rates are broken down by sex and by age, heterogeneity that we exploit in our analysis.

A basic OLS analysis regressing STI rates on PrEP rates show significant associations between male PrEP rate and male STIs. However, there are potential issues of endogeneity where states with increasing STI or HIV rates are most likely to adopt PrEP. We cannot estimate the effect of PrEP in a traditional difference-in-differences framework because it was introduced nationally in 2012. To ameliorate these endogeneity concerns, we exploit a pre-treatment measure of the intensity of PrEP exposure in a difference-in-differences framework. Specifically, we follow analyses by Bleakley (2007) and Alpert, Powell and Pacula (2018), which examine treatments without staggered rollouts using pre-treatment variation. Bleakley (2007) uses pre-treatment measures of hookworm exposure to examine the effect of hookworm eradication in the American South. Alpert, Powell and Pacula (2018) examines a nation-wide reformulation of OxyContin making abuse of the pills more difficult. They use the pre-treatment abuse of opioids before the national change to and show those states had the largest increase in heroin abuse following the OxyContin reformulation.

Following a similar strategy, we use pre-treatment variation in the gay male population, which we show are the areas that use PrEP the most. Given that PrEP is targeted and mostly used by MSM, we use female STIs as an additional control group for male STIs. We show that prior to the introduction of PrEP in 2012, the rate of male and female STIs are parallel in low and high PrEP states, and after 2012, STI rates diverge with male STIs increasing. However, we find that HIV rates are consistently declining before the introduction of PrEP in states with a large gay population with no break when PrEP is introduced, making it difficult

to estimate the casual effect of PrEP on aggregate HIV levels. Given that HIV infections are declining faster in states, our estimates on HIV infections will likely be downwardly biased, overstating the effect of PrEP on HIV infections. Specifically, we find that a 1 additional PrEP user results in 0.73 additional cases of male chlamydia and 0.83 additional cases of male gonorrhea and 0.1 fewer cases of male HIV<sup>1</sup>.

Next, we explore age heterogeneity, exploiting that people aged 25-45 take PrEP at a higher rate than other age groups. We show that the largest increases in male STIs occur in the age group that take PrEP the most. We then conduct several robustness checks. First, we replace our measurement of pre-treatment PrEP intensity with HIV prevalence instead of the gay population. While these measures are correlated, one may think that exposure to HIV would make a better measure of pre-treatment PrEP intensity. We show our results hold in that context as well. Next, we look at STI testing to see if our effect is due to increased reporting of STIs. We find no significant change in the number of HIV tests administered following the rollout of PrEP. Then, we conduct a simple counterfactual analysis where we subtract the number of PrEP users multiplied by the estimates of the effect of PrEP on that STI. We show that without PrEP in 2017, male chlamydia rates would be 7-16% lower in our counterfactual estimate than what was observed.

Finally, we conclude our analysis with basic back of the envelope calculations assessing the costs and benefits of PrEP. While PrEP may increase STIs like gonorrhea and chlamydia, the relative cost of treating HIV is much higher. We take lifetime cost estimates of chlamydia, gonorrhea, syphilis, and HIV and examine the costs and benefits of these STIs caused or prevented by PrEP. Given that HIV infections are downwardly trending before and after PrEP's introduction, our estimates of the effect of PrEP on HIV infections are likely overstated, making it difficult to get an accurate cost-benefit analysis. Alternatively, we will look conduct a break-even calculation. We find that in 2017, PrEP increased male chlamydia and gonorrhea rates to a level that cost approximately \$9 million. Given the

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<sup>1</sup>Again, the HIV estimate is likely overstating the effect of PrEP on HIV

lifetime cost of treating HIV is about \$300,000, the 88,151 male PrEP in 2017 would need to prevent only 31 cases of HIV to offset the costs of the additional STI treatment.

We show in the first analysis that PrEP has a significant, causal effect on aggregate STIs, costing millions of dollars for treatment. However, given the relative cost of STI treatments, PrEP can still be an effective public health tool. Our research suggests an increased need of condom usage and education for people who are using PrEP.

## 2 Literature Review

The medical literature has studied PrEP usage for several years, examining the effectiveness of PrEP along with examining potential moral hazard factors of the HIV-prevention drug. We are the first in the social science literature to examine PrEP and the potential moral hazard consequences of increased risky behavior and corresponding STIs. There are several reasons why one may want to examine this question through the lens of social science. First, the medical literature has not examined the effect of PrEP on aggregate STI levels. They have mostly been confined to looking at the people who are taking PrEP, and it seems plausible that there are potential spillovers of STIs to the non-PrEP community. Second, there is the potential of the Hawthorne effect where enrolling PrEP takers into a study may impact their behavior (Adair, 1984). Enrolling someone into a study has been shown to alter behavior and the medical literature on PrEP is not immune to those concerns. By using observational data on PrEP and STIs, we can circumvent this concern. Finally, the medical literature has found varying effects on how PrEP affects sexual behavior.

The medical literature varies in their approach and findings in examining the effect of PrEP on increased risky behavior. Even the meta-analyses differ in their findings of the effect of PrEP on STIs. Traeger et al. (2018) examines 8 studies on STI incidence and 13 studies on condom usage, and they find significant increases in rectal chlamydia and any STI diagnosis with a stronger association in the later studies. They also find that condomless

sex increases in most studies. However, Freeborn and Portillo (2018) conducts a different meta-analysis and found no conclusive evidence on increased STIs.

Some studies focus mostly on surveying MSM before and after administering PrEP while taking regular HIV and STI tests. Volk et al. (2015) used administrative data and surveys of MSM in San Francisco and found that after a year 50% had any STI, 33% had a rectal STI with 33% having chlamydia, 23% having gonorrhea, and 6% having syphilis. Volk et al. (2015) also found condom use decreased for 41% and number of sexual partners increased for 11%. Marcus et al. (2016) found similar results with total of 771 STI diagnoses for 972 PrEP users with many people having multiple STIs. They found that after a year, 42% had any STI, 27% had a rectal STI, 26% had chlamydia, and 23% had gonorrhea. There were significant increases over the baseline for chlamydia and gonorrhea diagnoses.

However, there are some studies that find no change in relative STI rates. Liu et al. (2016) surveyed MSMs before and after PrEP and found that the proportion of those having condomless receptive sex stayed constant at 65% with an insignificant increase in STIs. McCormack et al. (2016) conducted an RCT in the UK. They randomized their sample into people who received PrEP immediately and those who would receive it after 1 year. However, they cut the study short as some participants in deferred PrEP group began to contract HIV and felt ethically obliged to give people in the control group PrEP. Those who immediately received PrEP reported more condomless anal receptive sex and had higher incidences of STIs, but the significance of the increased STIs went away after controlling for additional STI screenings.

Even though the medical literature may have different findings on whether STIs increased or decreased as a result of PrEP, they consistently find that the STI incidence at the baseline was already high before administering PrEP (Volk et al. (2015); Liu et al. (2016); McCormack et al. (2016); Hosek et al. (2017)). Hosek et al. (2017) surveyed young MSM on PrEP and found that 80% reported condomless sex and 58% reported condomless receptive sex. The MSM population that would be taking PrEP already engages in relatively risky sexual

behavior that by some studies becomes even riskier following PrEP.

This research also contributes to the robust economics literature on moral hazard. Economics has a long literature on moral hazard and unintended consequences with seminal work by Peltzman (1975), which suggested that innovations in driving safety would be muted through increased risky behavior. Cohen and Einav (2003) found small changes in behavior from seat belts relative to what Peltzman hypothesized. However, Cohen and Dehejia (2004) found that automobile insurance incentivized riskier driving through moral hazard and caused an increase in traffic fatalities.

Moral hazard is not limited to instances of insurance though. There is a growing literature on medical breakthroughs having unintended consequences. In particular, broadening naloxone access, a drug preventing opioid led to more opioid related emergency room visits and opioid related crime with no decrease in opioid deaths (Doleac and Mukherjee, 2018). The same study showed that broadening naloxone access also increased fentanyl use, a more potent opioid than heroin (Doleac and Mukherjee, 2018).

In a context closer to our own, Lakdawalla, Sood and Goldman (2006) consider the moral hazard effects of HIV treatment breakthroughs on risky sexual behavior. They find that treating HIV-positive individuals more than doubles their number of sexual partners and contributed to a large increase in HIV incidence during the same period. Chan, Hamilton and Papageorge (2015) provide a dynamic model of this behavioral response to the availability of life-saving HIV treatment. They show that both HIV-negative and HIV-positive men increase their risky sexual behavior when the cost of contracting HIV falls.

We contribute to the literature in multiple ways. First, we are the first non-medical study examining the moral hazard impacts of PrEP. Second, we are the first to document the affect of PrEP on aggregate STI levels, which is critically important given that diseases can have spillovers and infect those that are not on PrEP. Third, while the medical literature has documented that PrEP is effective at preventing HIV infections, it is unclear if that finding translates to the aggregate level of HIV diagnoses as people may be substituting

away from condom use in replace of PrEP. We also contribute more broadly to the economics literature on moral hazard and unintended consequences and to the epidemiology literature on increasing STI rates.

### 3 Data

Data on four of the most common STDs: chlamydia, gonorrhea, HIV, and syphilis<sup>2</sup> comes from the CDC National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) database. It contains information on the number of cases of each STD at the state, year, sex, age group and ethnicity level; it also contains the population of each respective group. Using the number of cases and the population we construct our outcome variable – the STD rate per 100,000 population. Data is available for all of the 50 states and the District of Columbia. Our main sample includes male and female (separately) aged 20 and up for the years 2008-2017. Additional analyses use different age and race groups.

For our main sample, we use persons aged 13 and up. The CDC reports STDs in broad age bins, where the earliest age bins are 13-24. During our sample years, PrEP was only approved for persons aged 18 and up, although it was occasionally prescribed off-label for younger persons (Highlymen, 2018). Due to lack of awareness, no insurance coverage, or stigma, older adolescents also under use PrEP. Magnuson et al. (2018) reports that only 2,324 males aged 12-19 started using PrEP over the years 2012-2017 across the United States, compared to 16,739 males aged 20-24. For older males, PrEP usage is even higher, as will be detailed in section XX. Additional analyses using other age groups is detailed in section XX.

Our PrEP use data comes from AIDSVu, an online source for HIV related data. AIDSVu reports the number of PrEP users and rate per 100,000 at the state, year, and sex level as

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<sup>2</sup>CDC reports 3 types of Syphilis - primary and secondary, early latent and congenital. We use primary and secondary as that is what is a typical syphilis case with symptoms appears as. Latent syphilis has no symptoms, so one would be unlikely to seek treatment for it, and congenital syphilis is when a mother passes syphilis to a newborn child, which is not a relevant mode of transmission for this study.



well as separately by the state, year, and age level. The AIDSvu PrEP data was obtained by AIDSvu by researchers at the Rollins School of Public Health at Emory University in conjunction with Gilead Sciences, Inc., the manufacturer of PrEP. The data is based on Symphony Health patient-level prescription data from a sample of pharmacies, hospitals, outpatient facilities, and physician practices across the United States. It encompasses all prescription payment types (Including Medicare Part D and Medicaid). Since the prescriptions were for Emtricitabine/Tenofovir Disoproxil Fumarate, which besides PrEP is also used for other indications (such as HIV treatment), Gilead used a stringent algorithm to identify those prescriptions which were indeed PrEP. Prescriptions that could not be attributed to a specific indication were removed, although a certain share of those were PrEP. In addition, prescriptions from certain closed healthcare systems that did not share data with Symphony Health were not included. Therefore, the PrEP use data slightly underestimates the number of PrEP users. A minimum duration of 30 days was required for an individual to be considered a PrEP user, and to be considered a user in a given year, at least one day of that 30-day minimum period was required to fall within that calendar year.

Given that this drug is targeted toward gay men, we want to examine how this treatment differentially affects states with a higher gay male population. Unfortunately, there is little data on the distribution of the LGBT population, so we use data on same-sex partnerships from the 2000 Census. The 2000 Census asks about household composition, which we use to infer sexual orientation. We proxy for the gay male population in each state with data on male same sex partnerships from the 2000 Census. Measuring the gay male population using the Census would likely underestimate the amount of gay men since it is only capturing gay men in committed relationships. However, it should give an approximation of the relative ranks of states with respect to the size of their gay male population, i.e. California has a higher percentage of same-sex partnerships than Wyoming even if both are underestimated. We calculate the share of male same-sex partnerships by dividing the number of male same-sex partnerships and dividing that by the total number of partnerships in a state.

Additional demographic and economic covariates at the state and year level are derived from the yearly American Community Surveys for 2008-2016. These include the racial makeup of the state, the natural logarithm of state GDP, the percent on Supplemental Nutritional Assistance Program, the unemployment rate, the poverty rate, and the state minimum wage.

As will be explained in Section X, the FDA recommends increased STD testing for persons on PrEP, which could potentially confound our results. In order to tackle this, we proxy for STD testing by analyzing HIV testing data from the Behavioral Risk Factor Surveillance System (BRFSS). The BRFSS data is obtained through telephone interviews that ask participants regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. More than 400,000 adult interviews are conducted yearly in all 50 states and the District of Columbia. Participants were asked the month and year of their last HIV Test. In 2016 for example, the variable was available for 21.2% of participants<sup>3</sup>. Although the variable is not available for the majority of participants, it is likely that participants who had testing done in the months preceding the interview will remember it. Thus, recent testing data could be more complete, and that is the data we are interested in. From that variable, we construct the share of male participants aged 18-45 in each state that had HIV testing in the 6 months preceding the interview for the years 2008-2016.

### 3.1 Descriptive Statistics

Table 1 provides summary statistics for states throughout our time period as well as split by those states that had the lowest and highest PrEP expansion. We split the states in the quartiles based on their PrEP expansion. “Low PrEP” states are in the lowest quartile of PrEP take-up, whereas states labeled “High PrEP” states are in the highest quartile of PrEP take-up. We present the statistics for the whole sample as well as split between pre-PrEP in 2008-2011 and post-PrEP in 2012-2017.

