FUNDAÇÃO GETULIO VARGAS
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FILIPE MATHEUS SILVA CAVALCANTI

SCALING UP PREP: EVIDENCE FROM A POLICY TO PREVENT HIV IN BRAZIL

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Dissertação apresentada à Escola de Economia de São Paulo como pré-requisito à obtenção de título de mestre em Economia de Empresas.

Orientador: Bruno Ferman.

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Resumo

PrEP é um medicamento disponível em vários países que, se tomado frequentemente, pode eliminar o risco de ser infectado por HIV por meio de relações sexuais. No entanto, ao reduzir o custo de relações sexuais desprotegidas, sua distribuição pode promover comportamentos de risco, aumentando a incidência de infecções sexualmente transmissíveis, em um típico problema de risco moral. Neste trabalho, analiso os efeitos da distribuição de PrEP gratuitamente no Sistema Único de Saúde no Brasil. Utilizando o método de diferença-em-diferenças explorando a variabilidade temporal na adoção da política entre municípios, encontro que a PrEP reduziu em 7.8% a taxa de novos casos de HIV. O efeito é maior para os grupos de homens que se relacionam com homens, pessoas entre 25 a 39 anos e pessoas com ensino médio completo. Estas são as principais características dos indivíduos que utilizam PrEP. Em adição, não houve efeito substancial em sífilis, enquanto que houve redução nos novos casos de hepatite. Evidência sugere que este efeito é consistente com maior monitoramento dos indivíduos e com a focalização bem sucedida da política.

Palavras-chave: HIV, PrEP, políticas de saúde, risco moral

Abstract

PrEP is a drug that is available in many countries and, if taken frequently, can virtually eliminate the risk of being infected with HIV through sex. However, by reducing the cost of unsafe sex, it might promote risky behavior, increasing the incidence of sexually transmitted infections in a typical moral hazard problem. I analyze the effect of PrEP distribution for free in the public health system in Brazil. I find that PrEP is mainly distributed to high-risk individuals. In a difference-in-differences setting exploring temporal variability in the adoption of the policy by municipalities, I find that PrEP reduced by 7.8% the rate of new cases of HIV. The effect is higher for the groups of men who have sex with men, people aged between 25 to 39 years and people who completed high school. These are the main characteristics of PrEP takers. Additionally, there was no substantial effect on syphilis, while it has helped to reduce new cases of hepatitis. Evidence suggests that this is consistent with better screening of individuals and well targeting of the policy.

Keywords: HIV, PrEP, health policy, moral hazard

JEL Classification: I12, I18, D62

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1 Introduction

In 2020, 1.5 million people were newly infected with HIV and 680 thousand people were lost to AIDS-related illnesses, considered one of the deadliest pandemics of all time. Despite that, global efforts to reduce new HIV infections have not been as successful as expected (UNAIDS, 2021). In that same year, key populations (sex workers and their clients, gay men and other men who have sex with men - MSM, people who inject drugs, transgender people) and their sexual partners accounted for 65% of new HIV infections globally and 93% of new HIV infections outside of sub-Saharan Africa (UNAIDS, 2021). That scenario made The Lancet state in an editorial that "ending HIV cannot be achieved without targeted programs that are tailored to key populations" (The Lancet, 2021).

One of the most promising avenues to HIV prevention created in the last years is Pre-Exposure Prophylaxis (PrEP). PrEP is a pill that, if taken frequently by HIV-negative individuals, can eliminate the risk of HIV infection through sex (CDC, 2021c). According to the PrEP Watch, more than 90 countries have PrEP programs, that vary in scale and magnitude and mainly focus on the key populations cited above. However, in terms of public health, the expected effects of these policies are theoretically ambiguous. These interventions might not be as effective as expected and have unintended consequences by increasing the incidence of other widespread diseases. In this paper, I study the effect of PrEP introduction on HIV and other ailments and find that returns far outweigh its costs.

I analyze the effect of PrEP distribution on the public health system in Brazil. I exploit temporal variability in the adoption of the policy to uncover the causal effects of PrEP introduction in an event study analysis. First, I focus on the effect of the policy to prevent new cases of HIV. Theoretically, the expected effect is unclear. If PrEP is distributed to low-risk individuals, we expect it does not affect substantially new cases of HIV. However, if it efficiently targets individuals with high HIV risk, it must reduce new HIV cases.

I provide descriptive evidence that it indeed targeted high-risk individuals. Using a simple index based on risky behavior, I classify 87.10% of individuals using PrEP as high-risk of HIV. Consistent with what is expected, the main results indicate that PrEP helped to reduce the rate of new cases of HIV by 7.8% on average. However, the effect is

increasing through time and can reach -18.7%. The relative effect is higher for the groups of men that have sex with men, people who completed high school, and people aged between 25 to 39 years old. These groups represent the main characteristics of PrEP takers. Using back to envelope calculations, I find that every 100 doses of PrEP distributed in a quarter of a year reduces four new cases of HIV on average.

Next, I focus on the effect of the policy on new cases of other Sexually Transmitted Infections (STIs). Theoretically, it is expected that since PrEP reduces the risk of being infected with HIV, it can lower the cost of unsafe sex, leading to an increase in risky behavior. That is the classic moral hazard problem well known by economists. If this is the case, PrEP distribution would be followed by an increase in new cases of other STIs. Eilam and Delhommer (2021) found that this was true in the United States. However, PrEP individuals in Brazil are also more screened for STIs, since periodic tests are mandatory due to a high-enforced national protocol, and they are also vaccinated for some diseases. Additionally, frequent doctor visits might help individuals taking PrEP to acquire information about how to prevent getting sexually transmitted infections and how to have access to free condoms, for example. In that case, PrEP distribution could have the effect of decreasing other STIs.

I test the effect of PrEP introduction on syphilis and hepatitis, two common STIs in Brazil. I find that the PrEP delivery did not increase the rate of new cases of syphilis in the population. Although this is not a bulletproof result, since lack of power might explain it, I show that there is no effect for subgroups with high adherence to PrEP. Additionally, I find that PrEP introduction reduced the rate of new cases of hepatitis. The effect is concentrated in acute cases (recently infected) and is not present in chronic cases. It is also higher for men and people aged between 25 to 39 years old, two groups highly focused on PrEP policy. This heterogeneity bolsters the argument that it is an effect of the PrEP policy and not other policies simultaneously adopted. Additionally, it reduces both sexually transmitted and not sexually transmitted cases.

Cost-benefit analysis of the results shows that, considering only the effect of the policy on HIV, the *payback period* of the program is three years. However, considering the positive externality on other diseases, the returns of the program outweigh its costs in the same year that it was implemented.

This paper is closely related to the work of Eilam and Delhommer (2021). They analyze the moral hazard effects of PrEP introduction in the US, finding huge increases in

STI incidence after PrEP. The results from Brazil differ from the ones found in the US. I present some possible reasons in the discussion section. Additionally to their paper, this paper also analyzes the effect of PrEP introduction on the HIV rate, making it possible to do a proper cost-benefit analysis.

This paper contributes to the literature on unintended consequences of health interventions. For example, Lakdawalla et al. (2006) finds that treating people living with HIV increases risky sexual behavior. MacGregor et al. (2020) provides theoretical evidence that screening PrEP users for hepatitis C could reduce drastically new cases of this disease. This paper presents evidence that this is true using empirical evidence. Doleac and Mukherjee (2018) show that increasing access to naloxone, a drug that can save lives when administered during an overdose, has led to more opioid-related emergency room visits and more opioid-related theft. Donohue and Levitt (2001) found that legalized abortion has led to crime reductions in the US.

Also, this paper contributes to the literature on policies to prevent HIV infection. Greenwood et al. (2019) calibrated a theoretical model to analyze the effect of different preventive policies on HIV/AIDS in Malawi, but did not consider PrEP. Duflo et al. (2015) study the impact of educational policies on HIV using experimental evidence from Kenya. Björkman Nyqvist et al. (2018) study the impact of a lottery where the participation is conditional on negative test results for sexually transmitted infections. Goldstein et al. (2013) study the effect of nurse attendance on vertical transmission of HIV also in Kenya. For a systematic review of 36 RCT interventions, see Padian et al. (2010). None of these papers study PrEP intervention. Hence, this paper studies the effects of a new and promising policy. Additionally, the majority of papers study the African context. In the review of literature done by Padian et al. (2010), 32 of 37 studies selected were about Africa. Thus this paper also adds to the literature by studying the effect of policies in the context of a Latin American country.

This paper is organized as follows. Section 2 discusses the background of the empirical setting of the paper, by analyzing the scenario of HIV, other STIs, and PrEP in Brazil. Section 3 presents the data collected for this paper. Section 4 presents the empirical strategy designed to measure the effect of PrEP introduction. Section 5 presents some descriptive statistics of PrEP users in Brazil. Section 6 presents the main results of the paper, and Section 7 presents robustness and heterogeneity analysis of these results. Lastly, Section 8 discusses and compares the main findings with related literature and performs a

cost-benefit analysis. Section 9 states the main conclusions.

2 Background

2.1 HIV and STI in Brazil

The first case of AIDS in Brazil occurred in 1982. The cases were first concentrated on men that have sex with men who lived in big cities. In the following years, the cases continuously expanded, reaching almost the whole country and all segments of the population (Rachid and Schechter, 2017).

