Eric Tang
CRC Rotation: IRB for Patient PrEP Survey

Columbia University Human Subjects Study Description Data Sheet
Submitting To: Medical Center

Title: Effect of Different Educational Interventions in the Knowledge, Attitudes, and Willingness of High-Risk Adolescents and Young Adults to Use Systemic Antiretroviral Chemoprophylaxis for HIV Prevention

Abbreviated title: Effect of Educational Interventions on Attitudes Regarding PrEP for HIV Prevention

IRB of record: Columbia University Medical Center

Affiliated Institutions: New York Presbyterian Hospital

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Principal Investigator: Magdalena Sobieszczyk (527)
Co-Investigator: Eric Tang

1. STUDY PURPOSE AND RATIONALE

More than one million people are living with HIV in the United States and an estimated 56,300 Americans become infected with HIV each year. Domestically, men who have sex with men (MSM) remain the population most severely affected by HIV, accounting for more that 50% of all new infections in the US each year, and just under half (48%) of people living with HIV. Furthermore, new HIV diagnoses among MSM are more than 44 times that of other men (1). In New York City, the AIDS case rate is almost 3 times the United States average and MSM remain an important risk group (2). It is evident that risk reduction strategies for this population are imperative. While condom use is effective in HIV prevention, current strategies, such as educational programs, have not significantly reduced HIV incidence (3).

A recent press release from the CDC announced that adolescents and young MSM (age 13-29) of all races are severely affected by the HIV epidemic, but young black MSM are the only group to demonstrate a statistically significant increase in the number of HIV infections from 2006 to 2009. It is estimated that HIV infection rates increased by 48% for this group during this four-year period. In 2009, infection rates among all blacks and Hispanics were nearly 8 times and 3 times the rate of whites, respectively (4). High prevalence of HIV in these minority communities means that uninfected members of these communities are at higher risk of infection with every sexual encounter. New biomedical methods of HIV prevention can be utilized to target these high-risk populations, and must be assessed and used strategically in order to reduce the prevalence and rates of infection among these communities.

Biomedical strategies focusing on the use of antiretroviral (ART) drugs for prevention of HIV acquisition are an important strategy. Much of the data supporting use of pre-exposure prophylaxis (PrEP), are based on both animal models and studies in humans showing the effectiveness of post-exposure prophylaxis (PEP). The goal of ART administered as PEP and PrEP is to prevent the HIV virus from establishing around the time of exposure. The key difference between the two is that while one presumes exposure is infrequent and unpredictable (PEP), the other anticipates regular exposures to HIV (PrEP). The CDC currently recommends PEP after occupational or non-occupational exposure to HIV-infected fluids (5).

Pre-exposure prophylaxis (PrEP) is one of the new biomedical prevention techniques that has recently demonstrated efficacy in reducing HIV acquisition in MSM, high-risk heterosexual men and women, and serodiscordant couples. PrEP stands for Pre-Exposure Prophylaxis, an experimental approach to HIV

prevention where HIV negative people take HIV drugs to try to prevent HIV infection. PrEP is started **before** being exposed to HIV and continued during periods of risk. This is different from post-exposure prophylaxis (PEP) where the medication is started soon **after** exposure to HIV and continued for 28 days. PrEP can be in the form of a pill taken by mouth or a gel applied in the vagina or rectum. Current studies of oral PrEP (pills) have tested the HIV drug Tenofovir (also known as Viread) alone or in combination with emtricitabine (the combined drug is also known as Truvada) as a daily pill. Both tenofovir and Truvada are approved for the treatment of HIV infection in HIV-positive people. Preventing an infection by giving a drug that is also used to treat that infection has been a successful approach against other diseases such as malaria.

To date, results from four large efficacy studies have reported on the effectiveness of preventing HIV acquisition with oral PrEP. The results of 3 of the studies are very encouraging and show that taking an anti-HIV pill daily can be partially effective in protecting from HIV.

These efficacy studies include:
iPrEx: conducted among MSM and transgender women who have sex with men in South America, South Africa, Thailand and USA. The primary analysis of the iPrEx study were reported in the 4th quarter of 2010 and represents the first efficacy results of oral PrEP with once-daily TDF-FTC (Truvada). In the study there was a relative risk reduction in HIV acquisition of 44% among MSM and transgender women who have sex with men in combination with comprehensive prevention services such as monthly HIV testing, condom provision, counseling, and treatment of other sexually transmitted infections. The reduction of HIV-1 acquisition was strongly correlated with adherence measured by self-report and pill count/dispensing; for example a 73% reduction was noted at adherence levels greater than or equal to 90%. Furthermore, risk behavior among participants declined overall during the trial with respect to the number of sexual partners and condom use, which was likely a result of the risk reduction counseling provided as part of the trial (7).