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<sup>3</sup>The rest of the participants were either not sure, didn’t know, refused to answer, were not asked or their data is missing

We detail the male rate for different STDs for our overall sample and between low and high PrEP states before and after the adoption of PrEP. Before the introduction of PrEP, high and low take-up states had similar male chlamydia and gonorrhea rates with 298 cases per 100,000 of male chlamydia in high PrEP states compared to 293 cases per 100,000 for in low PrEP states and 110 cases of male gonorrhea in high PrEP states versus 121 cases per 100,000 low PrEP take-up states. High PrEP take-up states had much higher rates of male syphilis and HIV relative to the low-PrEP states though. We also show that our treatment in male PrEP rate, defined as users per 100,000, has a large difference between high and low PrEP take-up states. We also exploit the variation in the percentage of male same-sex partnerships in the 2000 Census, which is defined between 0 and 100 for interpretation of regression coefficients. High PrEP take-up states had higher percentage of male same-sex partnerships at 0.69% compared to 0.39% for low PrEP take-up states. We also present our state by year level control variables. High PrEP take-up states were also richer and had more Black and Hispanic people relative to the low PrEP take-up states.

First, Figure 1 illustrates the overall number of PrEP users per 100,000 population separately for male and female. Since its introduction in 2012, the number of male users grew rapidly, which makes sense given the appeal toward gay men for HIV prevention. By 2017, there were 94,146 male users and 6,045 female users which corresponds to a PrEP rate of 70.6 for male and 4.3 for female. While the female PrEP rate remained rather constant over time, the male PrEP rate grew 2,300% since its introduction. Given heavy marketing brought by the warm endorsement of various public health organizations, the introduction of generic PrEP, and the Trump administration plan to eradicate HIV infections by 2030<sup>4</sup>, the fast adoption of PrEP is unlikely to halt.

Next, we show that in some states, users barely adapted PrEP while other states saw large increase in PrEP users. In Figure 2, we show the male PrEP rate across states in 2017, illustrating this spatial variation. States in the West Coast and Northeast as well as Florida,

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<sup>4</sup><https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview>

Georgia, and Illinois were largest adopters of PrEP. Unsurprisingly, these states have a larger share of the gay population, which we show in Figure 3, displaying the percentage of the partnerships in a state that are same-sex and male in the 2000 Census. Given that this drug is marketed toward and taken by gay men, the distribution of the gay men before the introduction of PrEP should be indicative of the states that would be more likely to adopt PrEP.

Next, we plot the evolution of male STD rates for states with different PrEP take-up. We divide states based on their quartiles of PrEP take-up in 2017. We then plot the evolution of the average male STD rates for each quartile of states for the four STDs separately. Quartile 1 is the quartile of states that had the highest PrEP take-up, whereas quartile 4 is the quartile of states that experienced the lowest PrEP take-up. We present the trends in STDs rate in Figure 4.

Male STD rates, with the exception of HIV, were trending upwards in all states during the past few years, at a faster pace than previous years, to reach record highs each year. In just 5 years between 2012 to 2017, male chlamydia, gonorrhea and syphilis rates have increased on average by approximately 36%, 106% and 91%, respectively, compelling the CDC to call for urgent action<sup>5</sup>.

Figure 4 shows that the states that experienced the fastest increases in recent years in male chlamydia and gonorrhea rates were the states with in the highest quartile of PrEP take-up. The chlamydia and gonorrhea rates seem to be evolving in parallel for all of the states based on PrEP take-up before PrEP is introduced, suggesting these states may be good counterfactuals of each other. After PrEP is introduced, states with the largest increase in PrEP take up see the largest increases in STDs. In 2008, male chlamydia rates in states with high PrEP take-up were similar to states with lower PrEP take-up, but by 2017, they were approximately 20% higher with a similar finding for gonorrhea. Syphilis rates began increasing at a faster pace in states with high PrEP take-up 2 years prior to the introduction

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<sup>5</sup><https://www.cdc.gov/media/releases/2017/p0926-std-prevention.html>

of PrEP, and increased at a faster rate after.

With respect to male HIV rates, Figure 4 shows that rates were declining throughout the period for states in the top 3 quartiles of PrEP take-up. Moreover, the higher the PrEP take-up, the faster the decline in rates. This decline could be a result of efforts of numerous public health organizations groups that began in the early 2000's to combat HIV. These efforts were concentrated in states with high male HIV rates, which were the states that had large gay populations, which are also the states that had higher PrEP take-up once it was introduced. These efforts to reduce HIV could have been coupled with efforts to combat other public health concerns such as STDs. This simultaneous reduction does not seem the case, since although the reduction in HIV occurred throughout the period, most male STD rates were quite flat at the beginning of the period. The fact that male HIV rates were trending differently prior to the introduction of PrEP across states with different PrEP take-up, provides a challenge for the identification of the effect of PrEP on male HIV rates as states with lower PrEP take-up may not provide an accurate counterfactual for male HIV rates in states with higher PrEP take-up. Estimating the effect on HIV would likely bias the any negative effect downward from the downward trends of states with high PrEP take-up that existed before the introduction of PrEP. We mainly focus on the effects of PrEP on other STDs because of the difficulty in estimating the effect on HIV.

## 4 Identification Strategy

In order to best estimate the effect of PrEP on STDs we employ different specifications. First, we employ a simple differences-in-differences framework to see how the change in PrEP usage affects changes in STD, followed by a triple-differences analysis to compare the change between male and female PrEP usage and male and female STDs. Our difference-in-difference estimate is limited to men in this equation and is defined as:

$$STD_{st} = \beta PrEP_{st} + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{st} \quad (1)$$

Where  $STD_{st}$  is the rate of STDs defined as cases per 100,000 in state  $s$  in year  $t$ . We examine chlamydia, gonorrhea, syphilis, and HIV separately.  $PrEP_{st}$  is the PrEP rate per 100,000. We include a set a demographic and economic controls in  $X_{st}$ , which include racial demographics of each state, state GDP, and the SNAP, poverty, and unemployment rate. Finally we include state- and year-fixed effects in  $\mu_s$  and  $\tau_t$ , respectively.

Our coefficient of interest is  $\beta$ , which gives the effect of one additional male PrEP user on male STD cases because  $PrEP_{st}$  and  $STD_{st}$  are both defined as rates per 100,000 people. As we include state and year fixed effects, the effect is identified from the changes in PrEP rates within the same state over time and relative to the corresponding changes in other states. We run the regression separately for each STD. The regressions are population weighted and the errors are clustered at the state level.

Given that the use of PrEP is concentrated among gay men, women make a good comparison group for men, especially given that a small share of PrEP users are women. We are examining the how the difference between male and female STDs change in states with larger take-up of PrEP. Specifically, we estimate:

$$STD_{stg} = \beta_1 PrEP_{stg} + \beta_2 Male_g + \beta_3 Male_g * PrEP_{stg} + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{stg} \quad (2)$$

We maintain the past notation as before with an additional variable with  $Male_g$  as an indicator for male observations. We include an additional subscript  $g$  for gender  $g$ . The coefficient of interest  $\beta_3$ , identifies the the differential effect of one additional PrEP user on men compared to women, and  $\beta_1 + \beta_3$  identifies the effect of one additional PrEP user on male STDs.

The identifying assumptions in both of these specifications is that STDs and the dif-

ferences in male and female STDs in states with different PrEP rates would have evolved in parallel in the absence of PrEP. While this assumption is inherently untestable, we can examine what how the trends in STDs evolved before and after the treatment, which we will discuss further in the next section.

## 4.1 Intensity of Pre-Treatment Variation

One of the difficulties in estimating the effect of a national rollout of a treatment is that there is little temporal variation to examine how trends differed in a traditional event study. One common strategy to get around this lack of differential treatment starts is to use pre-treatment variation as an intensity of treatment. Use pre-treatment variation has been used to analyze the effect of hookworm eradication, the effect of making opioids harder to abuse, and the effect of the Affordable Care Act’s free contraception mandate (Bleakley (2007); Alpert, Powell and Pacula (2018); Willage (2020)). Given that PrEP is targeted toward gay men given their unique risk of contracting HIV, we exploit the pre-treatment variation in the gay population as the states with a larger gay population would likely be the states that had the largest increase in PrEP utilization. We use the household information in the 2000 Census to infer sexual orientation based on if someone is in a same-sex partnership, which is common in the literature on LGBT economics (Klawitter and Flatt (1998); Black et al. (2003); Gates (2009)). Specifically, we estimate the below equation:

$$STD_{st} = \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \beta_t \mathbb{1}(Year = t) * \%MaleSSP_s + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{st} \quad (3)$$

Where the notation is the same as the previous equations in this section with some additions.  $\%MaleSSP_s$  gives the percent of partnerships that are male same-sex partnerships in state  $s$  from the 2000 Census<sup>6</sup>.  $\%MaleSSP_s$  is defined between 0 to 100 for better interpretability of regression coefficients. We have indicators for each year that are interacted

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<sup>6</sup>The Census asks for people in a household to list their relationship to the head of the household. Partnerships are defined as households with two adults that are either married or in a partnership.

with  $\%MaleSSP_s$  with the exception of 2011, which is used as the comparison year because it is the year before PrEP was introduced. The interpretation on  $\beta_t$  is how many additional cases of per 100,000 of an STD occur in year  $t$  with a 1 p.p. increase in the percent of male same-sex partnerships. For context, the difference in the male same-sex partnerships between North Dakota and New York is about 0.5 p.p. We run the regression separately for each STD and for male and female. The regressions are population weighted and the errors are clustered at the state level.

We can also estimate the effect of the  $\%MaleSSP_s$  on PrEP to verify that the states with the largest gay male population would see the largest expansion in PrEP take-up. The notation is the same as in equation (3), where  $PrEP_{st}$  is now the dependent variable. Specifically, we estimate:

$$PrEP_{st} = \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \alpha_t \mathbb{1}(Year = t) * \%MaleSSP_s + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{st} \quad (4)$$

Following the same logic as detailed previously, we also estimate a similar specification that includes women as a third difference. Specifically, we estimate the following equation:

$$STD_{stg} = \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \beta_t^1 \mathbb{1}(Year = t) * \%MaleSSP_s + \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \beta_t^2 \mathbb{1}(Year = t) * Male_g + \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \beta_t^3 \mathbb{1}(Year = t) * \%MaleSSP_s * Male_g + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{stg} \quad (5)$$

Where all the variables are as defined in (3) and  $Male_g$  is an indicator for male observations. The coefficients of interest are the  $\beta_t^3$ s which are interpreted as the additional cases per 100,000 of a male STDs compared to female STDs in year  $t$ , compared to the baseline year, that occur with a 1 percentage point increase in male same-sex partnerships.

Our identifying assumptions are similar to ones mentioned in the previous specifications.



The assumption is that states with a larger gay population would have similar trends in STDs as those with a smaller gay population in the absence of PrEP. While this assumption is untestable, we can examine how STDs were evolving before the differential treatment of states, which will be seen by plotting  $\beta_{2008}^3$ ,  $\beta_{2009}^3$ , and  $\beta_{2010}^3$  in the results section. Our identifying variation, the percentage of male same-sex partnerships by state, is presented in Figure 3.

## 4.2 Using Instrumental Variables to Scale Effect

Using the pre-treatment variation in these difference-in-differences specifications scales the effect size in terms of the pre-treatment variation and not in terms of the treatment. This interpretation on the effects make it harder to scale the effect size in a meaningful way. One potential way to scale the effects sizes produced in using the pre-treatment variation is to examine how much the pre-treatment variation also affects PrEP usage. When we understand how pre-treatment variation affects the treatment and the outcome, we can then scale the effect to see how the treatment affects the outcomes. Specifically, if we estimate equation (4) on PrEP with this equation:

$$PrEP_{stg} = \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \alpha_t^1 \mathbb{1}(Year = t) * \%MaleSSP_s + \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \alpha_t^2 \mathbb{1}(Year = t) * Male_g + \sum_{\substack{t=2008 \\ t \neq 2011}}^{2017} \alpha_t^3 \mathbb{1}(Year = t) * \%MaleSSP_s * Male_g + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{stg} \quad (6)$$

In this specification,  $\alpha_t^3$  gives the additional male PrEP users per 100,000 compared to female PrEP users in year  $t$ , compared to the baseline year, that occur with a 1 percentage point increase in male same-sex partnerships. Now that the effect of the gay population on PrEP is established, and the effect of the gay population on STDs, we can then scale the effects to reflect the effect of PrEP on STDs. We represent that effect with  $\delta_t^3 \equiv$

$\beta_t^3/\alpha_t^3$ . Notably, this scaling method is essentially an instrumental variable approach where  $\beta_t^3$  represents the reduced form effect,  $\alpha_t^3$  represents the first stage, and  $\delta_t^3$  would represent the IV effect.

To get the effect of PrEP on STDs, we estimate these two equations with the first stage equation represented in equation (5), and the second stage equation represented here:

$$STD_{stg} = \delta_1 \widehat{PrEP_{stg}} + \delta_2 Male_g + \delta_3 \widehat{Male_g * PrEP_{stg}} + \gamma X_{st} + \mu_s + \tau_t + \epsilon_{stg} \quad (7)$$

Where the notation is the same as equation (2), but  $PrEP_{stg}$  and  $Male_g * PrEP_{stg}$  are instrumented for using equation (6). While this is an instrumental variable approach, these regressions are for helping to scale the effects shown in equation (4).

## 5 Results

### 5.1 PrEP Rate Specifications

Table 2 reports the results from estimating equations (1) and (2) separately by STDs. The first column for a STD gives the results from equation (1) and the second column gives the results from equation (2). The first equation is limited to male STDs and PrEP rate while the second one compares male to female STDs and PrEP rate. All specifications include state by year controls as well as state and year fixed effects and are weighted by population. Standard errors are clustered at the state level.