With the promulgation of a new constitution in 1988, health was considered a right of every citizen and a state responsibility in Brazil. This change paved the way for the creation of a Unified Public Health System (Sistema Único de Saúde, SUS), which was held responsible for providing centers for basic care, specialized centers, emergency centers, mental health services, and health surveillance. All of that with no cost for its users (Castro et al., 2019).

Through this system, the country started to distribute the first available treatments for AIDS, such as drugs for opportunist infections and the first antiretrovirals since 1991. However, it was only in 1996 that was approved a bill that assures every people living with HIV and AIDS the right to obtain all required medication for treating HIV infection in the public health system[1] (Galvão, 2002). It means that every new HIV infection represents a potential cost to the state. For example, in 2019, the Brazilian government spent more than R$ 1,8 billion on remedies for HIV treatment.[2]

The government also invested in prevention policies that are considered extremely successful (Okie, 2006). The efforts to fight HIV infection included "the promotion of HIV testing; promotion and education on condom use; the provision of disposable syringes; increasing the availability and provision of incentives for prenatal testing, and the prevention of other STD" (Levi and Vitória, 2002).[3]

Forty years after the start of the AIDS pandemic, Brazil still has more than 920

[1] Lei nº 9.313, de 13 de novembro de 1996.

[2] https://exame.com/brasil/pessoa-com-hiv-e-despesa-para-todos-no-brasil-diz-bolsonaro/

[3] Jim Yong Kim, former director of the World Health Organization's Department of HIV/AIDS said: "I think what they did was to say, 'We're going to scale up treatment, but we're going to scale up prevention along with it, because it doesn't make sense to do one without the other.´" (Okie, 2006)

thousand people living with HIV in 2019. In the same year, there were more than 40 thousand new cases of HIV infection, more than 37 thousand new cases of AIDS, and 10 thousand deaths related to HIV (Ministério da Saúde, 2020b).

The HIV epidemic in Brazil disproportionately affects the group of men that have sex with men (MSM). According to a survey by Kerr et al. (2018) in 12 capital cities of the country, 18.4% of this population lives with HIV, while this rate is 0.6% for the whole population.

Besides that, other groups also present rates of infection far above the overall population rate. Technical studies made by the Ministry of Health estimate that the proportion of infected individuals among sex workers is 4.9%, while it is 31.2% for transgender people (Ministério da Saúde, 2018b).

However, HIV is not the only sexually transmitted infection that is widespread across the country. A comprehensive representative national survey made by the Ministry of Health concluded that only in 2019 there were more than 1 million diagnoses of STIs in Brazil (IBGE, 2019). According to official notified cases, there were more than 200 thousand cases of syphilis and 30 thousand cases of viral hepatitis in the same year (Ministério da Saúde, 2020a,c). Other STIs are not tracked by the Ministry of Health.

2.2 PrEP in Brazil

Pre-exposure prophylaxis, also known as PrEP, is the use of antiretroviral drugs to prevent HIV infection in people not yet contaminated by the virus. Mainly, it is a drug prescribed to be taken daily, although there are other forms of using it.[4] The Centers for Disease Control and Prevention of the United States Government concluded, after reviewing the medical literature, that PrEP is highly effective in preventing HIV. When

[4] In July 2019, the World Health Organization (WHO) published guidelines for event-driven oral pre-exposure prophylaxis to prevent HIV for MSM and attested its efficacy. It consists of using a double dose of the same drug used in daily PrEP between two and 24 hours in advance of sex; then, a third pill 24 hours after the first two pills, and a fourth pill 48 hours after the first two pills. Event-driven PrEP has been described as "2+1+1" dosing, to better communicate with the general public. This method, however, was not included in the Brazilian official PrEP protocol, the official government document that provides guidelines to doctors able to prescribe PrEP. (World Health Organization, 2019)

In December 2021, the US Food and Drug Administration approved the first injectable treatment to prevent HIV infection. This prophylaxis is given first as two initiation injections administered one month apart and then every two months thereafter (FDA, 2021).

taken as prescribed, PrEP reduces the risk of getting HIV from sex by 99% and by injection drug use by at least 74% (CDC, 2021c).

This prophylaxis started to be distributed in the Brazilian public health system in January 2018. PrEP could not be obtained in Brazilian pharmacies, although it can be imported from other countries. Nevertheless, the cost is probably prohibitive for most citizens. According to Eilam and Delhommer (2021), PrEP could cost US$20,000 per year for a single individual, which represents more than 6 times the annual minimum wage in Brazil[5]. Therefore, although there are not enough data to make such a claim, it seems reasonable to believe that the vast majority of PrEP users obtain their drug in the public health system.

According to Brazilian PrEP protocol, the distribution of this type of drug must be indicated for some specific groups: men that have sex with men, transgender people, sex workers, and people in serodiscordant relationships (i.e., when one of the partners is living with HIV and the other is not). These groups have a high prevalence of HIV as shown in Section 2.1, but being part of one of them does not automatically make an individual eligible for PrEP. The Ministry of Health recommends that doctors also take into consideration contextual factors such as repeated sexual relations without condoms; quantity and diversity of sexual partners; repeated episodes of STIs; repeated use of Post-Exposure Prophylaxis (PEP)[6]; and practice of sex in exchange for money (Ministério da Saúde, 2018b).

Every patient willing to take PrEP must first proceed with tests for HIV, syphilis, hepatitis B, hepatitis C, and also exams to measure renal and hepatic function. These tests must be repeated quarterly and they are mandatory if the individual wants to continue on PrEP. This indicates that PrEP might induce a better screening in high-risk individuals, preventing the spread of these other diseases by stimulating early diagnosis and treatment. In addition, individuals recommended to PrEP must take the vaccine for hepatitis B if they did not complete this vaccine schedule and take the vaccine for hepatitis A if they are from a group with a high risk of contracting this disease sexually (mainly MSM with no antibodies) and also did not complete this vaccination schedule.

[5] Using 2018 values, 1 dollar costs R$ 3.8750, and hence PrEP (without importation costs) would cost R$ 77,500 for a single individual. The annual minimum salary in Brazil in the same year was R$ 11,448.

[6] According to the CDC, "PEP (post-exposure prophylaxis) means taking medicine to prevent HIV after a possible exposure. PEP should be used only in emergencies and must be started within 72 hours after a recent possible exposure to HIV" (CDC, 2021b).

Some studies attested high knowledge of PrEP among high-risk individuals in Brazil. For example, Torres et al. (2018) showed that 58% of MSM in dating apps are aware of PrEP. In addition, Assaf et al. (2021) in a more recent survey showed that this rate is 69% for MSM interviewed on social media in general.

A previous trial study by Grinsztejn et al. (2018) attested high adherence to PrEP among high-risk individuals in the country. Using a small sample of individuals, they showed that 83% of the individuals who initiated the treatment were retained for at least 48 weeks. Besides that, 74% of the participants had drug concentrations consistent with at least four doses per week in week 48.

In the past couple of years, the Ministry of Health is increasing access to PrEP. In December of 2021, they determined that the PrEP can be distributed in the Public Health System if the patient has a medic prescription from either a public or private doctor[7]. It means that the patient does not need to find a public doctor to obtain the drug for free anymore.

[7] Ofício Circular Nº 31/2021/CGAHV/DCCI/SVS/MS

3 Data

PrEP distribution I collected data from PrEP distribution in the Public Unified Health System (SUS) by opening a request for information to the Brazilian Ministry of Health. As I cited before, the SUS is the main source of PrEP distribution, and other sources are probably unfeasible for potential users, due to the high cost of the drug. I obtained a database containing information about PrEP distribution directly to users for each municipality by month.

Sexually transmitted infections Some diseases must be compulsorily notified to the Ministry of Health in the System for Notifiable Diseases (SINAN). This is valid for both public and private health centers. New cases of patients living with HIV that are not on AIDS must be obligatorily notified in the SINAN since 2014, while the notification of syphilis and hepatitis are mandatory since 2017. These last two diseases, however, were already implemented in the SINAN since 2010.

I collected microdata about these three diseases which might be transmitted sexually. I have detailed information about patients' characteristics, such as gender, age, race, schooling, and occupation. For HIV infections, I also have information about sexual orientation, which is not collected for other diseases.

I transformed the microdata about new infections of each disease in a balanced panel by quarter, using the date of diagnosis as the time of reference and the patients' city of residence as the unit of analysis. I restrict the analysis from the first quarter of 2016 until the first quarter of 2020. Using data about the population collected in the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatistica - IBGE), I transform the variables into rates of new cases per 100.000 inhabitants. I also create rates per subgroups of data (such as rates by gender, race, etc.) using the general population of the municipality as the denominator, since the size of each group is not available at traditional sources. I restrict the analysis to 4846 municipalities with at least 1 HIV case notified in the period.

In addition to the information about new infections of the cited diseases, I also

collected microdata about HIV related deaths[1] using the Brazilian Mortality Information System (Sistema de Informação sobre Mortalidade - SIM) for the years from 2016 to 2019. There is also information about gender, race, schooling, and age of each death. I transform the data similarly as before.