FemPrep: conducted among 1951 women in Kenya, Tanzania, and South Africa. After a regularly scheduled interim review of the data in April 2011, Independent Data Monitoring Committee (IDMC) recommended stopping the study because Truvada was not effective in reducing the risk of HIV infection. There were a total of 56 new HIV infections in the study. An equal number of infections occurred in participants assigned to Truvada and those assigned to a placebo pill. Retention was very high in the study (about 90%) and self-reported adherence to the medication was high at about 95%. It is not clear why Truvada was not effective in preventing HIV infection in this study. The data will be looked at more closely. But possible explanations include low adherence to the study pill, study pill sharing between the participants in the Truvada and placebo groups, chance, or some biological reasons, or a combination of these factors (8).

PARTNERS PrEP: a study of daily Tenofovir or Truvada pill conducted among serodiscordant heterosexual couples (one partner is HIV+) in Kenya and Uganda. In July 2011, after review of the study by the Data and Safety Monitoring Board, it was announced that Tenofovir and Truvada taken daily reduced the risk of HIV transmission among both men and women. In the trial, daily oral TDF reduced HIV risk by an estimated 62 percent infections and daily oral TDF/FTC reduced HIV risk by an estimated 73 percent (95% CI 49 to 85, $p<0.0001$) when compared to a placebo. Both drugs were effective in both men and women, and there were no significant safety events in the trial (9).

TDF2: conducted among 1,219 heterosexual male and female participants in Botswana. In this trial, PrEP using daily oral Truvada was found to reduce the risk of HIV infection by approximately 63 percent (95% CI 21.5 to 83.4, $p=0.0133$) among heterosexual men and women overall when compared to placebo. The data suggests efficacy for both men and women, but definitive conclusions cannot be drawn by gender due to the limited size of the study. Overall safety and efficacy findings are consistent with the Partners PrEP data, with only nausea, vomiting, and dizziness reported at significantly higher rates using Truvada

versus placebo (9).

While the results of these studies are promising, many questions remain regarding its application to clinical practice, the long-term safety of this regimen, and development of resistance to FTC/TDF, which is an important component of the preferred initial antiretroviral regimen in the US. Several ongoing studies of systemic and topical PrEP, administered daily or intermittently, will provide important answers for the field and will inform normative guidelines (10, 11). At present, however, PrEP would only be available through prescriptions and its use is dependent on patients' knowledge, attitudes, and acceptability of PrEP. This may serve as a barrier to the implementation of PrEP if education on its efficacy is not a routine part of clinical practice. Prior to the publication of these PrEP efficacy results, surveys conducted among at-risk MSM document limited knowledge of PrEP but high level of interest in considering its use (12,13). Now that there is hard evidence demonstrating partial efficacy of PrEP in preventing HIV infection, a study assessing patients' knowledge, attitudes, and intent to use PrEP based on these results is needed.

Identification of these barriers and limitations can help develop interventions that raise awareness among at risk adolescent and young adults about the use of anti-retrovirals to prevent HIV acquisition. Providing knowledge about these recent studies will be essential prior to successful implementation of PrEP as a public health strategy. Individual counseling on patient education has demonstrated to be effective in changing behavior, including smoking in diabetic patients (14). One-on-one counseling may also address patient and provider concerns (i.e. side effects, possibility of developing resistant strains, increase in risky behavior). Given the burden of HIV in New York City, characterization of barriers to the implementation of this prevention strategy and the method in which we should educate at-risk populations about PrEP is of great importance.

