HIV Pre-exposure Prophylaxis Prevalence's Influence on the Spread of Bacterial STDs

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Econ 6896: Research Methods
June 2018

1 Introduction

HIV/AIDS became a national epidemic in the early 1980's. Though the virus existed decades earlier, it was not understood or recognized. HIV can take over a decade to produce any symptoms and the US was underprepared to face the coming crisis. HIV, initially called GRID (gay-related immune deficiency), disproportionately affected the gay male community and many lost their friends and family to the disease. However, modern developments have made it so HIV is no longer a death sentence. Moreover, in 2012, the FDA approved Truvada, a drug often used to treat HIV, as a daily prescription drug to prevent acquiring HIV even if exposed.

Using Truvada daily if one does not have HIV/AIDS is referred to as Pre-exposure Prophylaxis or PrEP. This treatment is 99% effective if taken as prescribed (Anderson 2012). Some believe that this will encourage users to engaging in risky sexual behavior. That is, since PrEP users are very unlikely to get HIV from condom-less sex, they will engage in it more often. While this should not lead to an increase in HIV infections, it could lead to the spread of other STDs (sexually transmitted diseases/infections) since PrEP only offers protection against HIV. In this paper, I will attempt to test this theory that PrEP usage is associated with higher instances of other STDs. The idea that PrEP users are encouraged to be promiscuous and risky is commonly thrown around in gay circles as a sort of insult. The results are consistent with this idea and it suggests more education and accountability is needed with PrEP users and medical providers.

2 Background

Approved by the FDA in 2012, Truvada is the only medication currently used as PrEP in the US. Since this a very recent development, the literature is not as robust. Not surprisingly, there are many studies and trials that detail the efficacy of PrEP and Truvada on HIV transmission, but fewer on other health outcomes. Moreover, Truvada is owned and produced by Gilead Sciences. Inc. and they have good economic and ethical reason to be very controlling of their data.

One trail study of PrEP in Ghana (Guest et al. 2008) found that women participating in the trail did not increase their sexual risk behavior over the year long trial. They also found that counseling was effective and it is may be necessary to tailor

the messaging according to groups within a population. This result suggests there should be no effect, but it is very limited. First, it focuses on a small population in Ghana which is very different than the US. Second, the vast majority of PrEP users in the US are male and it is reasonable to think that US men are significantly different that Ghanaian women.

HIV is also easier to spread if another STD is present. In a double-blind trail, it was found that Syphilis was a good predictor of HIV infection (Solomon et al. 2014). Participants who contracted HIV during the trial often also contracted Syphilis during the same time period. In general, the conclusion was that HIV is easier to transmit in individuals who are infected with other STDs (both bacterial and viral). The CDC cites numerous other studies on their HIV and STD fact webpage that link STD infection and increased HIV infection.

3 Data

Data regarding PrEP Usage and HIV diagnoses was obtained from AIDSVu (aidsvu.org), a free online resource that focuses on visualization of the AIDS epidemic in the US. The project's source of HIV related data comes from the CDC's National HIV surveillance system. Information regarding PrEP was complied by the Rollin School of Public Health at Emory University with the support of Gilead Sciences, Inc. and Source Healthcare Analytics LLC. The US Census Bureau's American Community Survey provided population data used to determine rate per 100,000 (included in AIDSVu datasets). The previous information is available at the state and zip3 (first 3 digits of 5-digit zip code) level.

STD rates and cases were obtained from the Center for Disease Control and Prevention (https://gis.cdc.gov). These figures are based on county reporting. As with PrEP usage and HIV infection, US Census Bureau's American Community Survey informs population which is used to determine rate per 100,000.

The following figure contains basic summary statistics of key variables between the years of 2012-2016. PrEP has only been approved for general uses since 2012, so its is the obvious and only starting point. HIV diagnoses are lagged by one year (2011-2015). Analysis takes place at the US state level (including the District of Columbia and Puerto Rico).