PrEP users According to the PrEP protocol, all patients must fill out standardized questionnaires at regular intervals of time. Specifically, they must fill out one on the first visit, the next one month after the first visit, and then one every three months. I obtained data about these filled forms for all PrEP users in Brazil. The Ministry of Health provided the data completely anonymized. All sociodemographic information about the patients was deleted to respect patient confidentiality. Therefore, in this source, I am not able to identify patients' information about gender, race, schooling, etc. However, I obtained information about the number of sexual partners, frequency of condom use, repeated use of PEP, use of drugs, and practice of sex in exchange for objects or services.

In order to obtain the sociodemographic characteristics of PrEP users, I collected this aggregated information on the PrEP panel made available by the Ministry of Health. Specifically, I obtain information about age, sexual orientation, schooling, and race.

[1] I consider HIV related deaths the ones with primary cause classified as B20, B21, B22, B23, B24 (CID-10)

4 Empirical Strategy

I exploit the temporal variation of PrEP implementation that begins in the first quarter of 2018 until the first quarter of 2020. For that purpose, I use a difference-in-differences (DID) model to analyze the effect of PrEP distribution on HIV and other STIs rates in the municipality. Specifically, I procedure an event study analysis, where I will estimate the following equation:

$$Y_{it} = \alpha_i + \beta_t + \sum_{k=-M}^{8} \gamma_k 1\left(K_{it} = K\right) + \epsilon_{it} \tag{4.1}$$

Where i and t represent municipality and quarter of the year, respectively. Additionally, Y_{it} is the main outcome of interest; α_i and β_t are unit and time fixed effects; $1(K_{it} = K)$ is a dummy that takes value one if the municipality i is treated and if $t - g$ is equal to K, where g is the first quarter that the municipality is treated. I test both pre- and post-treatment effects. I consider that the municipality is treated after the first dose of PrEP is distributed to an individual in the city i. Municipalities that never distributed a dose of PrEP in the period of analysis are thus never treated; ϵ_{it} is an idiosyncratic shock. Hence, we expect that γ_k represents the causal effect of the policy in the outcome of interest k periods after (or before) the treatment starts.

Recent literature shows that event studies estimated with traditional Two-Way Fixed Effects (TWFE) estimator can lead to biased estimates in staggered settings with heterogeneous treatment effects (Sun and Abraham, 2021). Additionally, aggregate parameters are hard to interpret in scenarios with heterogeneity (Goodman-Bacon, 2021; de Chaisemartin and D'Haultfœuille, 2020). Therefore, in addition to TWFE estimation, I will estimate and consider the method proposed by Callaway and Sant'Anna (2021) (CS) as benchmark, since it provides a robust estimation procedure in settings with multiple time periods and variation in treatment timing. In addition to the event study analysis, I will aggregate event study parameters in average treatment effects for the treated.

The main identification hypothesis is that the trends in the treatment and control would be similar in the absence of treatment. The control group is every municipality that is not yet treated or never treated. I test the validity of the hypothesis before the treatment to provide indirect evidence that it is reasonable after the treatment.

The objective of this paper is twofold. First, I test if municipalities that started to distribute PrEP changed the rate of new cases of HIV per 100,000 population. Notice that the expected signal is not clear. It might be the case that PrEP was distributed to people with low risk of HIV, and thus it has a null effect on preventing infection. However, if PrEP was distributed mainly to high-risk individuals, we would expect that it would cause a significant decline in new rates of HIV infection since it virtually eliminates the risk of being infected. Notice that individuals who receive PrEP could also receive more information about how to prevent being infected with HIV, access testing services, and obtain free condoms given by the state. This could also affect the HIV rate. This paper analyzes the effect of PrEP distribution as a whole and does not try to disentangle these mechanisms.

Second, I aim to identify if PrEP introduction affects the incidence of other STIs. Again, the expected effects are not straightforward. HIV is the sexually transmitted infection with the highest cost for the individual. It still has no cure, and the infected individual must take medications for the rest of his life. Additionally, people living with HIV (PLHIV) suffer from prejudice and shame. A survey done by UNAIDS with PLHIV in Brazil concluded that 64% of them already suffered discrimination and that 81% find it hard to tell other people about their serology status (UNAIDS, 2019). Since PrEP eliminates the risk of HIV infection, it considerably lowers the expected cost of risky sexual behavior, thus possibly increasing the practice of risky sex among PrEP users and making them more vulnerable to acquiring other STIs. That is the classical moral hazard problem well known by economists.

In the opposite direction, PrEP users have to constantly go to a doctor to obtain the drug. In these visits, they could receive information about the importance of safe sex and the risks associated with other STIs. Therefore, we would expect that they change their behavior by favoring safe sex. In addition, PrEP users are tested regularly for STIs. Frequent testing might induce early diagnosis, preventing the widespread of STIs in the overall population. In that case, it is expected that PrEP introduction decreases the rate of new STIs.

All these mechanisms are valid and can exist mutually. However, we can only know which effect will prevail empirically. To test that, I estimate the effect of PrEP introduction on the rate of new cases of two STIs, hepatitis and syphilis, divided by 100,000 population.

As said, I do not expect to disentangle each effect of the policy, but to evaluate it as

a whole. Thus the fact that PrEP policy might affect individuals through many channels does not harm the identification hypothesis. However, if the adoption of treatment is correlated with other programs, such as programs to decrease syphilis or hepatitis, the results are probably biased, since it is combined with the effect of other policies. Although I found no evidence that this is the case, it is not possible to completely rule out the possibility that this can be true.

5 Descriptive Statistics

In Table 1 I present some sociodemographic characteristics of PrEP users in Brazil. We can see that the vast majority of users are in the group of MSM (84.6%), followed by cis women (7.1%) and heterosexual men (4.5%). Regarding the users' race, 56.7% self-identify as white, while 42.9% identify as black or brown. Furthermore, we can see that more than half of them have high levels of education since 71.2% of them have 12 or more years of school. Lastly, note that the majority of the public is in the age group of 25 to 39 years old, representing approximately 66% of the users.

In Table 2, I show some characteristics of the users in the first medical consultation to initiate PrEP. First, we can see that approximately 30% of the respondents used post-exposure prophylaxis in the last year. This indicates that these people had at least one experience where there was identified a risk of HIV infection.

We can also see that most of the patients had more than three sexual partners in the last three months (55.17%). In addition, 10.51% reported receiving money, valuable objects, drugs, housing, or services in exchange for sex.

Regarding condom use, 79% admitted having sexual relations without condoms in the last six months. Specifically, 27% reported having sexual relations with partners that live with HIV and 26.37% do not know if they had. In addition, 17.09% were diagnosed with STIs in the last six months.

Lastly, I create an aggregate index to measure if the individual can be considered at high risk of acquiring HIV. I define a variable that classifies an individual as high-risk if either: the individual used PEP last year, the individual accepted benefits in exchange for sex, the individual "Never" or "Less than half of the times" uses a condom during sex, the individual had any sexual relations with partners living with HIV without condoms in the last six months, the individual has more than 3 sexual partners or the individual was diagnosed with STI in the last six months. Notice that 87.10% of the individuals are classified as high-risk using these criteria.

These statistics show that PrEP is highly concentrated in a population that is more susceptible to HIV infection. Not only because it is highly concentrated in the group of MSM, which presents high rates of HIV among its population, but also because it focuses

on groups with sexual behaviors that are compatible with a higher risk of HIV.

6 Results

Before presenting the main results, I use the methodology proposed in 4 to show how PrEP distribution per 100,000 inhabitants evolved through time in Figure 1. Notice that the pre-treatment coefficients are all identically equal to zero since I define that the municipality is only treated after distributing at least one dose of PrEP. In the first quarter of treatment, the rate of doses of PrEP distributed per 100,000 was less than 10 on average, while it reached 40 in the last quarter, after continuously increasing this share through time. Using Callaway and Sant'anna to calculate the aggregated parameter, we find an ATT of 20.99.

Besides representing only a small fraction of the overall population, PrEP distribution is highly focused on the group of MSM with high-risk sexual behaviors, as shown in Section 5. There is no precise data about the size of the MSM population in each municipality of Brazil, which is why I do not use it as a denominator. However, Grey et al. (2016) estimates that the MSM population represents 3,9% of the overall population of the United States on average. Estimates collected by WHO and UNAIDS (2020) range from 1% for 4% in various countries. Hence, the rates presented would be at least 25 times bigger if divided by the MSM population instead of the overall population.

Now I turn to the results for the HIV rate. The Figure 2 plots the event study for this relation. The dependent variable is the rate of new cases of HIV. First, notice that TWFE and Callaway and Sant'anna estimators show very similar results. We see that the treatment and control groups follow a similar trend in pre-treatment periods but diverge in the later periods after treatment. Notice that the pattern of an increasing effect through time is consistent with PrEP being continuously expanded to the users. The aggregate parameter calculated by Callaway and Sant'anna is -0.88 (SE 0.36), representing a decrease of 7.8% in the rate of new cases of HIV per 100,000 inhabitants. However, we can see that this effect is heterogeneous through time, and is very close to -2.00 in the more distant treatment periods. In the 7 period, estimated effect is -2.11 (-18.7%). Using back to envelope calculations, we find that for each 100 distributed doses of PrEP, we reduce nearly 4 HIV cases on average in a quarter of a year.[1]

[1] Using the proportion of 4 fewer HIV cases for each 100 distributed doses of PrEP, if we sum all doses distributed and all new cases of HIV in the treated municipalities only in the periods that they are

Next, I analyze the effects of PrEP introduction in other STIs. In Figure 3, I report the results on syphilis. We can see no clear pattern of increase before or after PrEP introduction. The aggregate parameter is 1.06 (SE 1.13) and is not statistically significant. Despite that, we can see a small upward shift in the periods after the PrEP introduction, but with large standard errors. In general, the results indicate that there might not be enough power to reject the null hypothesis of no effect of the policy on syphilis. Therefore, those results must be interpreted with extra caution.