In column (1) for each STD, we find significant effects for the male PrEP rate on male chlamydia, gonorrhea, and HIV. We estimate that each additional male user of PrEP increases the incidences of male chlamydia and gonorrhea by 0.431 and 0.337, respectively, and reduces HIV diagnoses by 0.12. However, HIV diagnoses are likely downwardly biased given the discussion in the Identification Strategy Section.

We then compare men to women in column (2) for each STD. We report the estimates for the main effect coefficients and the interaction term  $Male * PrEP$ . We also report the overall effect of the male PrEP rate on male STDs, calculated as  $PrEP + Male * PrEP$ .

The coefficient on  $PrEP + Male * PrEP$  is our coefficient of interest in column (2). We estimate that each additional male user of PrEP increases the incidences of male chlamydia, gonorrhea and syphilis by 0.744, 0.629 and 0.071 cases, respectively, relative to female STDs. We also find that one additional male PrEP user decreases male HIV diagnoses by 0.024 cases relative to female HIV diagnoses, but again, the estimate on HIV may be downwardly biased, overstating the true effect.

The STD estimates other than HIV are higher than the difference-in-difference estimates. These estimates may be more believable though because comparing the changes in male and female rates within the same state may be a better comparison than comparing male rates across states. Another potential explanation for these differences in the estimates is differential trends in the STDs between the two specifications. We explore that possibility in depth next.

## 5.2 Intensity of Rollout from Variation in Gay Population in 2000

We examine how trends in STDs were evolving based in pre-treatment variation before the national approval of PrEP. Specifically, we use the percentage of the male same-sex partnership in a state in the 2000 Census as a proxy for pre-treatment variation in the gay male distribution. States with a larger gay population before PrEP would be more likely have more adopters of PrEP. Our specifications to estimate these effects are given in equations (3) and (4).

In Figure 5, we plot the  $\alpha_t$  from equation (4) to see how states with larger gay populations adopted PrEP at a faster rate. The interpretation of  $\alpha_{2017}$  is the predicted increase in PrEP usage in 2017 relative to 2011 based on a 1 percentage point increase in the percent of male same-sex partnerships. It's clear that states with larger gay populations are more likely to

adopt PrEP. Figure 5 actually looks nearly identical to Figure 1 for men and women.

Next, we plot the  $\beta_t$ s in equation (3) in Figure 6, which we estimate separately for male and female STD rates. The interpretation on a coefficient like  $\beta_{2017}$  is the increase in STDs in 2017 relative to 2011 for a state based on a 1 percentage point increase in the percent of male same-sex partnerships. We plot male and female STD rates separately with 2011 as the comparison year. For chlamydia, gonorrhea, and syphilis, we find that male and female STD rates tracked extremely similarly in states with large and small gay populations, and after 2012, states with larger gay populations saw male STDs increase while female STDs stayed constant. These event studies in Figures 5 and 6 support the hypothesis that the PrEP expansion would be largest in states with a larger gay population and those states would also see an increase in male STDs relative to female STDs other than HIV.

In Figure 6, we also estimate how trends were evolving for male and female HIV diagnoses. We see that the HIV diagnoses for men and women were both downwardly trending at different slopes before the introduction with little change afterwards. As discussed before, these differential trends in HIV diagnoses would make estimating an effect on HIV difficult.

In equation (5), we compare the differences between male and female STD rates. We compare men and women because women can make an appropriate comparison group to men in a given state because PrEP take-up was low among women and as shown in Figure 5, female STD rates tracked with male STD rates before PrEP.

In equation (6), we estimate the differences in PrEP take-up between men and women in states with larger gay populations. In Figure X, we plot the  $\alpha_t^3$ , which gives the additional men that adopt PrEP relative to women in states with a 1 percent point higher gay population in 2000.  $\alpha_t^3$ s plotted in Figure 7 are functionally the differences between the  $\alpha_t$ s plotted between men and women in Figure 5.

In Figure 8, we plot the  $\beta_t^3$ s estimated in equation (5), which gives the additional cases of male STDs relative to female STDs in year  $t$  relative to 2011 for a 1 percentage point increase in the gay male population.  $\beta_t^3$ s plotted in Figure 8 are effectively the differences

between the  $\beta_t$ s plotted between men and women in Figure 6 represented by green and orange, respectively. We present the  $\alpha_t^3$ s and  $\beta_t^3$ s in Table 5.

Figure 8 shows that the STDs other than HIV, there are extremely flat pre-trends in STDs centered around zero before the introduction of PrEP. States with a larger gay population adopted PrEP at a faster rate in Figure 8 after 2012, and the same states had a larger expansion in male STDs relative to female STDs after 2012 corresponding with the increase in PrEP. For chlamydia, gonorrhea, and syphilis, these figures suggest that the difference between STDs in men and women in states with large gay populations are reasonable counterfactuals compared to states with smaller gay populations. However, HIV rates are downwardly sloping before the introduction of PrEP in states with a larger gay population. This figure suggests that the finding for HIV in Table 2 is downwardly biased and would overstate the ability for PrEP to reduce HIV rates.

In Table 5, we present the coefficients in these figures. The interpretation on the coefficient  $\beta_{2017}^3$  for chlamydia in column (1) is that in 2017 a state with a 1 percentage point increase in their gay population had an additional 162.7 male cases of chlamydia per 100,000 people. In 2017, a state with a 1 percentage point increase in their gay population had 181.2 additional cases of male gonorrhea, and 15.83 additional cases of male syphilis. A state with a 1 percentage point increase in their gay population also saw 163.0 additional male PrEP users in 2017. For scaling purposes, the difference between the size of the gay population in New York and North Dakota in the 2000 Census is about 0.5 percentage points. The difference between New York and North Dakota would be about half of these estimates.

Another way to think about these estimates is that then for each predicted increase of 1 male PrEP user in 2017, there was a predicted increase in male chlamydia cases by about 1 case, a predicted increase in gonorrhea cases by about 1.11 cases, and a predicted increase in syphilis cases by about 0.10 cases. Thinking about the event study plot in this way is akin to using an instrumental variable. The relationship between the underlying gay population and the PrEP rate is the first stage while the relationship between the gay population and

STDs is the reduced form, and dividing the estimate from the reduced form by the first stage is essentially the process of an instrumental variable strategy.

### 5.3 Scaling Results by IV

We present the IV results in Table 6. They are displayed side-by-side with the analogous OLS results originally given in Table X. The variable of interest, similar to Table 6, is  $PrEPRate + Male * PrEPRate$ . For all of the STDs excluding syphilis, the IV results are insignificantly larger than the OLS results, while the results for the syphilis are nearly identical. We find that one additional male PrEP user for increases male chlamydia rates by 0.855 cases and increases male gonorrhea rates by 1.005 cases, which is higher than what we estimated in the OLS analysis at 0.763 cases additional cases of chlamydia and 0.898 additional cases of gonorrhea from one additional male PrEP user.

While the effect of PrEP is higher than in the OLS model, it is still within a plausible range. In the last section, we calculated  $\delta_{2017}^3 = \beta_{2017}^3 / \alpha_{2017}^3$ , which can the effect of the estimates in terms of the effect of one additional PrEP user on STDs in 2017. The  $\delta_{2017}^3$ s are higher than the estimated effect in the IV specifications, which is an intuitive finding given that the IV specifications will average across all of the  $\delta_{it}^3$ s and will be lower than the peak in 2017.

Most IV specifications go in-depth into the various assumptions in the analysis such as the relevance and exclusion assumptions. The relevance assumption should be satisfied in that the result is mechanical. As detailed in the PrEP expansion figures in Figures 5 and 7, it is clear that yearly indicator terms will be predictive of PrEP expansion after 2012. To satisfy the exclusion restriction, we need our instrument, the gay population, to be correlated with the PrEP rate, but uncorrelated with any other determinant of the dependent variable. This assumption may be stronger than our parallel trends assumption detailed earlier in our section using the intensity of the gay population before the introduction of PrEP to examine which places would expand PrEP the most. Our previous analysis was more akin to just

looking at the first-stage and the reduced form analysis, while this is taking the next step in calculating the IV estimate. While we find similar results to the OLS specifications, these IV results better reflect the effect of PrEP as estimated in equations (3) and (5), which demonstrates how the STDs evolved over time.

## 5.4 Heterogeneity: Results by Age

Our PrEP data reveals that PrEP take-up was different amongst age groups, which could be due to host of factors such as different health coverage, awareness, different risk aversion, etc. STDs also proliferated differentially across different age groups. We estimate our triple-difference specifications comparing the change in STDs rates between men and women given in equation (5). We estimate these equations separately for different age bins. One limitation is that the PrEP data given by age is not broken down by sex as well. We have the age bins broken up into 24 and younger, 25-34, 35-44, 45-54, and 55 and older.

We plot the different  $\beta_t^3$ s in Figures 9 – 13 for the different age bins analyzed. We give the PrEP rate by age in Figure 9, where it's clear that PrEP expansion was largest for people between 25-54. The two groups with the lowest adoption are the groups with 24 and younger and 55 and older. Given that people aged 25-54 had the largest increase in PrEP, we would expect that these are the age groups that would have the largest expansion in STDs as well after 2011. One caveat with this analysis though, is that people are not confined to having sexual partners that are the same age. People of any age are able to have legal sexual relations with anyone over 18, so there could be spillovers across age groups if someone who is 30 and on PrEP passes along an STD to someone who is 50.

In Figure 10, we present the results for chlamydia broken down by age. We see large significant increases in male chlamydia in the age groups that saw the largest expansion in PrEP with people aged 25-54 gaining the most in STDs and PrEP. We also see relatively flat pre-trends in chlamydia before the PrEP introduction for people aged 35-54. The estimates for 15-24 are extremely noisy with much larger confidence intervals. One potential

explanation for this finding is that the variance in chlamydia rates for people aged 15-24 is much higher.

In Figure 11, we present the results for gonorrhea broken down by age. Again, we find large significant increases in male gonorrhea in the age groups with the largest expansion in PrEP. Overall, the pre-trends are extremely flat before the expansion of PrEP with the exception of the 25-34 age group, which is slightly increasing. In Figure 12, we present the results for syphilis broken down by age. The only significant increase in male syphilis occurs in 2017 for ages 35-44. Again, the pre-trends look encouraging overall in that they are relatively flat and centered around zero. Finally, in figure 13, we present the results for HIV broken down by age. We find similar patterns with the largest affected group being the 35-44 age group. However, as we have seen with the other figures involving HIV, there is a significant downward trend in HIV diagnoses before PrEP's introduction making any estimation on HIV extremely difficult.

Overall, our results support a finding that PrEP's differential expansion across different age groups led to a differential expansion in male STDs across age groups as well. People aged 25-54 were the most likely to adopt PrEP, and these age groups saw the largest expansion in male chlamydia, gonorrhea, and syphilis, showing an important element of heterogeneity in the population. The costs and benefits of PrEP are likely not evenly distributed even within the gay community.

## 6 Robustness Checks and Discussion

### 6.1 Recommended STD Testing

The CDC recommends screening all patients for HIV infection before initiating PrEP and at least once every 3 months while taking PrEP<sup>7</sup>. The CDC also recommends testing for

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<sup>7</sup>Testing regimes are detailed on page 47 of <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>



STDs every 3 months for asymptomatic MSM who are in a high-risk group for STDs such as those with a history of STDs and multiple partners, and they recommend asymptomatic STD screenings every 6 months for everyone on PrEP.

One concern when trying to analyze the effect of PrEP on STDs is that it is possible that differential sexual behavior from PrEP isn't causing the uptick in STD, but that increased testing is causing more STDs to be uncovered. The overall rate of STDs in the population may be the same, and additional STD screens makes the reported rate increase and become closer to the overall rate of STDs that was being underreported before PrEP.

Given that this change in screening frequency could occur differentially across states in a highly correlated way with the PrEP expansion, we want to examine how testing was potentially impacted. While increased screening frequency may confound some results, screenings for MSM may not actually change much. For the broader MSM community, the CDC recommends STD screenings for sexually active MSM every year with screenings every 3 to 6 months for higher-risk MSM<sup>8</sup>. Some higher-risk MSM may not actually see a substantial change in the STD screenings they undergo since the CDC already recommends frequent STD screening, but CDC guidelines recommend increased testing when undergoing PrEP.

While the CDC does recommend screening for HIV every 3 months while on PrEP, it only recommends asymptomatic testing on that frequency for high-risk MSMs. In many cases though, doctors and STD clinics will sometime couple HIV infection screenings with screening for other STDs even for non-high-risk patients given low marginal costs of many STD screens. In this instance, people taking PrEP would undergo more frequent STD screenings. However, it is unclear whether medical practitioners indeed administer more frequent STD screening other than HIV for persons taking PrEP, since it is at their discretion. Furthermore, it could be the case that persons who take-up PrEP already screen for STDs more often than gay male that are not taking PrEP. For example, if people taking PrEP are more risk averse or engage in riskier sex, elevating the frequency in which the CDC recommends screening.

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<sup>8</sup>Screening guidelines for MSM are given on page 15 for the 2015 guidelines here <https://www.cdc.gov/std/tg2015/tg-2015-print.pdf>

Importantly, more frequent STD screening could have an ambiguous effect on STD incidences. Given that chlamydia, gonorrhea, and syphilis are often asymptomatic, increased STD screening could pick up instances of STD cases that would have otherwise gone undetected. In this case, the differential increases in STD incidences would partially be explained by increased testing. On the other hand though, increased screenings that result in increased diagnoses of asymptomatic STDs could decrease the overall incidence of STDs since asymptomatic patients get treated and cured instead of passing the disease on to others. Overall, it's difficult to say in which direction increased screening would bias our results.

Although we do not have suitable data on overall STD screening, we are able to provide evidence on HIV screening. Given that HIV screens are frequently conducted with other STD screens, we believe that our findings on HIV screening extend to STD screening as well. We use data from the BRFSS where we construct the share of male participants aged 18-45 in each state that had HIV in the 3 months preceding the interview for 2008-2016. We estimate equation (5) where the dependent variable is the share that had an HIV screen. We present those results in Figure X. The coefficients for all of the years are insignificant with no trends, suggesting that HIV screening did not increase differentially for states with higher PrEP rates.