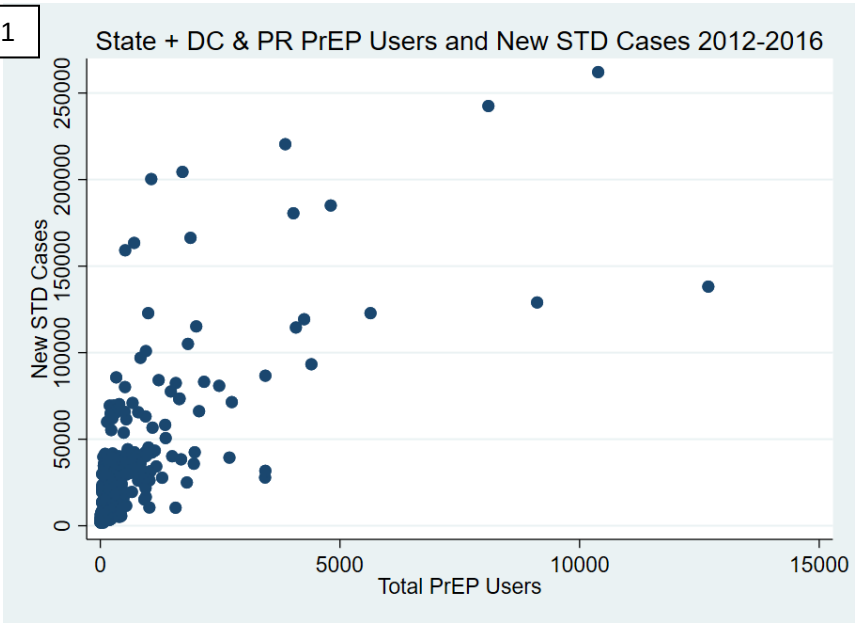
Summary Statistics 2012-2016 (Rates Per 100,000)

	Mean	SD	Min	Max
PrEP User Rates	12.45	22.29	0	268
STD Case Rate	668.18	236.05	176.85	1825.02
Gonorrhea Case Rate	127.07	76.75	9.2	553.6
Chlamydia Case Rate	541.11	164.32	161.8	1353.9
New HIV Diagnoses (previous year)	13.05	13.46	2	122
N	260			

The above table is averaged over 2012 to 2016. STD cases were generated by adding the total cases of Gonorrhea and Chlamydia. STD rate per 100,000 was then generated from this aggregate. Gonorrhea and Chlamydia were chosen to represent STDs as they are the two most common bacterial STDs in the US. Extreme values for PrEP user and for STD cases are driven by the District of Columbia. This is not surprising given the small population of DC and the African American population. African Americans at higher risk to contract HIV and PrEP guidelines encourage different distribution based on demographics.

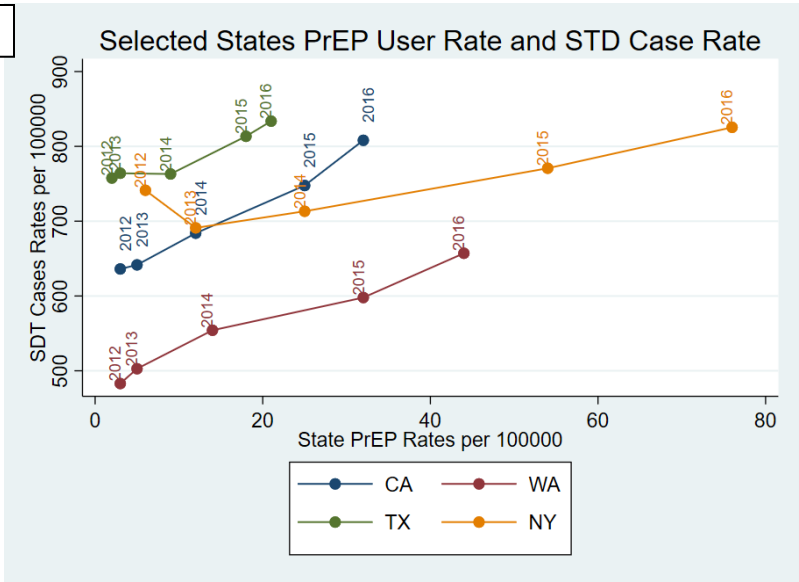
Graph 1 plots all PrEP users against new STD cases. Since there are so many data points a trend is not immediately evident.