In Figure 4 I show the effects for hepatitis. The results suggest that there are no pre-trends, but the rate of hepatitis per 100,000 inhabitants decreases after the introduction of PrEP, although treatment group and control means appear to converge to the same point in the last period. The pattern in which the size of the effect increases over time is also consistent with PrEP being expanded through time. The implied ATT coefficient is -0.53 (SE 0.18), which represents a decrease of 9.1% relative to the mean.

In general, those results appear to reject the hypothesis of huge moral hazard effects related to the studied intervention. If anything, the beneficial effects of PrEP policy appear to overshadow potential adverse effects that would be expected by classic economic theory.

treated, we found that PrEP reduced by 7.4% the total number of new HIV cases. Notice that this is very similar to the 7.8% reduction I reported by comparing the effect with the mean for treated units between 2016 and 2017. Similarly, if we consider all quarters, including both treated and untreated municipalities, the rate of new cases of HIV in Brazil would be 3.2% higher in the absence of PrEP.

7 Robustness and heterogeneity analysis

This section presents robustness and heterogeneity analysis of the previous results. Here, I divide the number of new cases of each STI for a specific subgroup by the entire population and multiply by 100,000. For example, for the group of MSM, I divide the number of new cases in the MSM population by the *overall* population and multiply it by 100,000. Note that this consistently underestimates the rates of new cases per 100,00 population of each group, as argued in Section 6, but since there is no precise information about the size of all populations in each municipality, there are no alternatives.

The first heterogeneity analysis comprises the gender and sexual orientation of the individuals. As shown in Section 5, the majority of the PrEP population is in the group of MSM. Therefore, if the results found in the last section are related to PrEP, we expect this group to be the most affected by the policy. This might not be the case if, for example, municipalities that engage in PrEP distribution also engage in a higher tracking of people living with HIV, offering treatment and making them undetectable for HIV, thus untransmittable, reducing HIV spread in the population. If this is true, however, it is reasonable to suppose that it equally affects all subgroups of the population.

In Figure 5 I plot the results for new HIV cases for 3 subgroups of the population: Straight men, MSM, and Women. I do not divide women by sexual orientation because new cases of HIV are very rare in women that have sex with women. Notice that we see no distinguishable effects for women and straight men, but we find a negative effect of the policy on the group of MSM.

In Table 3 there is the summarized results for heterogeneity for HIV rate per 100,000. As shown in Section 6 PrEP distribution reduced by 0.88 (-7.8%) new cases of HIV per 100k. The relative effect is higher for the groups of MSM, where the implied coefficient is -0.78 and represents a 13.44% reduction statistically significant at 5 percent. We see no significant effect for straight men (0.07). There is a modest negative yet not significant effect for women (-0.16) and other groups not focused on the policy. Additionally, we see significant effects for individuals aged between 25 and 39 years (-10.24%) and who completed high school (-11.38%). As shown in Section 5, this is also consistent with the PrEP users: 71.2% have 12 or more years of school, and 66,1% have between 25 and 39

years old. We do not see significant effects for other age groups or people who did not complete high school.

In general, the results for HIV are highly concentrated in the main groups focused on the policy. Since we are capturing a short period of time, this gives confidence that they are capturing the effect of PrEP introduction. However, over a long period, it might be the case that the reduction of cases in a specific group leads to a consistent reduction in other groups as well.

Lastly, I plot the results of the PrEP introduction in deaths related to HIV. Since this analysis is restricted to the short-run, it is expected that the policy affects new cases of HIV, but does not have any impact on long-run outcomes (thus, we expect it has no impact on deaths). In Figure 6 this hypothesis is confirmed. We see no overall impact in HIV-related deaths. In Table 4 I show the implied ATTs for subgroups. There are also no statistically significant impacts on all subgroups: men, women, age 13-24, age 25-39, age 40+, 12+ years of schooling, 12- years of schooling, white and non-white.

In Table 5, I plot heterogeneity analysis for syphilis. Notice that all subgroups' ATTs are positive but non-statistically significant. The coefficients are slightly higher for groups not focused on the policy. For example, notice that the effect is higher for women (0.68) than for men (0.38). Also, the coefficient is higher for people aged between 13 to 24 years old (0.44) than for people aged between 25 to 39 years. This provides suggestive evidence that syphilis is not increasing due to the PrEP policy.

In Table 6, I plot heterogeneity analysis for hepatitis. First, we see that the effect is mainly focused on hepatitis A and hepatitis C, and it is not significant for hepatitis B. Some mechanisms might be behind this result. All MSMs who are PrEP users are recommended to take the vaccine for hepatitis A, and thus it can lead to a reduction of cases. Hepatitis B vaccine is also recommended, and no effect is found for this disease. However, the hepatitis B vaccine is on Brazil's universal immunization program since the 90s, while the hepatitis A vaccine is only since 2014 (Brito and Souto, 2020; Costa et al., 2021). Therefore, it is likely that PrEP increased immunization against hepatitis A, while having little impact on hepatitis B. For hepatitis C, there exists no vaccine against it. However, PrEP users are tested quarterly for this disease. Thus, the effect probably comes from a higher screening preventing widespread disease.

Notice that the coefficient is significant for acute cases, but not statistically signifi-

cant for chronic cases.[1] This is consistent with PrEP introduction preventing short-run infections, but having no impact on long-run outcomes, which are probably determined before the PrEP policy. Also, notice that the results are statistically significant for men and individuals aged between 25 to 39 years old, two groups highly focused on the PrEP policy. In that case, however, the coefficient for the group who completed high school is not statistically significant, but it is for people who did not complete.

[1] Chronic hepatitis is inflammation of the liver that lasts at least 6 months. Usually, it means that the patient discovered the disease an extended period after infection

8 Discussion

8.1 Cost-benefit analysis

According to Luz et al. (2018), PrEP drug costs US$ 270 per year in Brazil. Additionally, they estimate HIV test costs US$ 1.57 per unit, clinic visit costs US$ 3.73 per visit, and creatinine testing costs US$ 0.69. The author does not provide costs for syphilis, hepatitis, and tests for other STIs. Let us assume that this represents an additional US$ 10 per doctor visit. Assuming four doctor visits per year, in which HIV and other STIs are screened and creatinine tests are performed, we obtain a yearly cost of approximately U$ 64 per patient. Therefore, an individual taking PrEP costs US$ 334 per year to the public health system.

In opposite, antiretroviral therapy for people living with HIV can cost from US$ 120 to US$ 6119, depending on the line of the treatment. Based on Brojan et al. (2020), I assume the following proportions: 60% individuals using first-line treatments, 30% using second-line treatments, and 10% using third-line treatments. Therefore, using the costs of each treatment line provided by Luz et al. (2018), I find an average cost of ARV per person of approximately US$ 964. Adding the cost of two CD4 count tests (US$ 13.57 each) recommended by Ministério da Saúde (2018a), and one viral load test per year (US$ 14.36), an HIV patient costs US$ 1006 to the public health system per year.

Using back to envelope calculations, we found that 100 distributed doses of PrEP reduce 4 new cases of HIV per quarter on average. Therefore, yearly, we would expect fewer 16 cases. Assuming an investment of US$ 334×100 in one year, the return would be US$ 1006×16 saved from the public spending yearly for all years that these persons would live being treated for HIV. This means that the Net Present Value (NPV) would be positive for this investment (assuming a 5% discount rate) as of 3 years after it was implemented.

However, until here I did not consider the effect of the PrEP policy in reducing new cases of hepatitis. Now I discuss this. In Section 7, it is shown that PrEP policy reduces 0.53 cases of hepatitis in a quarter on average. However, 0.23 are cases of Hepatitis A and 0.30 are cases of hepatitis C. No treatment exists for Hepatitis A. Most cases are cured on

their own (CDC, 2021a), implying few costs to the state. Therefore, the analysis here is focused on cases of hepatitis C. According to Schwambach et al. (2020) the average cost of treating an individual with genotype 1 of hepatitis[1] in Brazil is US$5,862.03.

Using back to envelope calculations, results show that each 100 distributed doses of PrEP would reduce 5,7 cases of hepatitis C per year. Therefore, if we round that to 6, the state would save US$ $5,862.03 \times 6$ yearly. Notice that this is higher than the annualized cost of PrEP. This means that the benefits generated by positive externalities associated with the policy are larger than the costs of the policy itself in the same year it was implemented.

8.2 Related Literature

Notice that the results found in this paper differ from the ones found for Eilam and Delhommer (2021) in the US case, where they find that PrEP introduction increased STIs. I suggest two main hypotheses to account for this fact: first, the PrEP distribution is very restricted in the Brazilian case. Since it is provided by the state, the government can enforce a rigid protocol for the whole country and determine which segments of the population are going to use it. The result is that only high-risk individuals have access to PrEP. Since these users engage in risky sexual before joining PrEP, there is no room for huge changes in sexual behavior favoring STI infection, although it is not possible to rule out them completely.