## 6.2 Counterfactual

We conduct a simple counterfactual analysis to examine how STIs would evolve in a counterfactual world without PrEP. We take our estimated effect of PrEP on STIs and subtract the amount of additional STIs caused by PrEP from aggregate STI numbers. For instance, we find in our IV model that 1 additional male PrEP user results in about 0.85 additional male cases of chlamydia, so for each additional male PrEP user relative to female users, we subtract 0.85 cases of chlamydia and recalculate the rate. The implicit assumption in this analysis is that the marginal effect of an additional PrEP user is constant over time and across states, which could be strong assumptions. However, we believe that this analysis can

still be instructive. We plot the new estimates for the STI rate for each year. We present the OLS and IV results together for comparison. We present the counterfactual estimates for chlamydia, gonorrhea and syphilis in Figure X. We omit HIV rates because of our lack of confidence in accurately estimating the correct effect of PrEP on HIV.

In the top left quadrant, we present the counterfactual for the aggregate chlamydia rate in the absence of PrEP with the top right quadrant showing the counterfactual for gonorrhea and the bottom left quadrant showing the counterfactual for syphilis. We also give how large of a decline the STD cases would be in the absence of PrEP with our different estimates. We present the differences in counterfactual cases for our OLS and IV results separately with the percent change from the observed cases in Table X.

For chlamydia, gonorrhea, and syphilis, the IV and OLS results are extremely similar, which is unsurprising given that the estimates are extremely similar with the IV results being slightly higher. We discussed these results more in full in the Results section and in Table X. In the chlamydia figure, our OLS estimates suggest that chlamydia cases would be 11.7% lower in aggregate in the absence of PrEP with the IV estimates suggesting about a 13% decline. For gonorrhea, our estimates suggest that the gonorrhea rate would be 25 to 28% lower in the absence of PrEP. For syphilis, our estimates suggest that the syphilis rate would be about 31% lower in the absence of PrEP. We do not perform the counterfactual analysis for HIV diagnoses as the estimates are likely biased away from zero, and the estimate sizes are likely too large.

One potential concern with this analysis is that the results are possibly too large to be plausible. The counterfactual changes for chlamydia, gonorrhea, and syphilis are relatively high given that the LGBT population is relatively small compared to the non-LGBT population. However, the amount of people that identify as part of the LGBT population is significantly different from the population that engages in sexual behavior with a member of the same-sex. For instance, about 3.5% of the population identifies with the LGBT title but about 8% of the population has engaged in same-sex sexual behavior and about 11% have some

same-sex sexual attraction (Gates, 2011). These estimates are from surveys though, and people could be underreporting same-sex attraction or behavior given the stigma around same-sex attraction.

The CDC reports on their website that the majority of male syphilis cases are from MSM at about 78% in 2018<sup>9</sup>. This finding would suggest that our estimates of the effect of PrEP on syphilis are potentially plausible. Gonorrhea is also growing specifically among the MSM community. The CDC shows that the rate of gonorrhea among men and women were relatively equal until 2012 when gonorrhea among men starting to shoot up while the rate for women stayed the same, which the CDC suggests is due to increased infections among MSMs who are less likely to have sexual interaction with women<sup>10</sup>. The CDC has a STI surveillance network giving them greater information on STI in certain cities. There's a wide range in the share of gonorrhea attributed to MSM with about 86% of gonorrhea cases in San Francisco attributed to MSM to about 20% in Baltimore. The CDC estimates about 43% of gonorrhea cases are attributable to MSM, 21% are attributable to heterosexual men, and 32% attributable to women in their surveillance cities. The figures for men suggest that about 67% of male cases of gonorrhea are attributable to MSM, suggesting that our estimates are again plausible. The CDC does not present the rate of male chlamydia cases attributable to MSM, making any inference about plausibility of counterfactual estimates difficult. If the prevalence of chlamydia is the same or slightly smaller among MSM as gonorrhea is then our estimates would be plausible.

Overall, our estimates suggest that a large amount of the STIs are potentially attributable to PrEP and the rollout of the new HIV-prevention drug. Importantly, our findings are plausible given how many STIs are attributable to MSM, who are most likely to use PrEP. At the high end of our estimates, chlamydia cases would be 13% lower, gonorrhea cases would be 28% lower, and syphilis cases would be 31% lower in the absence of PrEP in 2017, suggesting that PrEP contributes to a sizeable amount of current STIs.

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<sup>9</sup><https://www.cdc.gov/std/stats18/msm.htm>

<sup>10</sup><https://www.cdc.gov/std/stats18/gonorrhea.htm>

### 6.3 Back of Envelope Calculations

We conduct back of the envelope calculations that estimate the additional costs relative to the benefits associated with additional STDs that occurred due to the introduction of PrEP using STD costs estimates from the medical literature. Ideally, we would want to do a cost-benefit analysis to compare the costs of PrEP – the additional STDs caused from a moral hazard effect – to the benefits of PrEP – the reduced cases of HIV. However, any benefit we estimate will likely be overestimated due to the differential pre-trends in the diagnoses of HIV. We present a naïve cost-benefit analysis where we detail how to calculate the costs and benefits in Table X. Again, we will over-estimate any potential benefit from the PrEP expansion.

The first column gives the lifetime cost to treat the given STD based on Owusu-Edusei Jr et al. (2013) which gives figures in dollars amount. The estimate includes the costs of common complications of STDs weighted by the likelihood of said complication. We take the estimated effect of PrEP on STDs for OLS and IV in our triple difference model given in Table X and multiply that effect by the cost for each STD to get an average cost of STD per PrEP user. We then multiply the average cost by the number of additional male PrEP users relative to female users. In 2017, there were 88,151 additional male PrEP users, which we use to get the total cost of PrEP in 2017 with respect to additional STDs caused. For the estimates of HIV, the benefits are given as negative costs. Finally, we sum up the costs for all of the STDs and the non-HIV STDs separately, given that the effects of PrEP on HIV will be overstated. If one were to take the effect of PrEP on HIV as the true effect that is not biased, then our findings suggest that in 2017, PrEP had a positive benefit of \$630 million based on the OLS estimates and \$2.2 billion based on the IV estimates.

Since we cannot be confident in identifying the reduction of PrEP on HIV due to the differential pre-trends in states with high gay populations to those with low gay populations, we can instead calculate how many cases of HIV that PrEP would need to prevent in order to justify the additional costs of the STDs. We present this break-even analysis in Table X.

In Table X, we present the total costs for each STD and for the OLS and IV estimates separately. Next, we divide the total cost for each STD by the lifetime cost of contracting HIV – \$304,500, giving us the number of HIV cases that would need to be prevented to offset the cost of the additional STDs. Finally, we calculate the total cost for all of the non-HIV STDs together. For PrEP to break-even on the cost of the additional STDs, PrEP would need to prevent 46.4 cases based on our OLS estimate and 49.8 cases based on our IV estimates. The 88,151 additional male PrEP users would need to prevent 47 or 50 HIV cases for the benefits of PrEP to outweigh the costs, suggesting a needed prevention rate of 0.05%.

In summation, if we were confident in our estimates of the effect of PrEP on HIV, then our results suggest a benefit of \$630 million. However, as we’ve discussed extensively, given the downward trend in HIV diagnoses before the introduction of PrEP, our estimates of PrEP on HIV would be biased downward and overstate any effect. Given the difficulty in estimating the benefits, we conduct a break-even analysis to put the costs of the additional STDs from PrEP into context. We find that only about 50 cases of HIV need to be prevented in 2017 for PrEP to have a net benefit effect with respect to the transmission of STDs.

## 6.4 The Proliferation of Dating Applications

A potential omitted variable in our analysis is the rise of the dating apps, especially Grindr which is targeted at the male gay population and had a large expansion of users at a similar time to the adaption of PrEP. If Grindr increased the availability of sex among the gay population, it could lead to an increased number of sexual partners and consequently, increased STD incidences in states with a larger gay population. Given that we identify of the share of the population that is gay, our estimates could be picking up some of the effect of Grindr on STDs and not of PrEP.

Although there is no publicly available data on the adaption of Grindr that would have enabled us to test this hypothesis, it is unlikely that our results are driven by the growth

of Grindr given what we saw in our event study plots. Grindr was introduced in 2009 and by 2012, the year of PrEP introduction, it already had about 4 million users<sup>11</sup>. If indeed the use of Grindr increased STDs, it should show up as positive coefficients in our event study specification (illustrated in Figure X), for the years 2009, 2010, 2012, which is not the case. Nonetheless, we cannot rule out the possibility that Grindr growing its user base was responsible for an increase in STDs amongst gay men.

## 7 Conclusion

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<sup>11</sup><https://techcrunch.com/2012/06/17/grindr-joe-simkhani-announces-4m-users-1m-daily-uniques-and-weighs-in-on-the-skout-disaster/>

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# Tables

Table 1: Summary Statistics

Variable	2008-2017	2008-2011		2012-2017	
	All States	Low PrEP States	High PrEP States	Low PrEP States	High PrEP States
Male Chlamydia Rate	328	293	298	356	387
Male Gonorrhea Rate	149	122	110	158	184
Male Syphilis Rate	13.22	5.73	12.44	8.87	20.93
Male HIV Diagnosis Rate	25.75	17.11	34.33	16.65	28.58
Male PrEP Rate	19.36	0.00	0.00	11.04	48.47
Percent Male Same-Sex Partners in 2000	0.56	0.39	0.69	0.39	0.69
Percent White	0.614	0.740	0.546	0.724	0.518
Percent Hispanic	0.103	0.033	0.125	0.040	0.134
Percent Black	0.119	0.134	0.107	0.133	0.106
Percent Asian	0.049	0.013	0.071	0.016	0.078
Unemployment rate	0.070	0.073	0.091	0.054	0.065
Poverty Rate	0.140	0.150	0.141	0.151	0.134
SNAP Recipients	1766285	401184.5	2033476	454479.5	2807407
Natural Log of GSP (in Millions)	13.13	11.42	13.63	11.58	13.81

The table provides summary statistics for states according to their PrEP takeup for the years before the introduction of PrEP (2008-2011) and the years after the introduction of PrEP (2012-2017). States were ranked according to their male PrEP rate in 2017; "Low" are states that are in the lowest quartile of PrEP takeup, whereas "High" are states that are in the highest quartile of PrEP takeup. All summary statistics are population weighted. "Rate" refers to the rate per 100,000.

Table 2: Effect of PrEP on STDs and HIV

VARIABLES	Chlamydia		Gonorrhea		Syphilis		HIV	
	(1a)	(1b)	(2a)	(2b)	(3a)	(3b)	(4a)	(4b)
PrEP Rate	0.431*** (0.131)	-5.974*** (1.177)	0.337** (0.136)	-2.954** (1.220)	0.0148 (0.00927)	-0.277* (0.154)	-0.119*** (0.0305)	-0.283 (0.205)
Male		-450.1*** (22.60)		-8.482 (8.008)		8.929*** (1.145)		19.12*** (1.685)
PrEP Rate*Male		6.738*** (1.135)		3.852*** (1.128)		0.376** (0.143)		0.259 (0.201)
PrEP Rate + PrEP Rate*Male		0.763*** (0.139)		0.898*** (0.138)		0.0986*** (0.0182)		-0.0240*** (0.00765)
Dependent Var. Mean	323	529	133	129	10.6	5.9	21.7	13.8
Observations	510	1,020	510	1,020	503	1,006	510	1,020
R-squared	0.949	0.865	0.936	0.865	0.914	0.842	0.954	0.860

The table provides the results from estimating equation (1) and (2) where the outcomes variables are either Chlamydia, Gonorrhea or Syphilis. For each STD, column (1) are the results of difference-in-difference equation (1), estimated for male. Columns (2a), (2b) and (2C) are the results of triple-difference equation (2) without controls, with controls and with state-specific linear time trends, respectively. All specifications include year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. Robust standard errors clustered at the state level are in parentheses. The dependent variable mean is calculated from the period before the introduction of PrEP (2008-2011). \*  $p < 0.1$ ; \*\*  $p < 0.05$ ; \*\*\*  $p < 0.01$

Table 3: Intensity of Treatment Difference-in-Differences for Male STDs

VARIABLES	(1) Chlamydia	(2) Gonorrhea	(3) Syphilis	(4) HIV	(5) PrEP
$\beta_{2008}$	47.50*** (16.75)	-4.661 (19.92)	2.000 (2.760)	29.43*** (6.145)	-3.767 (7.453)
$\beta_{2009}$	35.51** (16.70)	4.258 (13.96)	-0.169 (2.197)	13.58*** (3.345)	0.731 (5.556)
$\beta_{2010}$	-17.20 (14.73)	-15.10 (10.22)	-2.387** (1.076)	8.822*** (3.215)	-0.109 (2.426)
$\beta_{2011}$ (Omitted)	-	-	-	-	-
$\beta_{2012}$	-10.74 (10.64)	-0.00467 (7.420)	0.00868 (1.370)	-5.548*** (1.678)	11.00* (5.802)
$\beta_{2013}$	-5.116 (13.03)	20.00* (11.07)	-0.0586 (1.760)	-13.39*** (1.599)	20.10* (10.70)
$\beta_{2014}$	-50.97 (36.11)	1.250 (40.31)	-2.236 (4.483)	-14.10*** (3.163)	44.58*** (8.345)
$\beta_{2015}$	60.82*** (14.25)	61.04** (26.33)	-1.281 (7.126)	-18.79*** (4.336)	99.18*** (9.313)
$\beta_{2016}$	71.04*** (19.80)	89.92*** (20.34)	4.364 (6.297)	-21.61*** (4.296)	141.0*** (15.82)
$\beta_{2017}$	162.8*** (21.24)	144.3*** (19.45)	12.59*** (3.957)	-24.03*** (3.869)	165.3*** (20.52)
Observations	510	510	503	510	510
R-squared	0.958	0.945	0.923	0.971	0.891