Graph 1



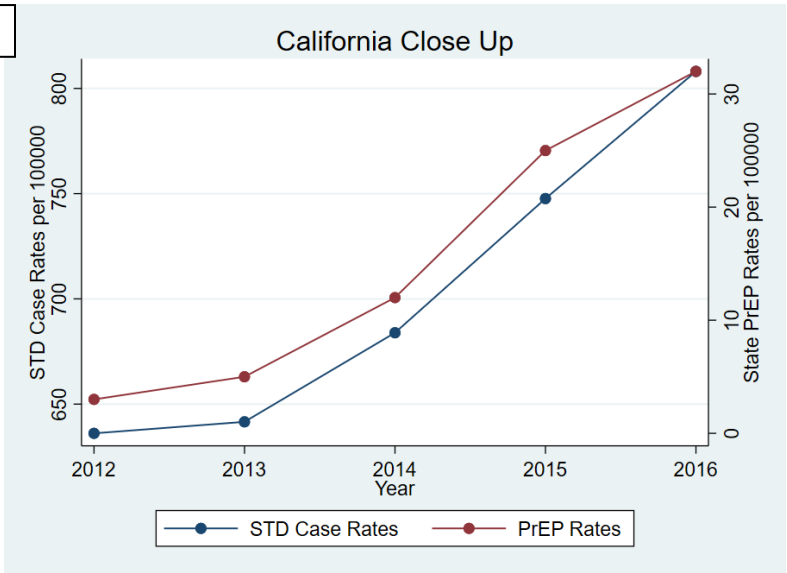
To clarify, Graph 2 shows only 4 selected states. It also shows the relevant rates, where Graph 1 shows the total users or cases. The markers are labeled by year. One can see that both STD Rates and PrEP usage rates tend to increase over time.

Graph 2



Graph 3 shows only data from California. STD rates are on the left Y axis and PrEP user rates are on the right Y axis. This was done since PrEP is only used by a small portion of any community and STDs effect a much wider group. In this case, they seem to comove.

Graph 3



4 Methods

This paper seeks to understand if increased PrEP usage leads to an increase in bacterial STD infections. In order to test this, I use the following model:

$$STD\ Rate_{it} = \beta_{it} \cdot PrEP\ User\ Rate + \alpha_i \cdot\ State_i + \delta_t \cdot Year_t + \gamma_{it} \cdot Controls_{it} + \varepsilon_{it}$$

STD rate of infection is the dependent variable and the key independent variable is PrEP user rate. The subscript *i* refers to the US state and the subscript *t* refers to the year (2012-2016). I include binary variables for state fixed effects. A binary variable for year is also included to account for increasing rates over time. A control, new HIV diagnoses rate, which is the rate of new HIV diagnoses the previous year is included. This is likely correlated with both PrEP usage, as providers would be incentivized to provide PrEP in areas with growing HIV infection, and with STD rate, since HIV infection facilitates the spread of other STDs.

I will conduct a two-sided test that PrEP has no effect on the STD rate against the alternative:

$$H_0: \beta = 0$$
$$H_A: \beta \neq 0$$

A fixed effects model will be used to account for time invariant state characteristics. The Hausman Test, when conducted on the first model, also suggests that fixed effects should be used over random. I will test for significance at the 95% level using a t-test. The critical value will be $t^* = 1.96$.

5 Results

Table 1 shows results both with and without the inclusion of the new HIV diagnosis rate of the previous year. We can easily reject the null at the 95% in both models. Interesting, when HIV diagnosis rate is included, the coefficient on PrEP user rate increases significantly.