On the contrary, Eilam and Delhommer (2021) suggest that the majority of users in the US case are not high-risk individuals. In that case, there is plenty of room for changes in sexual behavior due to moral hazard effects. In that case, the authors argue that "PrEP essentially subsidizes risky sex without the benefit of a reduction in HIV risk."

This is consistent with results on sexual behavior. In the US, Eilam and Delhommer (2021) argue that, after PrEP, gay men reported engaging more in sex without condoms, while the median number of partners remained constant. On the contrary, in a trial with high-risk individuals in Brazil conducted by Grinsztejn et al. (2018), they found that the proportion of participants reporting condomless sex with their last three partners did not vary substantially over time, but the mean number of sexual partners decreased from 11.4 to 8.3 (p=0.0013).

[1] This represents the majority (66.8%) of cases identified in the study, that was conducted in a large city of Brazil

Second, the authors argue that there is no increase in STI testing in the US due to PrEP. Thus, if PrEP users do not frequently test and change their behavior by engaging in risky sex, this may increase the probability of acquiring an STI and spread them to other people. Theoretical models have provided some evidence that screening for STIs might have an impact on diminishing its spread. Using a mathematical model calibrated for the UK prevalence of HIV and Hepatitis C virus (HCV) infection among MSM, MacGregor et al. (2020) conclude that screening and treating PrEP users for HCV every 12 or 6-months decreases HCV incidence by 67,3%. The results change little with behavioral changes due to PrEP. However, according to the authors, this country does not require HCV testing for PrEP users.

In Brazil, using data from the first visits to the doctor after PrEP prescription is possible to see that the majority of users realized screening for other STIs. For example, 88,1% take tests for syphilis, 80,6% take tests for hepatitis B[2] and 86,4% take tests for hepatitis C.

Lastly, the PrEP policy in Brazil also offered vaccines for some STIs at no cost to the individuals, a well-studied and effective way of preventing infection. Therefore, by combining PrEP with such measures, even if individuals engage in riskier sex, there is some degree of confidence that they will not catch some diseases.

Therefore, the results of this article reflect that Brazil conducted a very target public policy, focusing on the individuals with a higher risk of HIV, effectively tracked STIs, and protected individuals in advance, being able to counterbalance moral hazard effects. Regarding policy recommendations, the results suggest that other countries would benefit from introducing screening for STIs for all PrEP users and enforcing their already existing protocols to become more strict about PrEP eligibility. Lastly, they could also benefit from increased access to vaccines to protect PrEP users in advance for some STIs.

[2] Since users are required to take the hepatitis B vaccine, this disease is less tracked than the others

9 Conclusion

In 2019, the US announced a bold plan to eradicate HIV from the country by 2030[1]. Other countries have similar goals, such as Australia[2] and United Kingdom[3]. Ending HIV now seems reachable, but progress is not being made at the pace it is expected to achieve this goal (UNAIDS, 2021).

This paper documents the effects of a public policy to prevent HIV infection in a large developing country. It is found that a very targeted public policy can reduce new cases of HIV. Additionally, if the design of the policy incorporates high screening among the patients and measures to prevent the widespread of other STIs, it can help to reduce the incidence of other diseases and counterbalance potential moral hazard effects. Because of that, the benefits of the program are higher than its costs. Therefore, the distribution of Pre-Exposure Prophylaxis must be in the toolkit of policymakers to achieve the aim of ending new cases of HIV.

Despite that, the results above might be taken with caution. First, it was only possible to assess the impact of the policy on two STIs, because data was not available for other diseases. Each one of them might have its own characteristics, and effects may differ because of that. Second, this paper covers only a short period of time (2 years and a quarter), and effects might take a longer time to appear. Future research could address these problems.

[1] https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/
[2] https://www.afao.org.au/our-work/agenda-2025/
[3] https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00038-8/fulltext

Bibliography

Assaf, R., K. Konda, T. Torres, H. Vega-Ramirez, O. Elorreaga, D. Diaz-Sosa, S. Diaz, C. Pimenta, R. García, M. Medina-Mora, B. Grinsztejn, C. Caceres, and V. Veloso (2021, 08). Are men who have sex with men at higher risk for HIV in latin america more aware of PrEP? *PLOS ONE 16*, e0255557.

Björkman Nyqvist, M., L. Corno, D. de Walque, and J. Svensson (2018, July). Incentivizing safer sexual behavior: Evidence from a lottery experiment on HIV prevention. *American Economic Journal: Applied Economics 10*(3), 287–314.

Brito, W. I. d. and F. J. D. Souto (2020). Universal hepatitis a vaccination in brazil: analysis of vaccination coverage and incidence five years after program implementation. *Revista Brasileira de Epidemiologia*.

Brojan, L. E. F., L. M. Marca, F. A. Dias, and Y. D. Rattmann (2020). Antiretroviral drug use by individuals living with HIV/AIDS and compliance with the clinical protocol and therapy guidelines. *einstein (São Paulo) 18:eAO4995*.

Callaway, B. and P. H. Sant'Anna (2021). Difference-in-differences with multiple time periods. *Journal of Econometrics 225*(2), 200–230. Themed Issue: Treatment Effect 1.

Castro, M. C., A. Massuda, G. Almeida, N. A. Menezes-Filho, M. V. Andrade, K. V. M. de Souza Noronha, R. Rocha, J. Macinko, T. Hone, R. Tasca, L. Giovanella, A. M. Malik, H. Werneck, L. A. Fachini, and R. Atun (2019). Brazil's unified health system: the first 30 years and prospects for the future. *The Lancet 394*(10195), 345–356.

CDC (2021a). Hepatitis A guidelines. https://www.cdc.gov/hepatitis/hav/afaq.htm. Accessed: 2022-03-28.

CDC (2021b). Post-exposure prophylaxis (PEP). https://www.cdc.gov/hiv/basics/pep.html. Accessed: 2021-03-01.

CDC (2021c). Pre-exposure prophylaxis (PrEP). https://www.cdc.gov/hiv/risk/prep/index.html. Accessed: 2021-12-28.

Costa, G., I. Bezerra, and S. Gadelha (2021, 07). Clinical, epidemiological aspects, and trends of hepatitis b in brazil from 2007 to 2018. *Scientific Reports 11*, 1–10.

de Chaisemartin, C. and X. D'Haultfœuille (2020, September). Two-way fixed effects estimators with heterogeneous treatment effects. *American Economic Review 110*(9), 2964–96.

Doleac, J. and A. Mukherjee (2018). The moral hazard of lifesaving innovations: Naloxone access, opioid abuse, and crime. *IZA Discussion paper 11489*.

Donohue, John J., I. and S. D. Levitt (2001, 05). The impact of legalized abortion on crime. *The Quarterly Journal of Economics 116*(2), 379–420.

Duflo, E., P. Dupas, and M. Kremer (2015, September). Education, HIV, and early fertility: Experimental evidence from Kenya. *American Economic Review 105*(9), 2757–97.

Eilam, N. and S. Delhommer (2021). PrEP and moral hazard. *Working paper*.

FDA, U. (2021). FDA approves first injectable treatment for HIV pre-exposure prevention. https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention. Accessed: 2021-12-28.

Galvão, J. (2002). Access to antiretroviral drugs in brazil. *The Lancet 360*(9348), 1862–1865.

Goldstein, M., J. Graff Zivin, J. Habyarimana, C. Pop-Eleches, and H. Thirumurthy (2013, April). The effect of absenteeism and clinic protocol on health outcomes: The case of mother-to-child transmission of HIV in kenya. *American Economic Journal: Applied Economics 5*(2), 58–85.

Goodman-Bacon, A. (2021). Difference-in-differences with variation in treatment timing. *Journal of Econometrics 225*(2), 254–277. Themed Issue: Treatment Effect 1.

Greenwood, J., P. Kircher, C. Santos, and M. Tertilt (2019). An equilibrium model of the african HIV/AIDS epidemic. *Econometrica 87*(4), 1081–1113.

Grey, J. A., K. T. Bernstein, P. S. Sullivan, D. W. Purcell, H. W. Chesson, T. L. Gift, and E. S. Rosenberg (2016, Apr). Estimating the population sizes of men who have sex

with men in us states and counties using data from the american community survey. *JMIR Public Health Surveill 2*(1), e14.

Grinsztejn, B., B. Hoagland, R. Moreira, E. Kallas, J. Madruga, S. Goulart, I. Leite, L. Freitas, L. Marins, T. Torres, R. Vasconcelos, R. De Boni, P. Anderson, A. Liu, P. Luz, V. Veloso, V. Adão, P. Alencastro, A. Amaral, and N. Zuccaro (2018, 02). Retention, engagement, and adherence to pre-exposure prophylaxis for men who have sex with men and transgender women in PrEP Brasil: 48 week results of a demonstration study. *The Lancet HIV 5*.

IBGE, I. (2019). Pesquisa nacional de saúde - 2019 - acidentes, violências, doenças transmissíveis, atividade sexual, características do trabalho e apoio social. Technical report, IBGE, Rio de Janeiro.