The table provides the results from estimating equation (1) and (2) where the outcomes variables are either Chlamydia, Gonorrhea or Syphilis. For each STD, column (1) are the results of difference-in-difference equation (1), estimated for male. Columns (2a), (2b) and (2C) are the results of triple-difference equation (2) without controls, with controls and with state-specific linear time trends, respectively. All specifications include year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. Robust standard errors clustered at the state level are in parentheses. The dependent variable mean is calculated from the period before the introduction of PrEP (2008-2011). \*  $p < 0.1$ ; \*\*  $p < 0.05$ ; \*\*\*  $p < 0.01$

Table 4: Intensity of Treatment Difference-in-Differences for Female STDs

VARIABLES	(1) Chlamydia	(2) Gonorrhea	(3) Syphilis	(4) HIV	(5) PrEP
$\beta_{2008}$	40.26 (37.53)	5.172 (14.36)	-0.384 (0.694)	11.56*** (3.506)	-0.484 (1.273)
$\beta_{2009}$	-7.274 (33.40)	7.042 (12.84)	-0.311 (0.712)	5.899*** (2.055)	0.182 (1.120)
$\beta_{2010}$	-49.64** (19.02)	-1.299 (7.188)	-0.504 (0.325)	4.064** (1.587)	0.0470 (0.499)
$\beta_{2011}$ (Omitted)	-	-	-	-	-
$\beta_{2012}$	-19.15 (19.08)	-10.56 (11.47)	-0.539 (0.636)	-1.896*** (0.513)	2.359** (1.079)
$\beta_{2013}$	-26.90 (26.45)	3.987 (21.36)	0.302 (1.015)	-5.800*** (0.785)	3.760* (1.940)
$\beta_{2014}$	-64.40* (35.10)	-4.229 (28.34)	-0.631 (0.728)	-8.184*** (1.705)	4.961** (2.369)
$\beta_{2015}$	20.28 (35.28)	1.704 (31.52)	-0.527 (0.817)	-8.928*** (1.183)	6.297** (2.900)
$\beta_{2016}$	-15.86 (45.67)	-18.89 (24.52)	-0.0798 (0.873)	-9.682*** (1.215)	5.427*** (1.386)
$\beta_{2017}$	44.78 (45.40)	-16.58 (18.89)	0.400 (1.070)	-10.52*** (1.255)	6.236*** (1.578)
Observations	510	510	503	510	510
R-squared	0.933	0.908	0.789	0.940	0.793

The table provides the results from estimating equation (1) and (2) where the outcomes variables are either Chlamydia, Gonorrhea or Syphilis. For each STD, column (1) are the results of difference-in-difference equation (1), estimated for male. Columns (2a), (2b) and (2C) are the results of triple-difference equation (2) without controls, with controls and with state-specific linear time trends, respectively. All specifications include year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. Robust standard errors clustered at the state level are in parentheses. The dependent variable mean is calculated from the period before the introduction of PrEP (2008-2011). \*  $p < 0.1$ ; \*\*  $p < 0.05$ ; \*\*\*  $p < 0.01$

Table 5: Intensity of Treatment Triple Difference-in-Differences

VARIABLES	(1) Chlamydia	(2) Gonorrhea	(3) Syphilis	(4) HIV	(5) PrEP
$\beta_{2008}^3$	-11.20 (25.89)	-16.40 (15.27)	0.0953 (1.234)	15.90*** (4.119)	0.00851 (0.175)
$\beta_{2009}^3$	24.34 (21.34)	-9.435 (6.300)	-1.552 (1.982)	6.760*** (2.121)	0.0216 (0.123)
$\beta_{2010}^3$	29.45 (25.39)	-15.01** (6.392)	-2.655*** (0.844)	4.312* (2.177)	-0.0435 (0.0588)
$\beta_{2011}^3$ (Omitted)	-	-	-	-	-
$\beta_{2012}^3$	17.33 (14.86)	15.16*** (4.922)	2.071 (1.792)	-3.343* (1.977)	5.539*** (1.032)
$\beta_{2013}^3$	41.92** (19.83)	24.51*** (8.320)	1.688 (3.717)	-6.744*** (0.655)	10.17*** (2.125)
$\beta_{2014}^3$	30.21 (35.49)	14.71 (20.69)	1.275 (5.470)	-5.024*** (1.732)	37.45*** (3.170)
$\beta_{2015}^3$	69.85*** (23.60)	74.26*** (7.514)	2.888 (8.633)	-9.065** (4.224)	90.37*** (12.19)
$\beta_{2016}^3$	124.6*** (27.31)	126.4*** (10.93)	8.333 (7.545)	-11.49*** (4.070)	136.3*** (26.30)
$\beta_{2017}^3$	162.7*** (36.44)	181.2*** (14.57)	15.83*** (5.046)	-13.85*** (3.111)	163.0*** (35.12)
Observations	1,020	1,020	1,020	1,006	1,020
R-squared	0.870	0.935	0.900	0.915	0.939

The table provides the results from estimating equation (1) and (2) where the outcomes variables are either Chlamydia, Gonorrhea or Syphilis. For each STD, column (1) are the results of difference-in-difference equation (1), estimated for male. Columns (2a), (2b) and (2C) are the results of triple-difference equation (2) without controls, with controls and with state-specific linear time trends, respectively. All specifications include year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. Robust standard errors clustered at the state level are in parentheses. The dependent variable mean is calculated from the period before the introduction of PrEP (2008-2011). \*  $p < 0.1$ ; \*\*  $p < 0.05$ ; \*\*\*  $p < 0.01$

Table 6: IV for Scaling Effect

VARIABLES	Chlamydia		Gonorrhea		Syphilis		HIV	
	OLS	IV	OLS	IV	OLS	IV	OLS	IV
PrEP Rate	-5.974*** (1.177)	-2.933*** (0.968)	-2.954** (1.220)	-3.349*** (0.808)	-0.277* (0.154)	-0.525*** (0.141)	-0.283 (0.205)	-0.449 (0.274)
PrEP Rate*Male	6.738*** (1.135)	3.788*** (0.970)	3.852*** (1.128)	4.354*** (0.781)	0.376** (0.143)	0.619*** (0.138)	0.259 (0.201)	0.365 (0.242)
PrEP Rate + PrEP Rate*Male	0.763*** (0.139)	0.855*** (0.0843)	0.898*** (0.138)	1.005*** (0.139)	0.0986*** (0.0182)	0.0943*** (0.0267)	-0.0240*** (0.00765)	-0.0833** (0.0336)
Dependent Var. Mean	529	529	129	129	5.9	5.9	13.8	13.8
Observations	1,020	1,020	1,020	1,020	1,006	1,006	1,020	1,020
R-squared	0.949	0.937	0.936	0.882	0.914	0.886	0.954	0.926

Table 7: Estimated 2017 Counterfactuals in absence of PrEP

STD	Observed Cases	OLS		IV	
		Counterfactual Cases	Percent Change	Counterfactual Cases	Percent Change
Chlamydia	576,857	509,565	-11.7%	501,458	-13.1%
Gonorrhea	321,857	242,728	-24.6%	233,258	-27.5%
Syphilis	26,869	18,176	-32.4%	18,559	-30.9%

Table 8: Naive Cost-Benefit Analysis in 2017

STDs	Cost to Treat	OLS		IV	
		Avg Cost Per PrEP User	Total Cost	Avg Cost Per PrEP User	Total Cost
Chlamydia	30	22.89	2,017,776	25.65	2,261,073
Gonorrhea	79	67.55	5,954,159	79.40	6,998,749
Syphilis	709	69.91	6,162,407	66.86	5,893,661
HIV	304,500	-7,308	-644,207,508	-25,365	-2,235,936,892
Total (Non-HIV STDs)	818	160	14134343	172	15153483
Total		-7,148	-630,073,165	-25,193	-2,220,783,409

Table 9: Break-Even Analysis in 2017

Non-HIV STDs	OLS		IV	
	Total Cost	Number of HIV Cases to Offset	Total Cost	Number of HIV Cases to Offset
Chlamydia	2,017,776	6.6	2,261,073	7.4
Gonorrhea	5,954,159	19.6	6,998,749	23.0
Syphilis	6,162,407	20.2	5,893,661	19.4
Total	14,134,343	46.4	15,153,483	49.8



## Figures

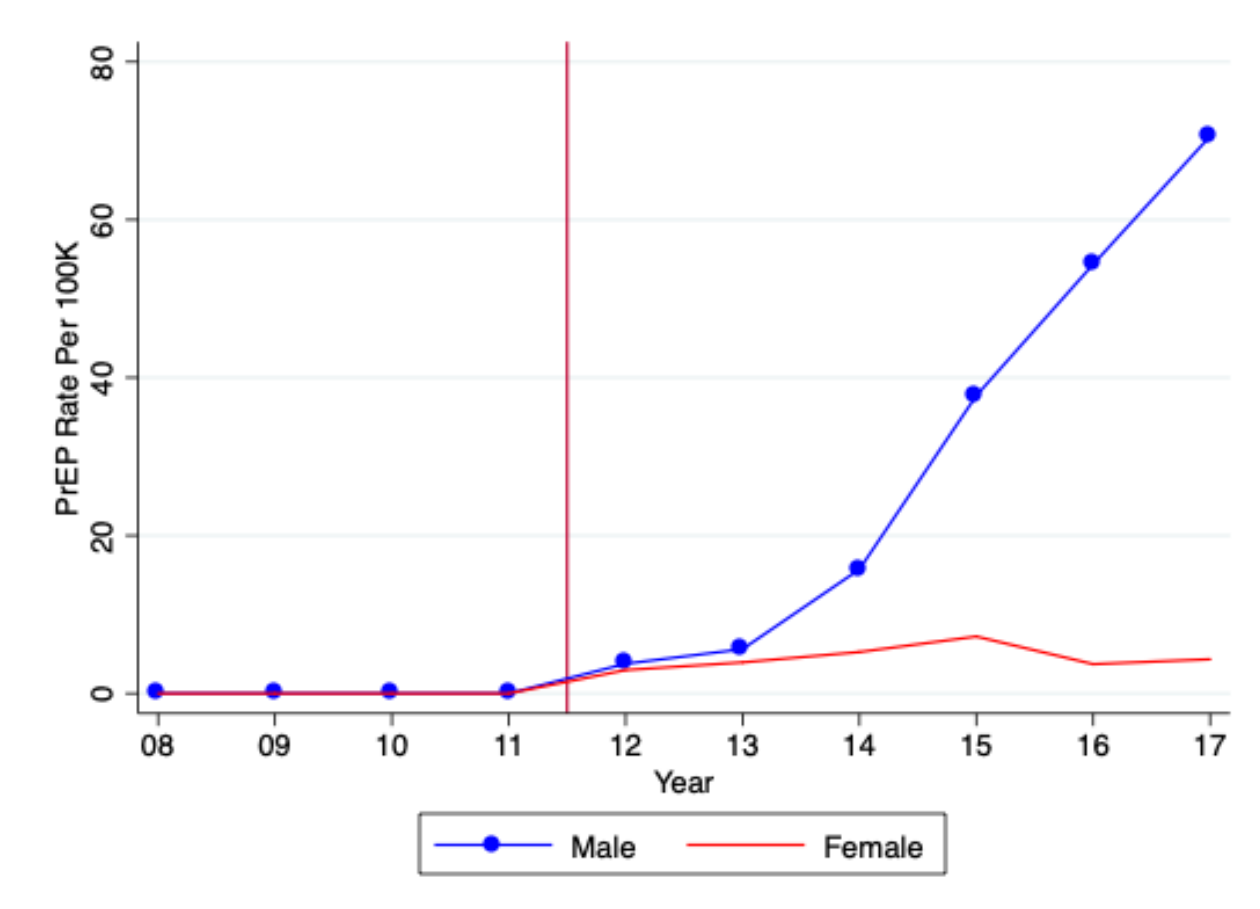


Figure 1: PrEP Use Over Time

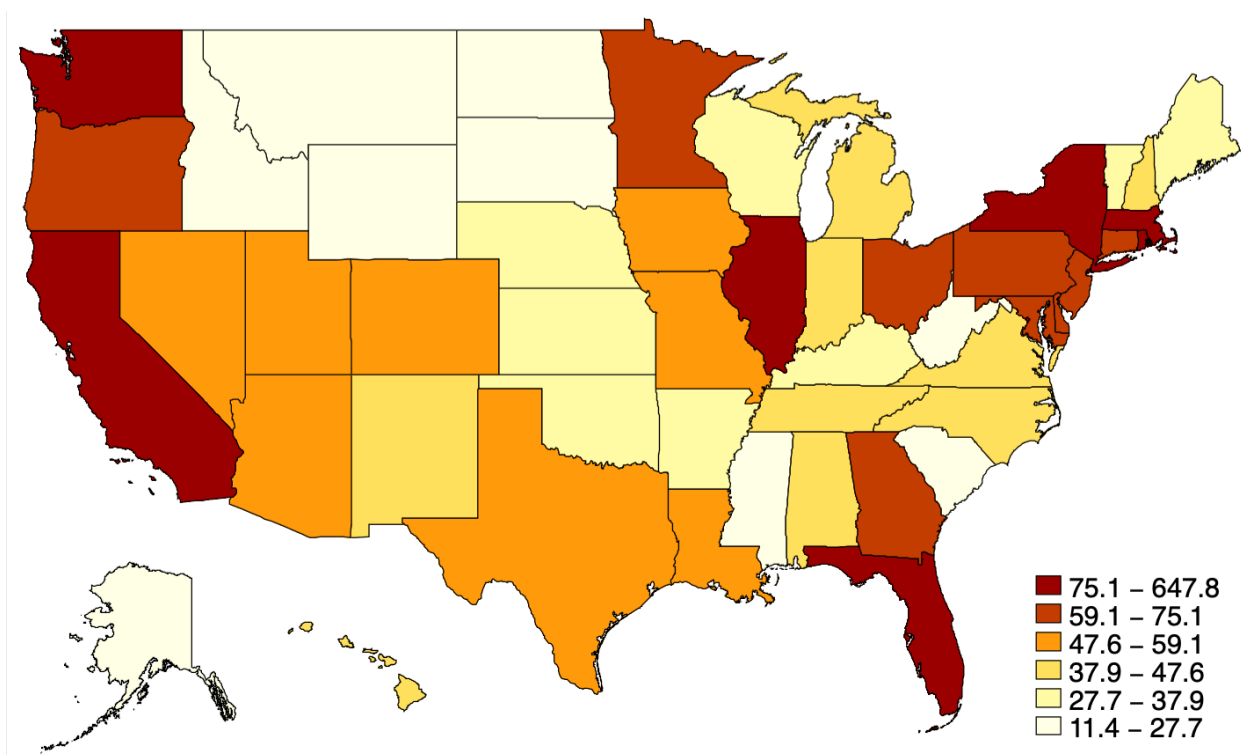


Figure 2: **PrEP Use Across States**

*Notes:* The figure details the male PrEP rate per 100,000 across states.