2. STUDY DESIGN AND STATISTICAL PROCEDURES

We propose to survey HIV negative young adults (age 18-25) waiting to see their providers at Project Stay, a Columbia-affiliated clinic for high-risk youth. After obtaining demographic information, including health insurance status, education level, and sexual health, participants will be asked about their baselines knowledge, attitudes, and willingness to use PrEP. They will then be educated on the recent PrEP results by randomization to either the control group (given a pamphlet on PrEP) or the intervention group (a one-on-one counselor session + the pamphlet on PrEP). Randomization will include stratifying by MSM demographic using a block randomization put together by a third-party. The counselor will be blinded to which arm the participant will be randomized to until the survey has been completed. After their educational intervention, they will see their provider, who will be asked if the participants inquired about PrEP or if the provider brought up the subject him or herself, and if the participant had asked for a prescription. One week following their appointment, they will be e-mailed an electronic survey asking them the same questions on their knowledge, attitudes, and willingness to use PrEP. Finally, we will assess the number of prescriptions for PrEP that were prescribed/filled at 0 months, 6 months, and 1 year. In addition to elucidating baseline willingness to use PrEP and how different modes of education can influence knowledge, interest, and uptake, we also aim to measure the acceptability of other methods of HIV prevention, including alternative ways to administer PrEP, including vaginal and rectal microbicides, IM injection, intermittent oral PrEP use, condoms, circumcision, and vaccines.

The primary research questions are as follows:

Primary Objective #1: To determine if one-on-one counseling on recent PrEP results can increase the proportion of high-risk adolescent and young adults who ask their providers for PrEP

Primary Objective #2: To determine if one-on-one counseling on recent PrEP results can increase the proportion of high-risk adolescent and young adults who are prescribed PrEP and have filled prescriptions at 0, 6, and 12 months.

Secondary Objective #1: To determine current knowledge, attitudes, and willingness to use PrEP for HIV prevention amongst high-risk adolescents and young adults age 18-25 in light of recently announced oral PrEP study results.

Secondary Objective #2: To determine specific concerns or barriers (e.g., concerns about potential side effects, concerns that I would increase risk taking behavior, don't feel that I am at risk for HIV, don't like taking pills, don't think the pill will protect me from getting HIV infected, concerns that if HIV medications are used now, they won't work in the future if I became HIV+, concerns that others might think I am HIV positive, concerns this would limit the availability of HIV medications for people infected with HIV, already using a strategy for prevention that is effective, concerned it is too expensive) that would prevent high-risk adolescents and young adults to use oral PrEP, and how this may be influenced by different modes of education.

Secondary Objective #3: To assess the acceptability of various methods of HIV prevention, including variations in the timing and way of administering PrEP (i.e. via IM, via microbicides, or intermittent dosing).

Statistical analysis of the questionnaire survey data will be performed using SAS software. Frequencies of responses to survey questions will be described. Chi square and Fisher's exact tests will be computed to compare pamphlet-educated participants' survey responses and PrEP prescriptions to the responses and prescriptions of participants educated by one-on-one counseling. Variables with p-value < 0.05 will be considered significant and will be included in multivariate logistic regression model. Forward selection will be used in the logistic regression model to evaluate variables independently associated with willingness to use PrEP. The outcome variables, whether or not they would use PrEP and bring the issue up with their provider, will be evaluated using a proportion and compared between groups; PrEP prescriptions written and filled at 0, 6, and 12 months will also be evaluated, proportion will be computed and then compared between groups.

The primary endpoint is the difference between the proportion of participants who asked their providers about PrEP in the intervention group versus control group. Because of the limited ability to survey 100 participants (50 in each group), we will use this fixed number of subjects in our power analysis to determine the smallest difference for which the available number of subjects will lead to statistical significance.

A study in Boston found that 74% of MSM were interested in using PrEP after being educated in-person about its potential (12). Based off this information, one can assume that the proportion of those willing to use PrEP will be approximately 74% for the group with one-on-one counseling (+ pamphlet) on the recent PrEP results, and could lead to a corresponding 74% who will ask their providers about it. Using backward power calculation using our predetermined sample size of 50 in each group, with $\alpha = .05$ and power = .80, we would find a difference between the two groups if the proportion of those who ask their provider about PrEP in the control group is < .46 (or > .96). Thus, the smallest difference for which our study will find a statistical difference between each group is .28.