Kerr, L. R., C. Kendall, M. Guimarães, R. Mota, M. A. Veras, I. Dourado, A. Brito, E. Merchan-Hamann, A. Kerr Pontes, A. Fachel Leal, D. Knauth, A. Castro, R. Macena, L. Lima, L. Oliveira, M. Cavalcantee, A. Benzaken, G. Pereira, C. Pimenta, and L. Johnston (2018, 05). HIV prevalence among men who have sex with men in brazil: results of the 2nd national survey using respondent-driven sampling. *Medicine 97*, S9–S15.

Lakdawalla, D., N. Sood, and D. Goldman (2006). HIV breakthroughs and risky sexual behavior. *The Quarterly Journal of Economics 121*(3), 1063–1102.

Levi, G. C. and M. A. A. Vitória (2002). Fighting against AIDS: the Brazilian experience. *AIDS 16*(18).

Luz, P., B. Osher, B. Grinsztejn, R. Maclean, E. Losina, M. Stern, C. Struchiner, R. Parker, K. Freedberg, F. Mesquita, R. Walensky, V. Veloso, and A. Paltiel (2018, 03). The cost-effectiveness of HIV pre-exposure prophylaxis in men who have sex with men and transgender women at high risk of HIV infection in Brazil. *Journal of the International AIDS Society 21*, e25096.

MacGregor, L., M. Desai, N. K. Martin, J. E. Nicholls, F. Hickson, P. Weatherburn, M. Hickman, and P. T. Vickerman (2020). Scaling up screening and treatment for elimination of hepatitis C among men who have sex with men in the era of HIV pre-exposure prophylaxis. *EClinicalMedicine 19*.

Ministério da Saúde (2018a). Protocolo clínico e diretrizes terapêuticas para manejo da infecção pelo HIV em adultos. Technical report, Ministério da Saúde, Brasília.

Ministério da Saúde (2018b). Protocolo clínico e diretrizes terapêuticas para profilaxia pré-exposição (PrEP) de risco à infecção pelo HIV. Technical report, Ministério da Saúde, Brasília.

Ministério da Saúde (2020a). Boletim epidemiológico - Hepatities Virais - 2020. Technical report, Ministério da Saúde, Brasília.

Ministério da Saúde (2020b). Boletim epidemiológico - HIV - 2020. Technical report, Ministério da Saúde, Brasília.

Ministério da Saúde (2020c). Boletim epidemiológico - Sífilis - 2020. Technical report, Ministério da Saúde, Brasília.

Okie, S. (2006). Fighting hiv — lessons from brazil. *New England Journal of Medicine 354*(19), 1977–1981. PMID: 16687709.

Padian, N., S. McCoy, J. Balkus, and J. Wasserheit (2010, 02). Weighing the gold in the gold standard: Challenges in HIV prevention research. *AIDS (London, England) 24*, 621–35.

Rachid, M. and M. Schechter (2017). *Manual de HIV / Aids.* Thieme Revinter.

Schwambach, K. H., M. R. Farias, G. B. Neto, and C. R. Blatt (2020). Cost and effectiveness of the treatment of chronic hepatitis c in brazil: Real-world data. *Value in Health Regional Issues 23*, 49–54.

Sun, L. and S. Abraham (2021). Estimating dynamic treatment effects in event studies with heterogeneous treatment effects. *Journal of Econometrics 225*(2), 175–199. Themed Issue: Treatment Effect 1.

The Lancet (2021). 40 years of HIV/AIDS: a painful anniversary. *The Lancet 397*(10290), 2125.

Torres, T., R. De Boni, M. Vasconcellos, P. Luz, B. Hoagland, R. Moreira, V. Veloso, and B. Grinsztejn (2018, 01). Awareness of prevention strategies and willingness to use pre-exposure prophylaxis in brazilian men who have sex with men using apps for sexual encounters: Online cross-sectional study. *JMIR Public Health and Surveillance 4*, e11.

UNAIDS (2019). PLHIV stigma index 2.0 report from Brazil 2019. Technical report, United Nations Programme on HIV/AIDS.

UNAIDS (2021). Global AIDS update. Technical report, UNAIDS.

WHO and UNAIDS (2020). Recommended population size of men who have sex with men. Technical report, WHO and UNAIDS.

World Health Organization (2019). What's the 2+1+1? event-drivel oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: update to WHO's recommendation on oral PrEP. Technical report, World Health Organization, Brasília.

Figure 1 – PrEP per 100,000 inhabitants

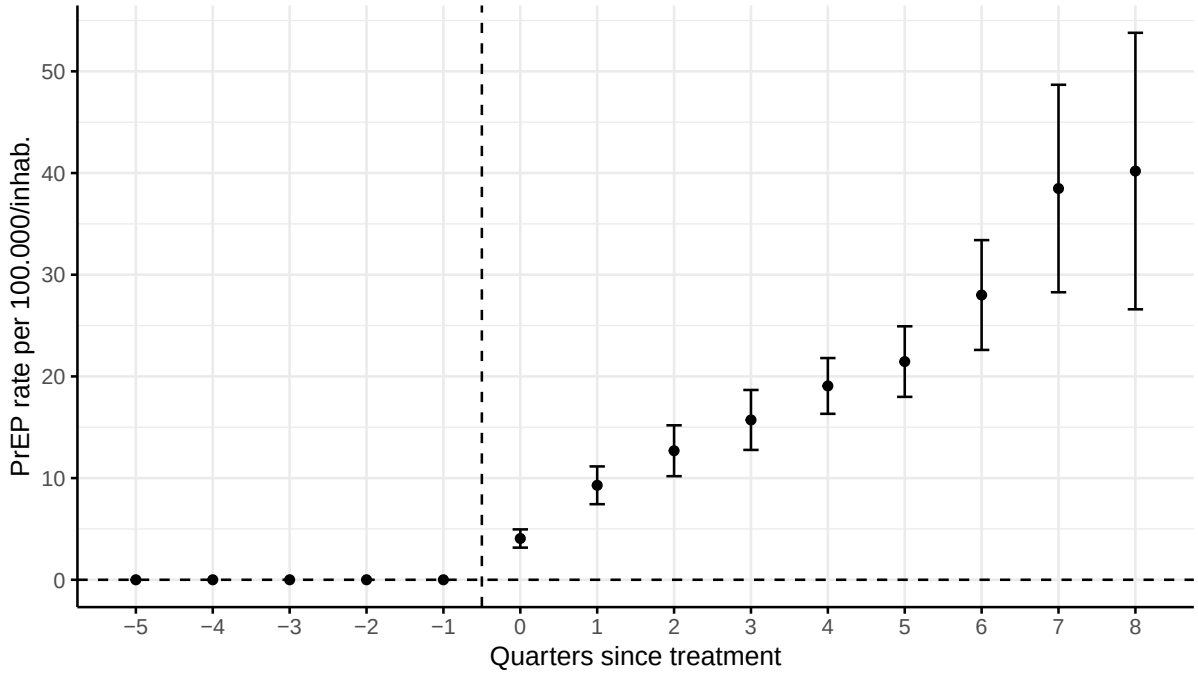
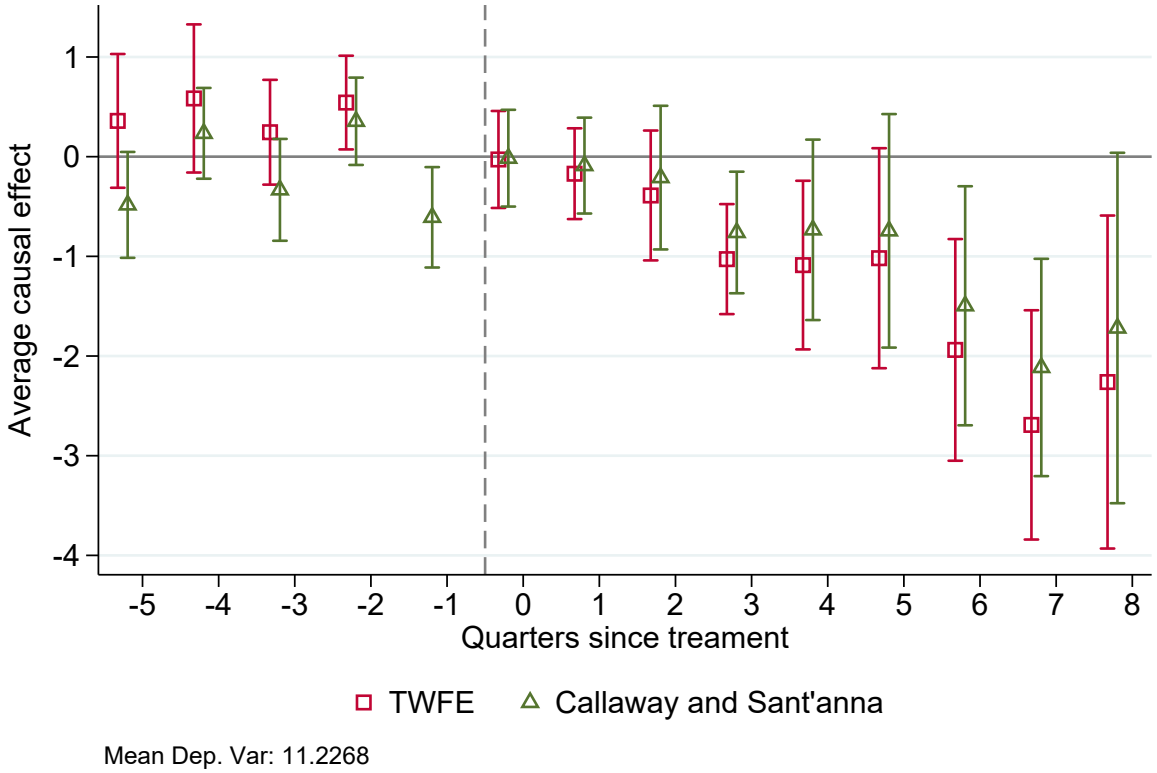
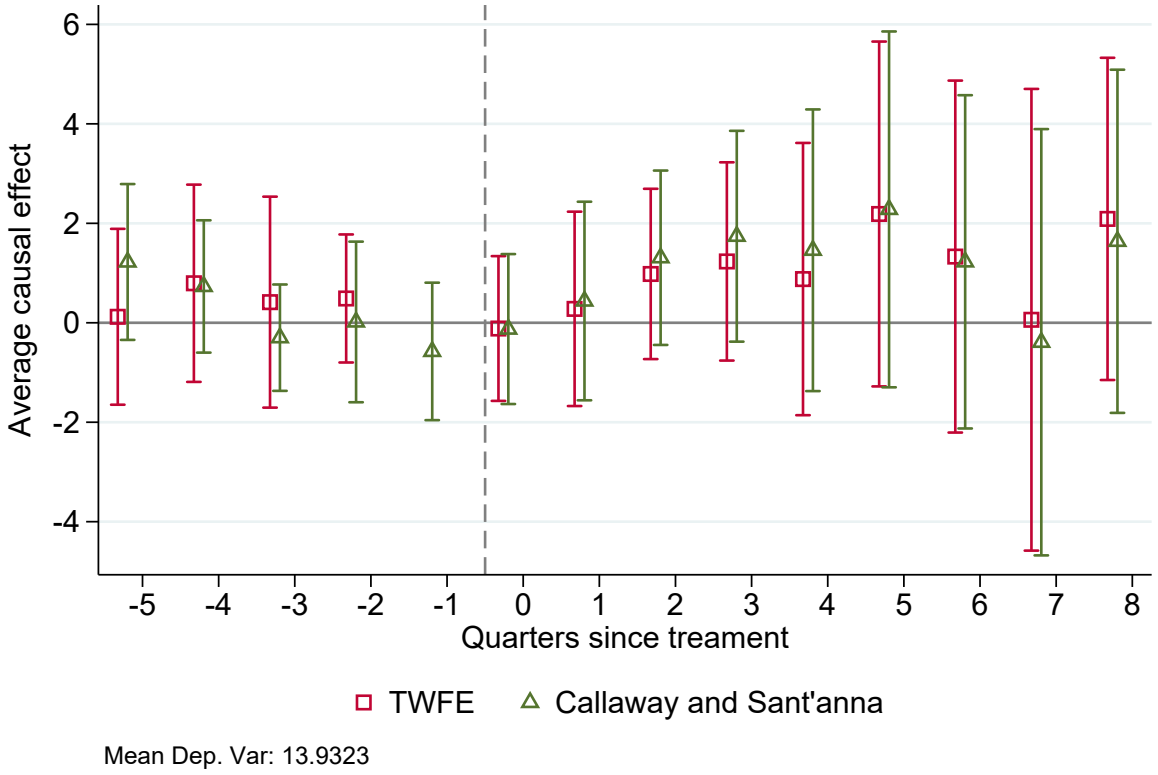