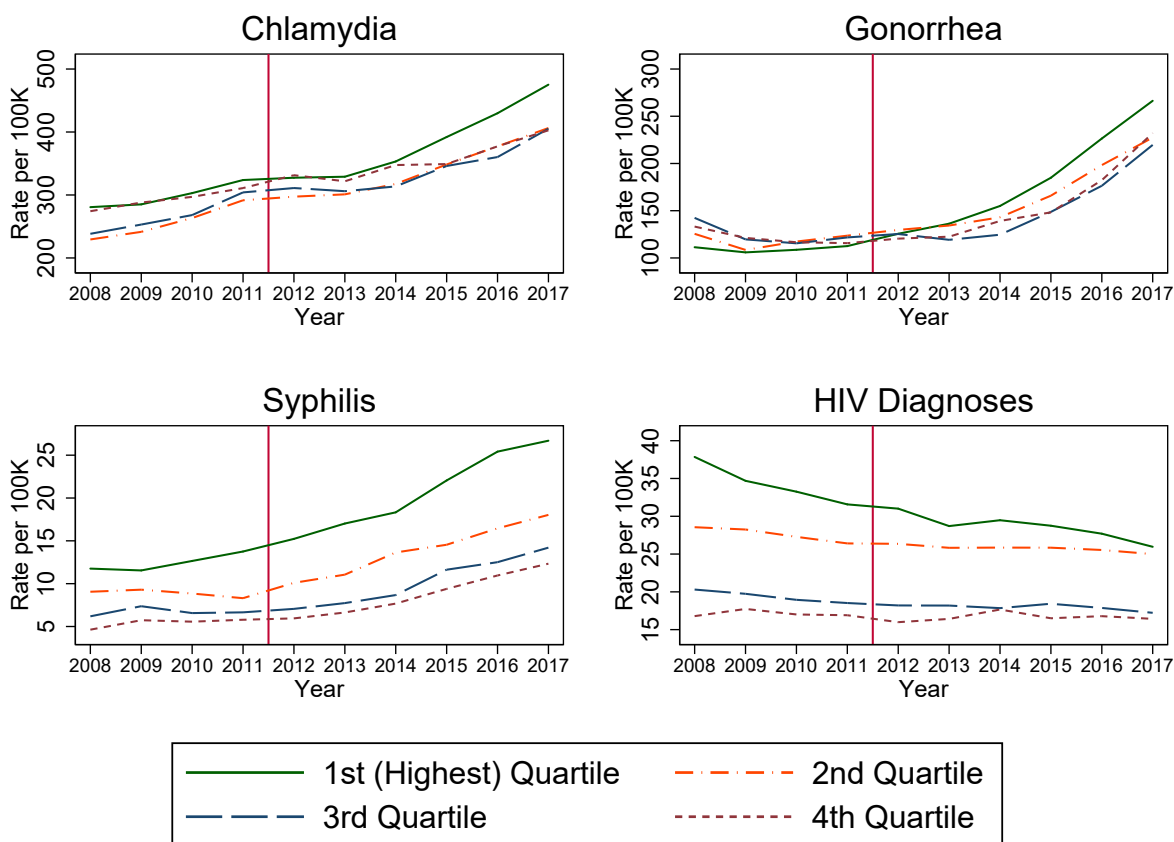


Figure 4: **Evolution of Male STD Rates by Quartile of PrEP Take-up**

*Notes:* The figure plots the male STD rates per 100,000 over time for states with different PrEP take-up. States were ranked according to their male PrEP rate in 2017 and put into quartiles, where quartile 1 includes states with the highest PrEP rate in 2007, and quartile 4 includes states with the lowest PrEP rate in 2017. The variables are population weighted.

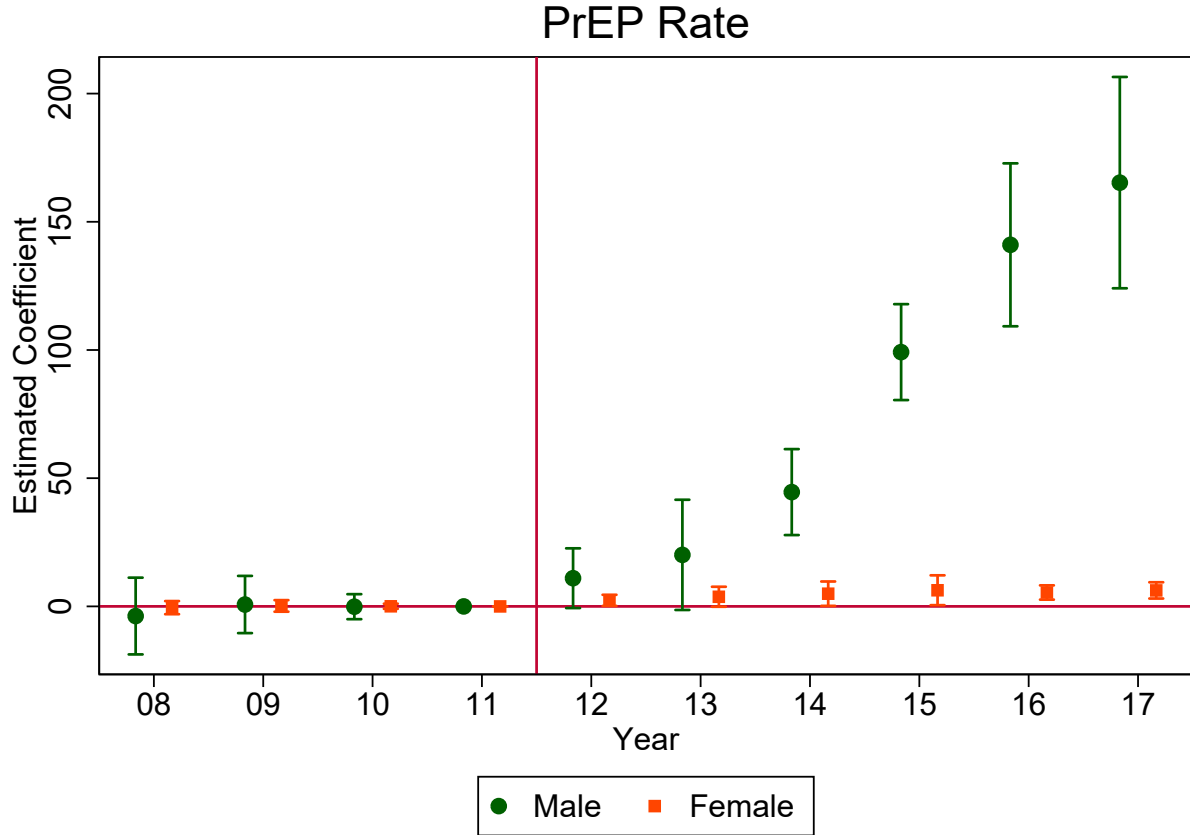


Figure 5: **DD Treatment Intensity Specification Results - PrEP**

*Notes:* The figure plots the event-study estimates from estimating difference-in-difference Equation (3) separately for male and female. The dependent variable is the PrEP rate per 100K. The year prior to the introduction of PrEP (2011) is omitted. Estimation includes year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. The bands represent the 95% confidence interval, calculated using robust standard error clustered at the state level.

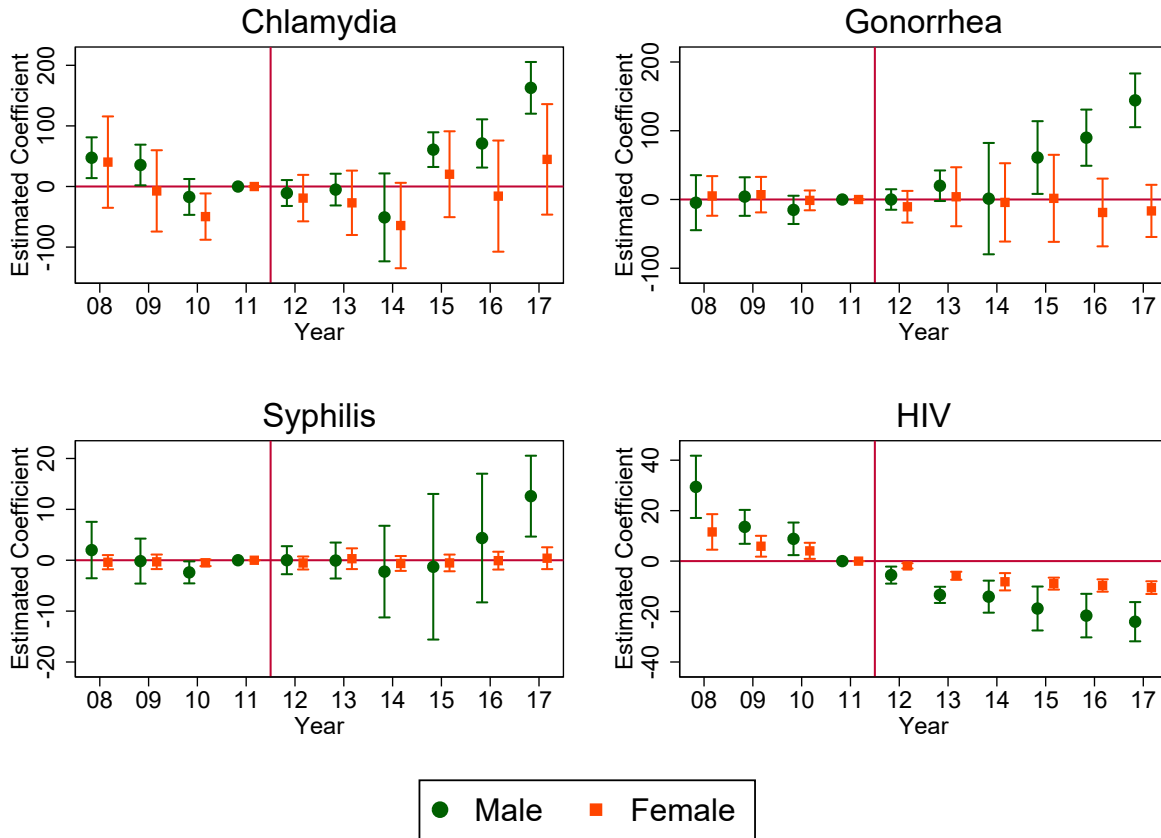


Figure 6: DD Treatment Intensity Specification Results - STDs

*Notes:* The figure plots the event-study estimates from estimating difference-in-difference Equation (3) separately for male and female for the different STDs. The dependent variables are the STD rates per 100K. The year prior to the introduction of PrEP (2011) is omitted. Estimation includes year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. The bands represent the 95% confidence interval, calculated using robust standard error clustered at the state level.

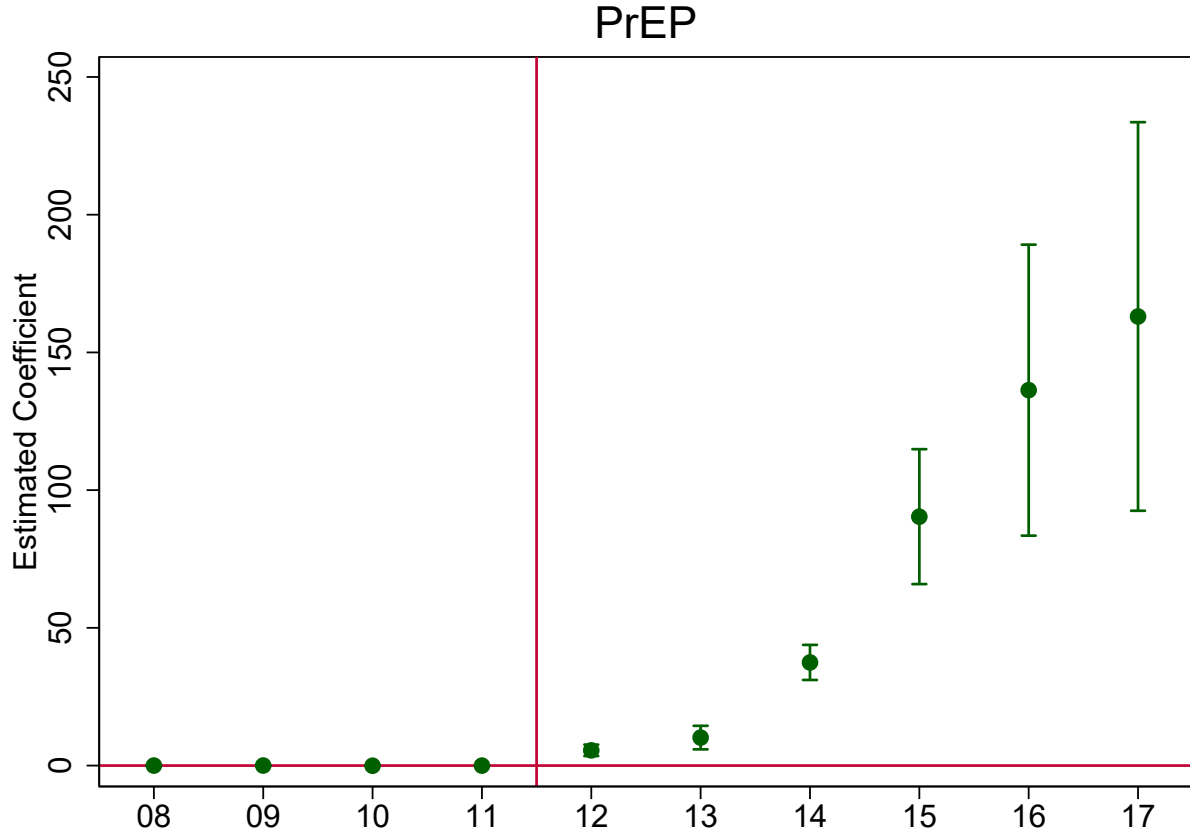


Figure 7: **DDD Treatment Intensity Specification Results - PrEP**

*Notes:* The figure plots the event-study estimates from estimating triple-difference Equation (4). The dependent variable is the PrEP rate per 100K. The year prior to the introduction of PrEP (2011) is omitted. Estimation includes year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. The bands represent the 95% confidence interval, calculated using robust standard error clustered at the state level.