Table 1: STD Rate Per 100,000 in US States Including DC and PR

	FE Model 1	FE Model 2
PrEP User Rate	0.924***	2.976***
	(0.233)	(0.393)
New HIV Diagnoses Rate		11.09***
		(1.782)
2013	-8.837	-3.563
	(9.785)	(9.025)
2014	-2.226	-0.234
	(9.891)	(9.088)
2015	24.01*	6.145
	(10.55)	(10.10)
2016	71.02***	47.22***
	(11.16)	(10.94)
Observations	260	260

Standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 2 reports the same models as table 1, except STD rate has been broken up into its component STD, Chlamydia and Gonorrhea. As Chlamydia is much more prevalent than Gonorrhea, I thought it was prudent to check if one infection was driving the results. Again, we easily reject the null at the 95% level in all cases.

Table 2: Individual STD Rate Per 100,000 in US States Including DC and PR

	FE Chlamydia 1	FE Chlamydia 2	FE Gonorrhea 1	FE Gonorrhea 2
PrEP User Rates	0.584***	1.992***	0.340***	0.984***
	(0.171)	(0.292)	(0.0840)	(0.145)
New HIV Diagnoses Rate		7.612***		3.484***
		(1.325)		(0.657)
2013	-9.332	-5.713	0.492	2.148
	(7.188)	(6.710)	(3.526)	(3.327)
2014	-6.236	-4.869	4.009	4.634
	(7.266)	(6.757)	(3.565)	(3.350)
2015	9.756	-2.504	14.26***	8.653*
	(7.747)	(7.510)	(3.801)	(3.723)
2016	31.01***	14.68	40.00***	32.53***
	(8.196)	(8.131)	(4.021)	(4.031)
Observations	260	260	260	260

Standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

From these tests, it appears that there is a relationship between increased usage of PrEP and an increase in instances of bacterial STDs. Indeed, these results are consistent with the idea that PrEP users are more likely to engage in otherwise risky sexual behavior. Unsurprising, the new HIV Infection rate is highly positively associated with the STD rate. However, it is interesting that including this as a control greatly increases the coefficient on PrEP user rate. This also suggests that there is something unique in the relationship of bacterial STDs and PrEP usage.

I should note that I tested the models dropping the states that correspond to the most extreme observations. The results did not change significantly, so I chose not to include them.

6 Limitations

Originally, I wanted to test at the county level since that is the most detailed level of reporting regarding STDs. The model I used accounts for differences in states, but states can have a lot of variation internally. For example, California has 58 counties that are often very different in terms of health services and attitudes. Liberal San Francisco County is going to have different attitude toward PrEP than the very conservative Kern County. I thought it would not be a problem, since the PrEP data was given in by zip code (first 3 digits). However, a problem arose when trying to combine the data. The 3-digit zip codes do not match up with county since some exist in multiple counties. Given

time limitations, it was not feasible to test at the county level. Given more time and resources (such as $495 to purchase zip code mapping data) I would still pursue county level analysis.

Additionally, PrEP usage is supposed to come along with a set of guidelines for medical providers (Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline). Among other things, the CDC recommends follow-up (3-month intervals) and monitoring (HIV/STD testing). The PrEP data I used only provided information on prescriptions provided. I have no way to know if clinical guidelines are being followed and this could have an effect on the results (Guest et al. 2008).

PrEP might also show a positive association with STD rates since it encourages regular testing. therefore, more STDs are diagnosed that would have gone untreated otherwise.

7 Conclusions

At the state level, it seems that more PrEP use is associated with more STD infections. I believe that the results are compelling enough to warrant further study into this issue. If the link between increased PrEP use and increased STD transmission is indeed causal, then it has serious policy implications. Sexual education and counseling would need to be altered in such a way that further emphasizes the risks of condom-less sexual activity.

These results should not suggest that PrEP is a negative program or to pass a lifestyle judgment on users of PrEP. I believe it will save many lives in the long run. However, it is important to look at the externalities the program creates and address them in a way that creates more positive and economically efficient health outcomes.

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