Figure 2 – Effect of PrEP introduction on HIV



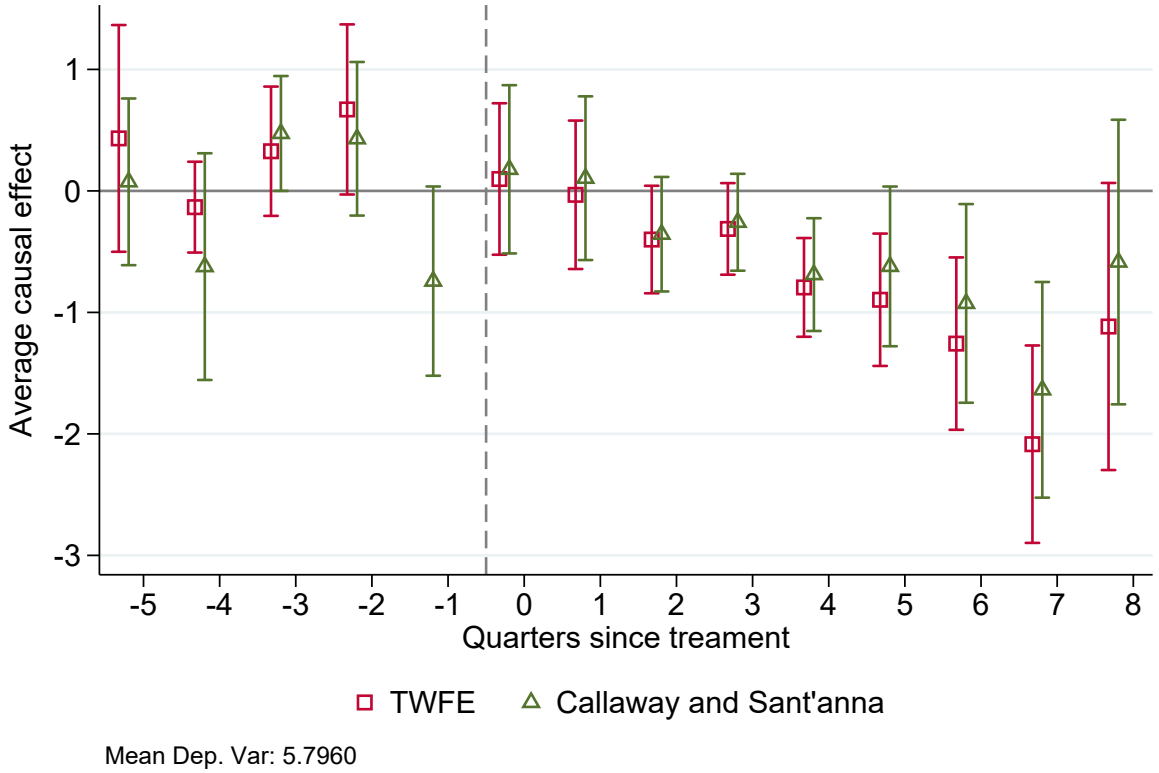
Notes: Event-study is calculated using TWFE and Callaway and Sant'anna estimators. "Mean dep. var." is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Figure 3 – Effect of PrEP introduction on Syphilis



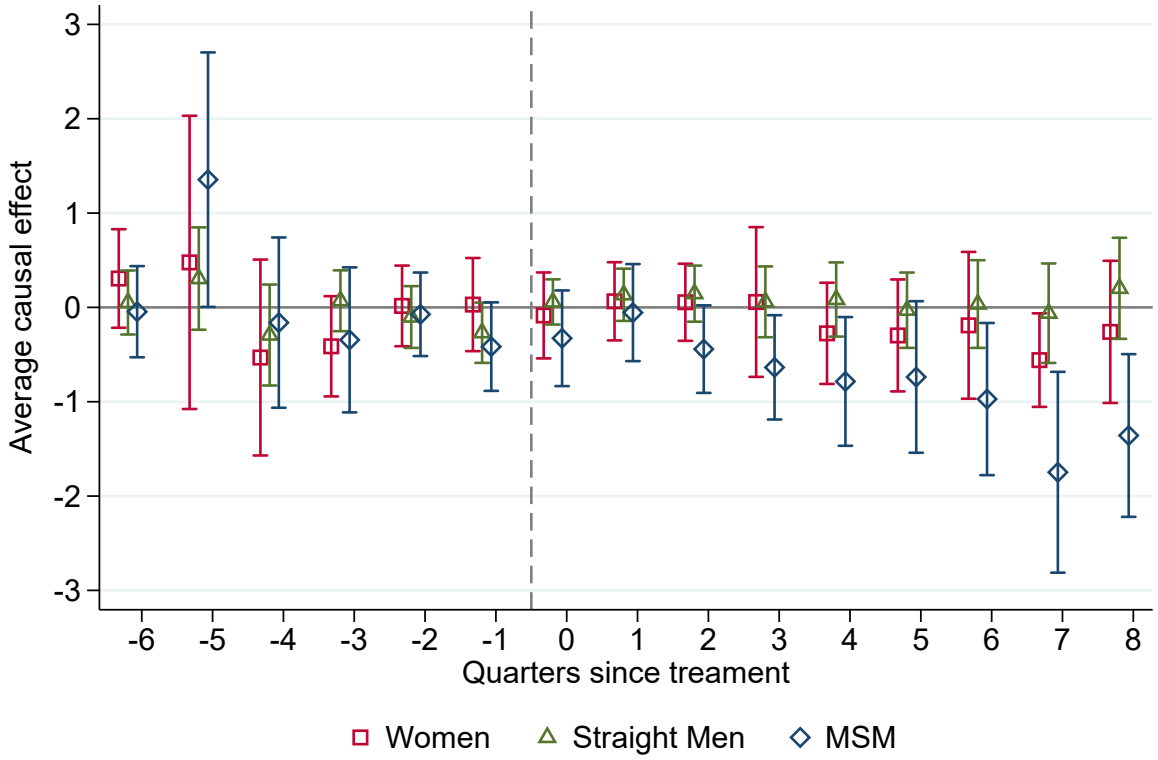
Notes: Event-study is calculated using TWFE and Callaway and Sant'anna estimators. "Mean dep. var." is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Figure 4 – Effect of PrEP introduction on hepatitis