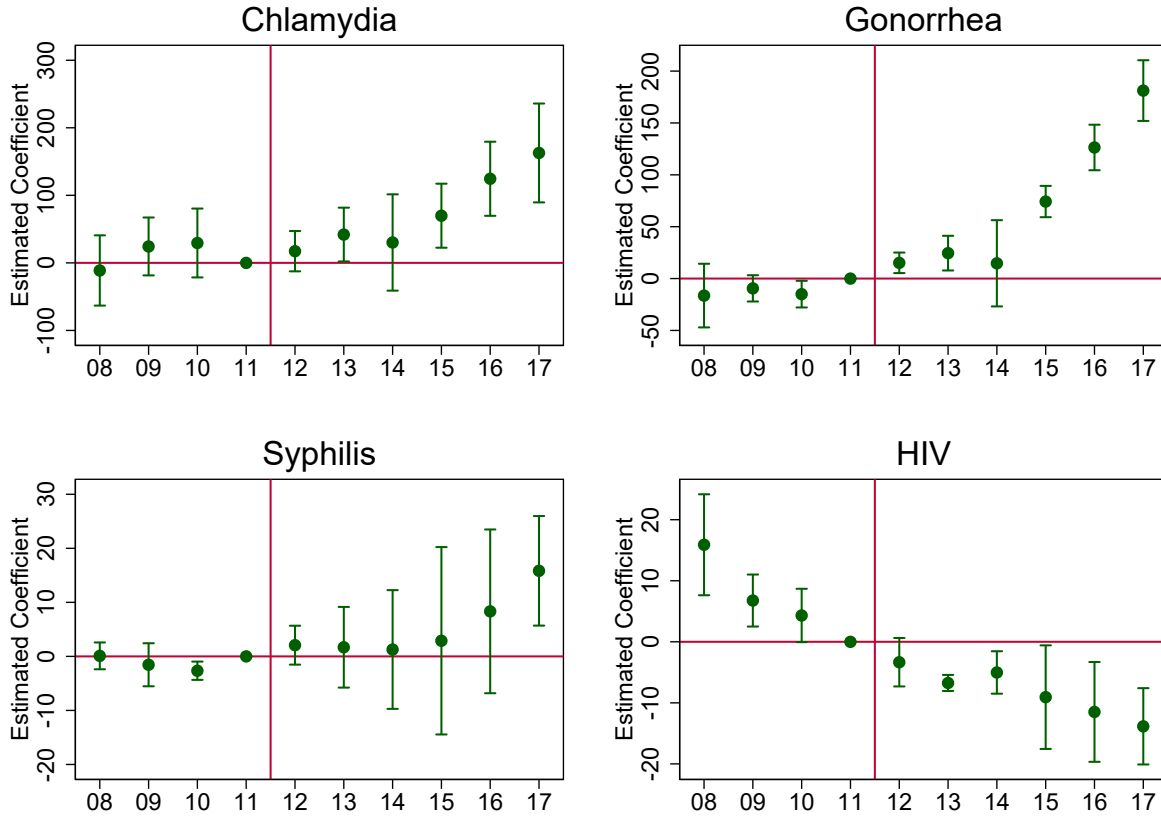


Figure 8: **DDD Treatment Intensity Specification Results - STDs**

*Notes:* The figure plots the event-study estimates from estimating triple-difference Equation (4) for different STDs. The dependent variables are the STD rates per 100K. The year prior to the introduction of PrEP (2011) is omitted. Estimation includes year and state fixed effects and are population weighted. Controls include the share of the population that is either White, Hispanic, Black, Asian, Native American or other, log GDP, log of the population and the unemployment rate. The bands represent the 95% confidence interval, calculated using robust standard error clustered at the state level.



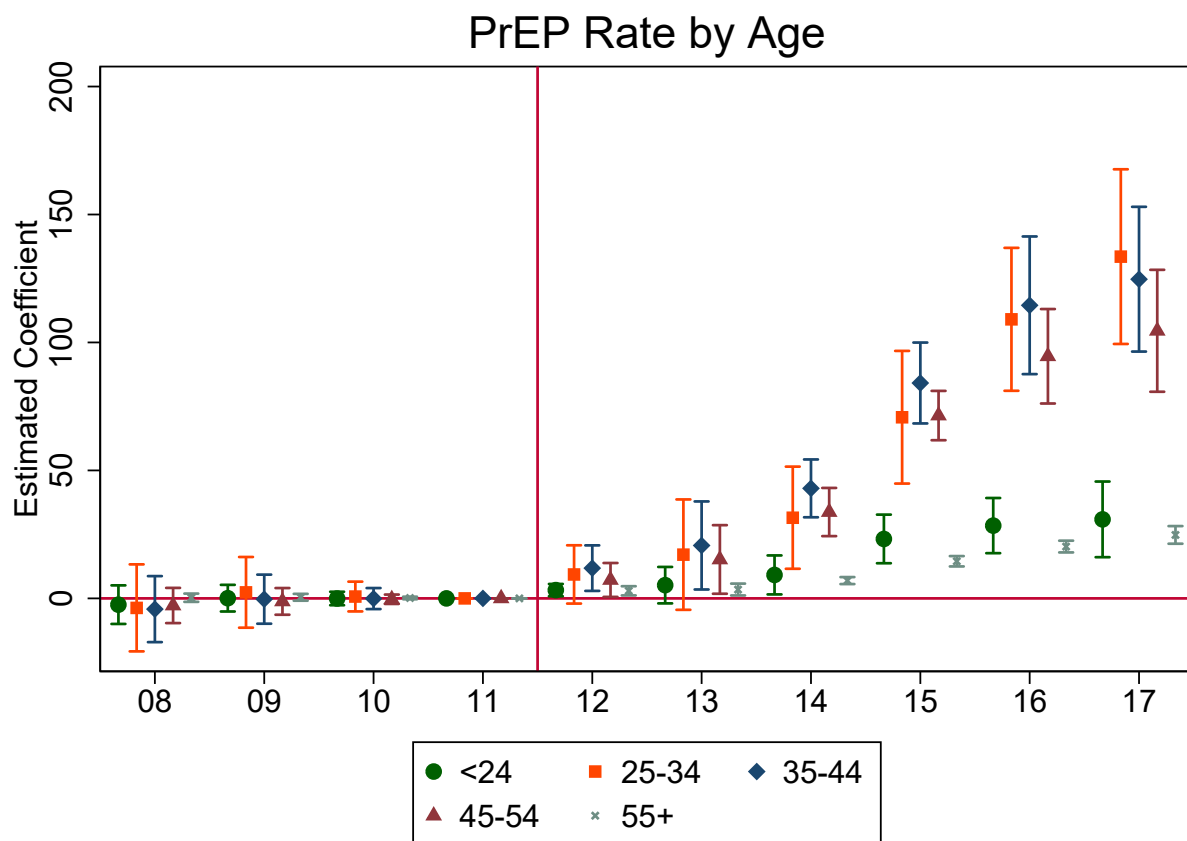


Figure 9: **Blank**

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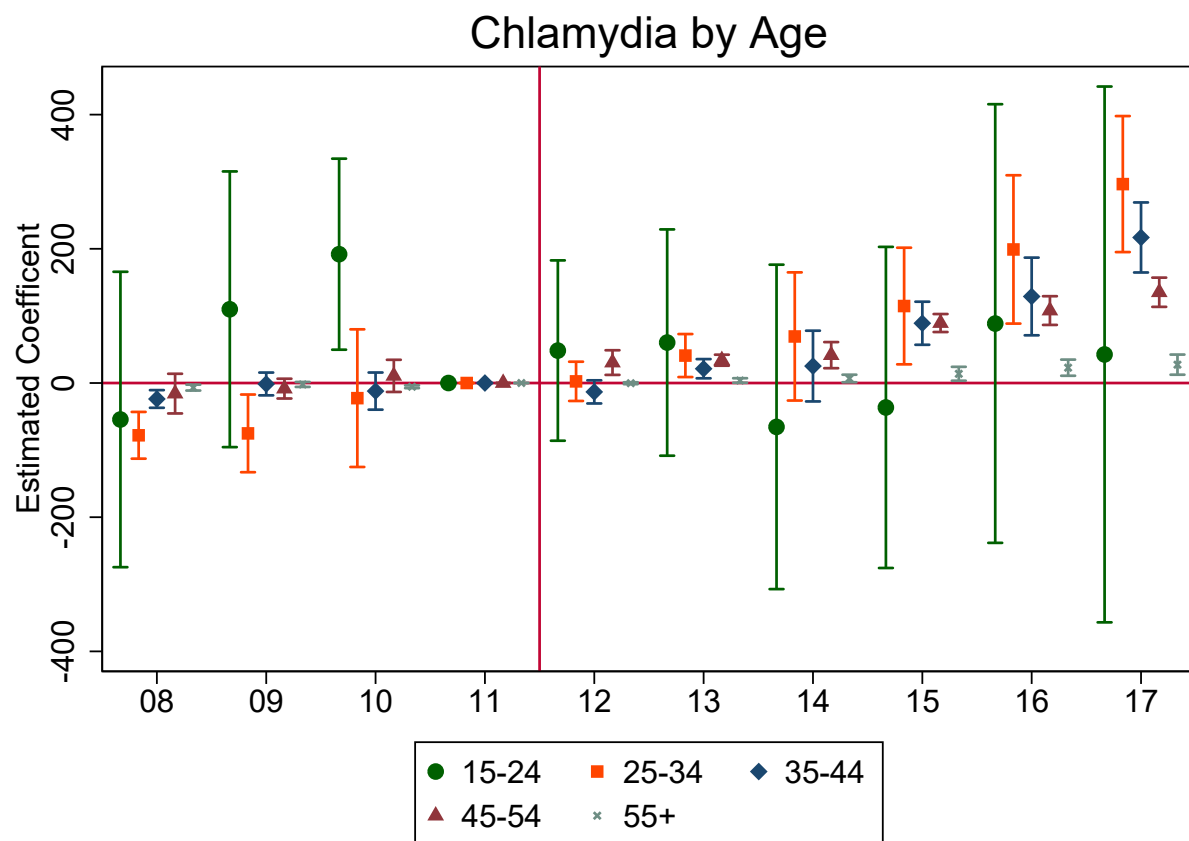


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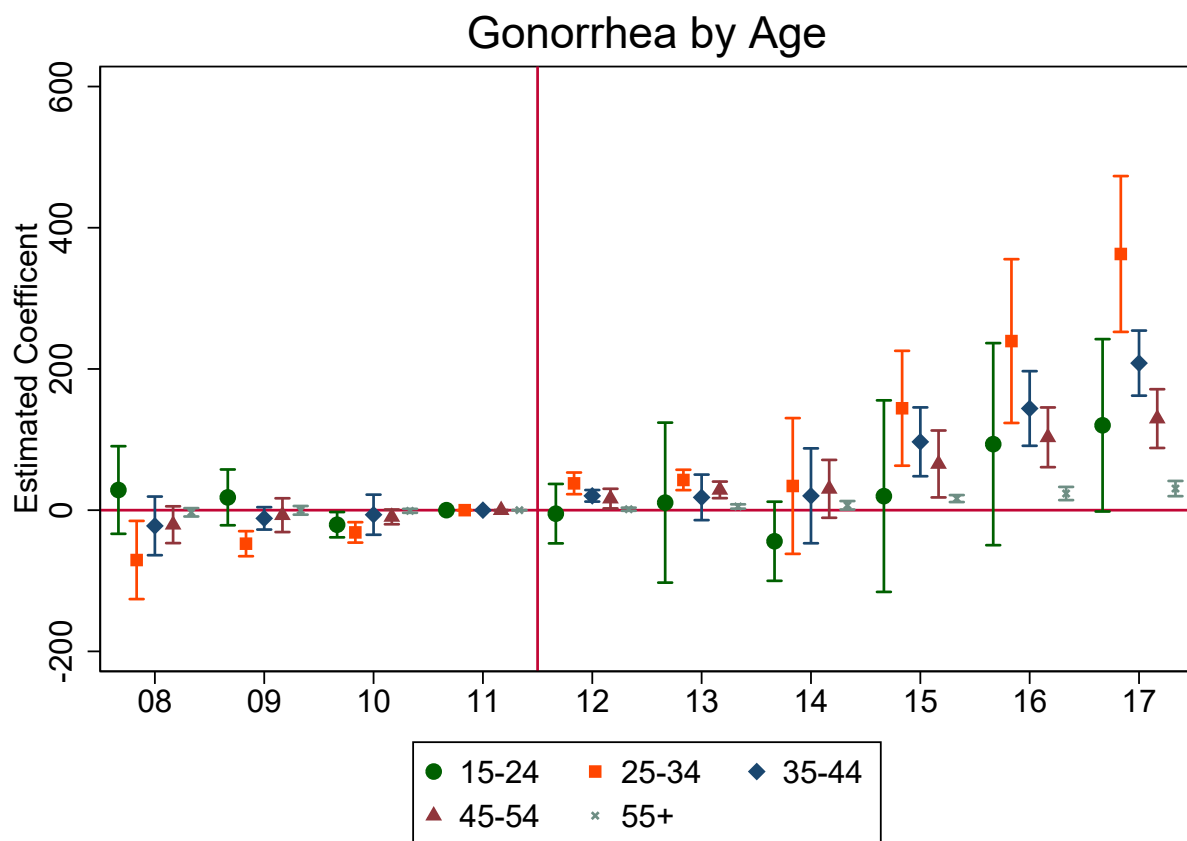