3. STUDY PROCEDURES

After screening for HIV-negative patients ages 18-25 waiting to be seen by providers at Project Stay, informed consent will be given about the study. If the patient decides to participate in the study and agrees to the informed consent, the initial survey will be distributed either in hard-copy form or on an iPad (using a computer-assisted self-interview assessment) to obtain the data. Following the survey, the counselor will see whether or the patient is MSM, and perform stratified randomization based off this demographic. A third-party statistician will provide assignments in premade envelopes assigning participants based off blocked and stratified randomization to each arm of the study, which will not be opened until the participants has completed the survey. If the participant is assigned the control arm,

s/he will receive a pamphlet on the recent PrEP studies and asked to read over the information prior to seeing their provider. If the participant is assigned the interventional arm, the counselor will provide a one-on-one session on the recent PrEP results and answer any questions they might have, in addition to receiving the aforementioned pamphlet. All participants will then be asked to bring a sealed envelope to the provider, which will have three questions that the provider will fill out after their encounter with the patient:

1. Did the patient ask you about PrEP?
2. Did you bring up the subject of PrEP with the patient?
3. If yes to either, approximately how much time did you spend talking to the patient about PrEP?
4. Did the patient ask for a prescription for PrEP?

One week following the initial survey, participants will be contacted via e-mail about completing the final part of the study, which will include some of the same questions regarding knowledge, attitudes, and willing to use PrEP, as well as acceptability of other HIV prevention methods. This survey will be given using Survey Gizmo, a secure online survey provider service. Reminder e-mails will be sent up to 3 times, with a phone call follow up if the survey has not yet been completed. Participants will received a $5 gift certificate to either Starbucks or McDonalds for completing the first portion of the study, and another $5 gift certificate for completing the second/final part of the study.

Finally, we will look up patient's medical records to determine if prescriptions for PrEP were prescribed and whether or not they were filled at 0, 6, and 12 months.

4. STUDY DRUGS AND DEVICES

Not Applicable

5. STUDY INSTRUMENTS

We will be distributing an initial questionnaire (either in electronic or hard-copy format) to collect data on:

1. Patients' demographic information, sexual behavior and health, and drug use
2. Patients' baseline knowledge, attitudes, and willingness to use oral PrEP
3. Patient's acceptance of other methods of prevention HIV methods

The second questionnaire (e-mailed to the patients using SurveyGizmo) will ask the same questions in 2 and 3 as above.

Questionnaires attached:

1. Initial Survey to Assess Knowledge, Attitudes, and Willingness to Use PrEP Among High-Risk Adolescents and Young Adults.doc
2. Follow-up Survey to Assess Knowledge, Attitudes, and Willingness to Use PrEP Among High-Risk Adolescents and Young Adults.doc

6. STUDY SUBJECTS

We plan to study HIV-negative, young adults age 18-25 who see providers at Project Stay, a Columbia-affiliated clinic catered to adolescents at high-risk for acquiring HIV infection.

7. RECRUITMENT

We will work with Project Stay to figure out the best way to approach and talk to patients about the study, which will likely be when they are waiting to be see their providers.

8. INFORMED CONSENT PROCESS

After reading about the purpose of our study, informed consent will be obtained using a hard-copy that must be signed before participation in the study. Participants will be provided with a copy of the informed consent and may withdraw from the study at any time.

9. CONFIDENTIALITY OF STUDY DATA

Study data will be collected both via hard-copy materials and electronically, using participant ID numbers. In addition, their MRN will be used to obtain information on provider prescribed PrEP medications and filled PrEP prescriptions. The records of this study will be kept in a secure fashion. In any sort of report we make public we will not include any information that will make it possible to identify participants and data will be reported in aggregate. Research records will be kept in a password-protected file and locked cabinet; only the investigators will have access to the records.

10. PRIVACY PROTECTIONS

Only those conducting the study will have access to participants' information. Furthermore, participants may choose to not answer any question in the questionnaire if it makes them feel uncomfortable or skip a question for any reason.

11. POTENTIAL RISKS

We do not foresee any potential risks associated with participating in our study other than providing potentially sensitive information about their social history. However, this is no different from what may be asked in obtaining a normal patient history.

12. DATA AND SAFETY MONITORING

Not applicable

13. POTENTIAL BENEFITS

Personal benefits for participants to partake in our study may include increased knowledge of a potentially effective HIV prevention method. In addition, information gained as a result of this research may advance knowledge in this area and help others in the future, including informing educational interventions on PrEP use and the direction of future research in the use of PrEP for the prevention of HIV. It may also aid in the development of educational materials geared toward increasing awareness among high-risk adolescents and adults on risks and concerns of using antiretrovirals for prevention of HIV.

14. ALTERNATIVES

The study participants can choose not to participate.

15. RESEARCH AT EXTERNAL SITES

Not Applicable

16. COLUMBIA AS LEAD INSTITUTION

Not Applicable

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