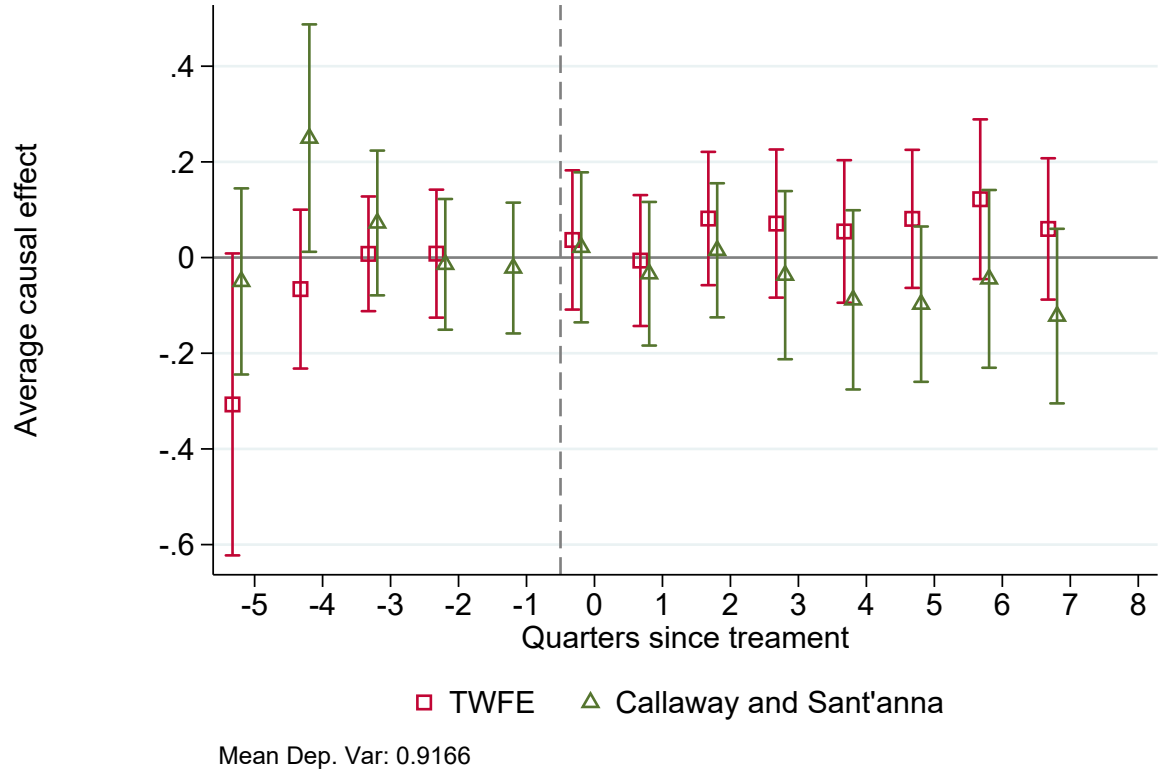
Notes: Event-study is calculated using TWFE and Callaway and Sant'anna estimators. "Mean dep. var." is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Figure 5 – Heterogeneity of PrEP introduction on rate of new HIV cases per subgroup



Notes: Event-study is calculated using Callaway and Sant'anna estimator. "Mean dep. var." is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Figure 6 – Effect of PrEP introduction on HIV deaths



Notes: Event-study is calculated using TWFE and Callaway and Sant'anna estimators. "Mean dep. var." is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Table 1 – PrEP user's profile

Population group	
Men that have sex with men	84.6%
Cis women	7.1%
Heterosexual cis men	4.5%
Trans women	3.3%
Trans men	0.4%
Race	
White/Yellow	56.7%
Black	42.9%
Indigenous	0.4%
School	
0-3 years of school	0.8%
4-7 years of school	3.5%
8-11 years of school	24.5%
12 or more years of school	71.2%
Age	
18-24 years	12.2%
25-29 years	24.9%
30-39 years	41.2%
40-49 years	15.8%
50 or more years	5.9%

Notes: Data by the Ministry of Health in the Panel of PrEP indicators. The data was collected in November of 2021.

Table 2 – Descriptive statistics about patients at first visit to PrEP

1. How many dosis of PEP did you use last year?	
0	69.80%
1	20.78%
2	6.21%
3+	3.20%
2. In the last three months, how many sexual partners did you had?	
0	2.48%
1	32.25%
2	10.10%
3+	55.17%
3. In the last six months, did you received money, valuable objects, drugs, housing or services in exchange of sex?	
No	89.49%
Yes	10.51%
4. In the last three months, how often did you use a condom during intercourse?	
Never	11.10%
Less than half of the times	12.41%
Half of the times	10.70%
More than half of the times	34.75%
Everytime	31.05%
5. In the last six months, did you have any sexual relation without condom?	
No	20.09%
Yes	79.91%
6. In the last six months, did you have any sexual relation without condom with partners living with HIV?	
No	39.49%
Don't know	26.37%
Yes	27.00%
Don't apply	7.14%
7. In the last six months, did you have any symptom or was diagnosed with any STI?	
No	82.91%
Yes	17.09%
8. (Proxy) High-Risk for HIV	
No	12.90%
Yes	87.10%

Notes: Data from the Ministry of Health. The variable for "high-risk" for HIV was created by the author and the individual is considered as high-risk if either: used PEP last year, accepted benefits in exchange for sex, "Never" or "Less than half of the times" uses condom during sex, had any sexual relations with partners living with HIV without condoms in the last six months, has more than 3 sexual partners, or was diagnosed with STI in the last six months.

Table 3 – Heterogeneity for HIV

Variable	ATT	SE	Sign 5%	Mean
Overall	-0.88	0.36	*	11.23
MSM	-0.78	0.28	*	5.84
Straight	-0.04	0.28		6.38
Straight Men	0.07	0.16		2.99
Women	-0.16	0.16		4.04
Age 13-24	-0.27	0.16		3.15
Age 25-39	-0.74	0.29	*	7.23
Age 40+	-0.16	0.22		4.43
High School	-0.70	0.35	*	6.14
Without High School	-0.27	0.21		4.71
White	-0.38	0.28		6.28
Non White	-0.78	0.41		7.19

Notes: ATT is calculated using Callaway and Sant'anna (2020), with population as weights. "Sign 5%" is filled with an $*$ if the results are significant at a 5% level. "Mean" is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Table 4 – Heterogeneity for HIV deaths

Variable	ATT	SE	Sign 5%	Mean
Overall	-0.05	0.07		0.92
Men	-0.04	0.06		0.62
Women	-0.01	0.04		0.30
Age 13-24	-0.01	0.01		0.05
Age 25-39	-0.01	0.03		0.30
Age 40+	-0.03	0.06		0.56
School 12+ years	-0.03	0.02		0.08
School 12- years	-0.04	0.06		0.67
White	-0.01	0.04		0.36
Non White	-0.04	0.06		0.53

Notes: ATT is calculated using Callaway and Sant'anna (2020), with population as weights. "Sign 5%" is filled with an $*$ if the results are significant at a 5% level. "Mean" is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Table 5 – Heterogeneity for syphilis

Variable	ATT	SE	Sign 5%	Mean
Overall	1.06	1.12		13.93
Men	0.38	0.74		8.58
Women	0.68	0.41		5.34
Age 13-24	0.44	0.32		4.02
Age 25-39	0.32	0.43		5.21
Age 40+	0.30	0.42		4.70
High School	0.38	0.42		3.66
Without High School	0.02	0.47		4.99
White	0.07	0.42		5.66
Non White	0.76	0.81		5.83

Notes: ATT is calculated using Callaway and Sant'anna (2020), with population as weights. "Sign 5%" is filled with an $*$ if the results are significant at a 5% level. "Mean" is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.

Table 6 – Heterogeneity for hepatitis

Variable	ATT	SE	Sign. 5%	Mean
Overall	-0.53	0.18	*	5.80
Hepatitis A	-0.23	0.08	*	0.27
Hepatitis B	-0.10	0.11		1.90
Hepatitis C	-0.30	0.13	*	4.24
Acute	-0.30	0.10	*	0.51
Chronic	-0.22	0.18		4.72
Sexual	-0.17	0.06	*	1.14
Non Sexual	-0.29	0.08	*	1.54
Men	-0.43	0.14	*	4.17
Women	-0.14	0.10		3.20
Age 13-14	-0.12	0.07		0.46
Age 25-39	-0.20	0.07	*	1.79
Age 40+	-0.24	0.16		5.12
High School	-0.10	0.11		2.05
Without High School	-0.36	0.12	*	2.77
White	-0.20	0.12		3.54
Non White	-0.28	0.16		2.82

Notes: ATT is calculated using Callaway and Sant'anna (2020), with population as weights. "Sign 5%" is filled with an $*$ if the results are significant at a 5% level. "Mean" is the mean for the treated group in the years of 2016 and 2017, when nobody was treated.