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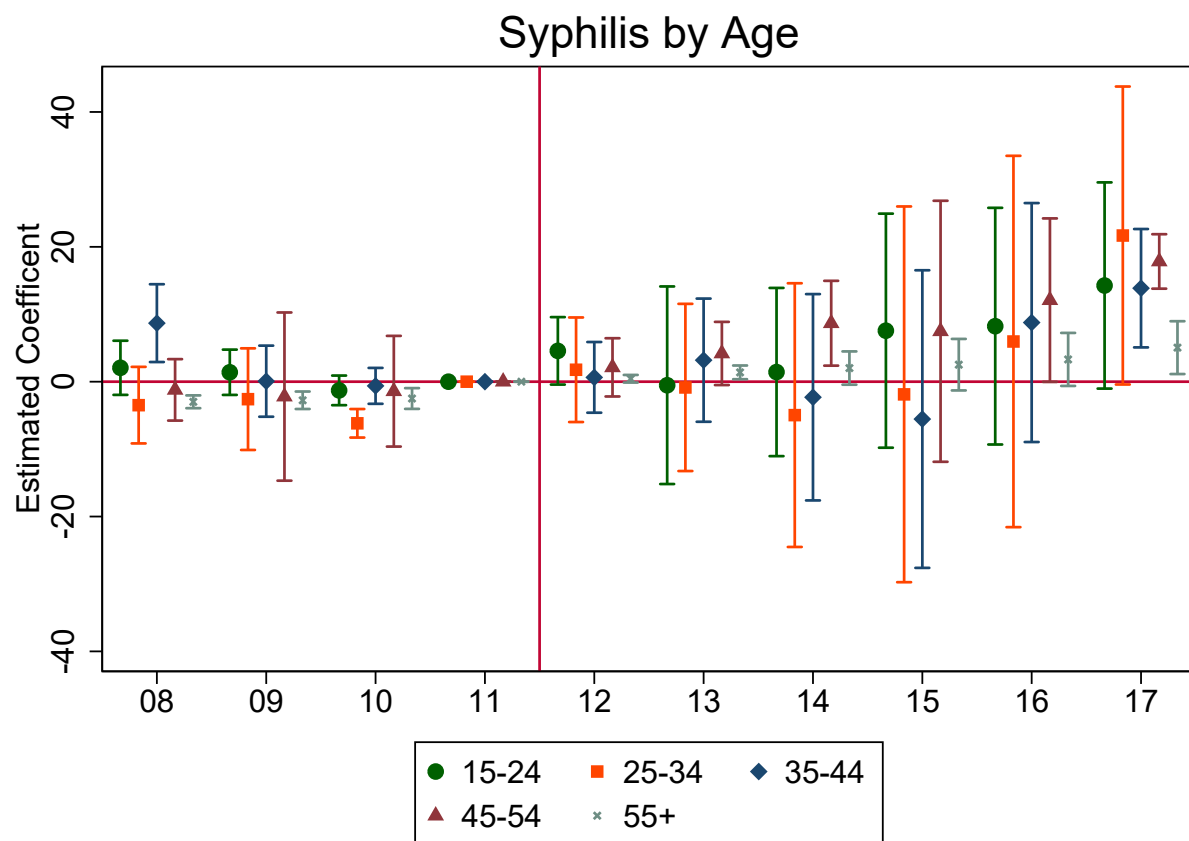


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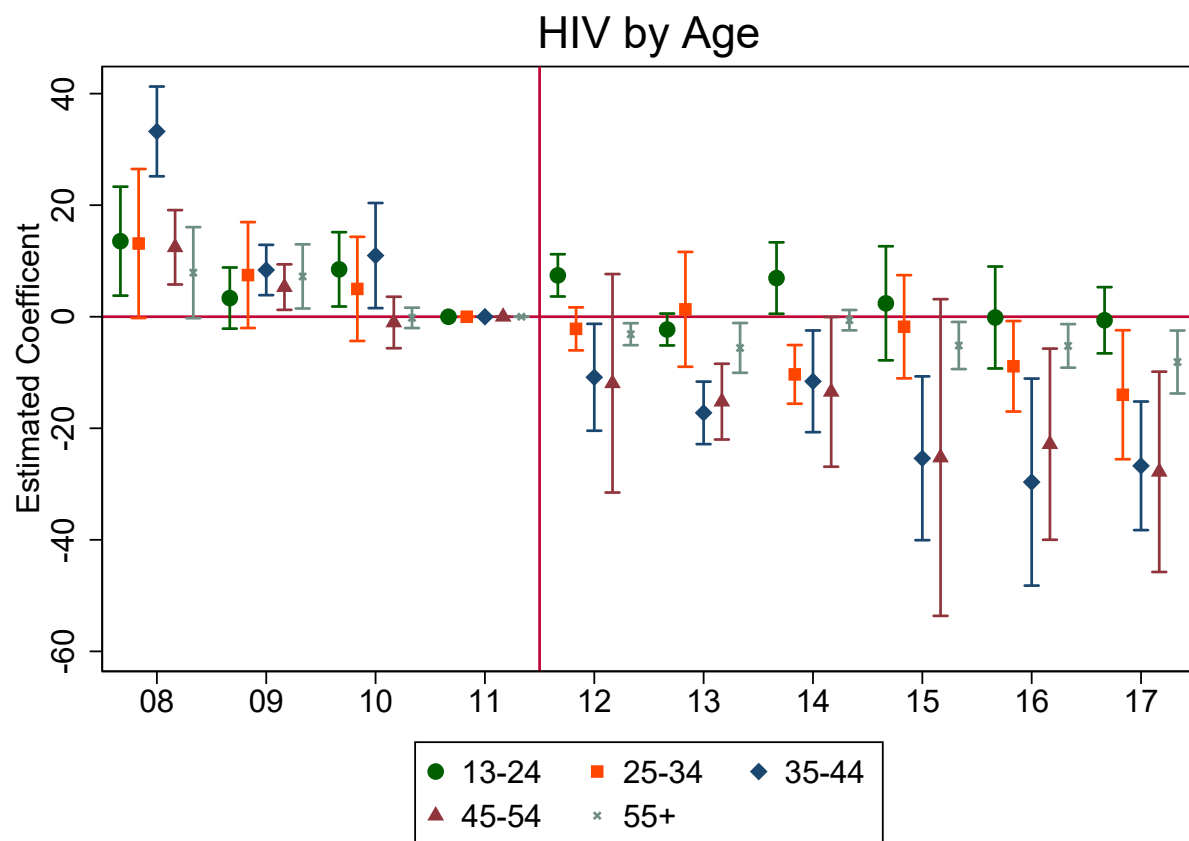


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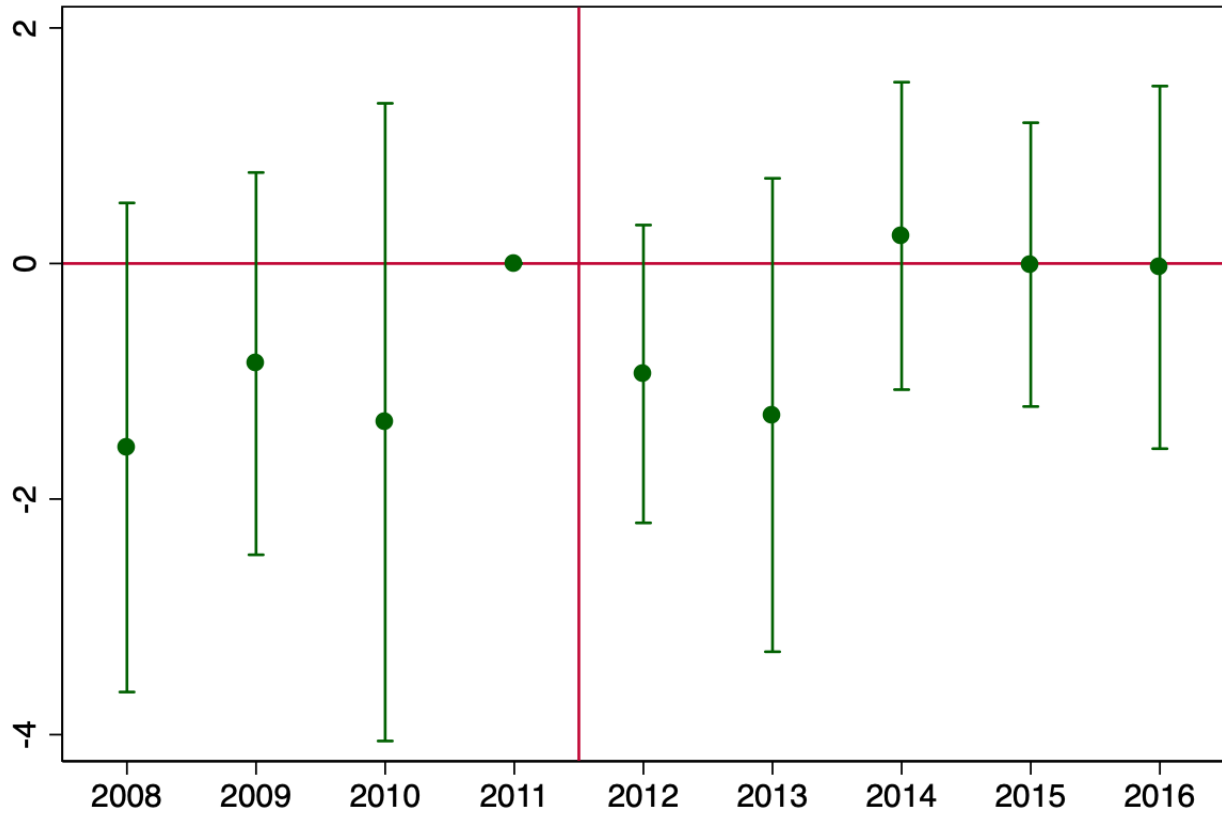


Figure 14: **Event Study - HIV Testing**

*Notes:* The figure plots the event-study estimates from estimating Equation (4); the dependent variable is the share of individuals tested for HIV in the past 3 months.

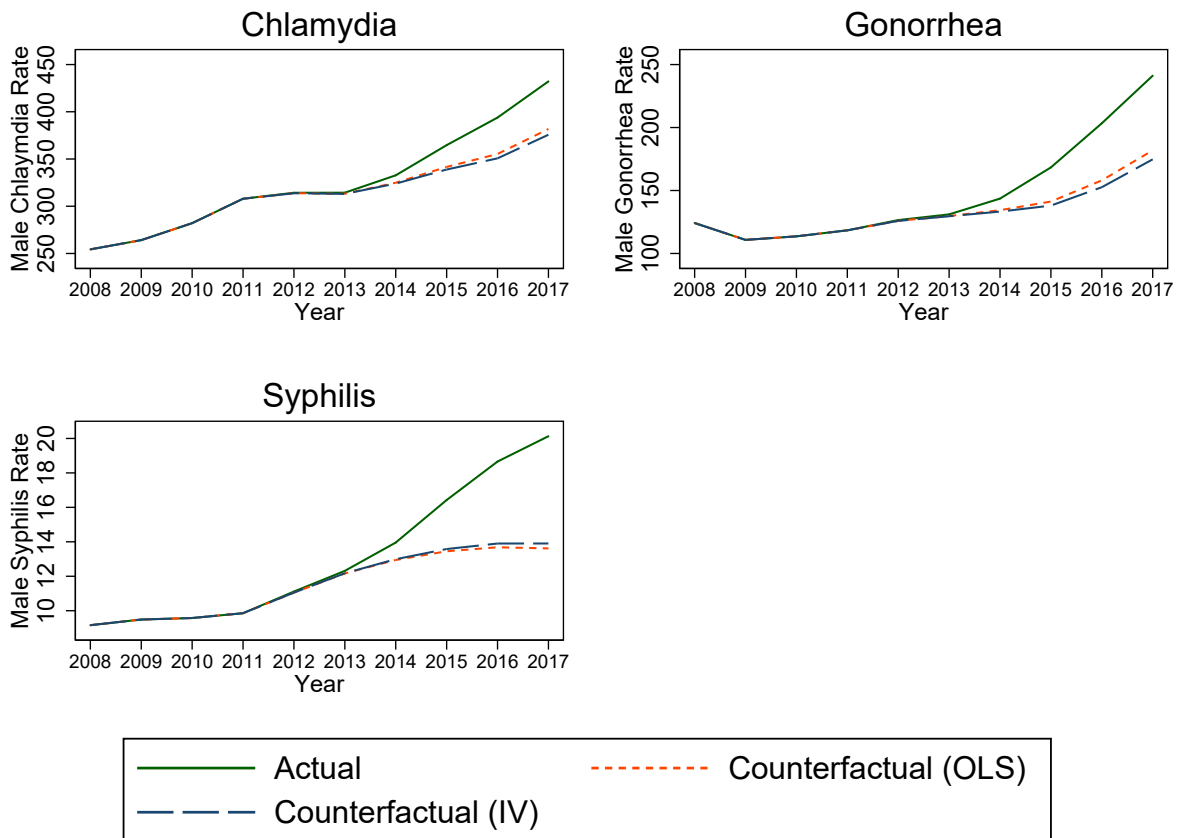


Figure 15: **Counterfactual STI development in absence of PrEP**

*Notes:* These figures plot how the aggregate STI rate would have developed in the absence of PrEP using two different estimates.