Peer-driven intervention prompting pre-exposure prophylaxis and improving access to health care among African American and Hispanic/Latino men who have sex with men

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Protocol Version 1.3

OBJECTIVE

The objective of this study is to seek knowledge of components of an effective peer-driven intervention (PDI) approach assess the feasibility and efficacy of a PDI on PrEP uptake for the purpose of expanding this PDI to promote PrEP in a large scale study.

BACKGROUND

African American (AA) and Hispanic/Latino (H/L) MSM each represent less than 1% of the total population [1], but accounted for 31% and 22% of all new HIV diagnoses in 2016 [2]. Given this concentrated epidemic, a key benchmark of the 2020 National HIV/AIDS Strategy is to reduce disparities in the rate of new HIV diagnoses among AA and H/L MSM by 15%, in addition to reducing overall diagnoses among all MSM by 25% [3]. Pre-exposure prophylaxis (PrEP) holds promise for reducing HIV transmission rates among MSM. The efficacy of PrEP in preventing HIV acquisition has been demonstrated in numerous randomized controlled trials and open-label studies among populations at risk[4-6], including MSM [7-9]. PrEP has the potential to dramatically reduce HIV incidence among MSM in the US [10,11].

PrEP uptake has been slow across the US [12], despite proven efficacy and recommendations by the Centers for Disease Control and Prevention (CDC) [13]. Disparities exist among AA and H/L MSM with worse outcomes in PrEP awareness and access, adherence, and retention in care (e.g. the PrEP care cascade)[14]. Reasons for these disparities include lack of access to health care, limited awareness about PrEP, stigma, cost, and low perceived HIV risk [15-18]. Lack of health care access may include suboptimal engagement in culturally-competent PrEP care as well as primary care and treatment services for mental health, unhealthy alcohol use, and substance use. This lack of health care access may significantly increase risk of HIV acquisition [19]. In current PrEP implementation efforts in Rhode Island, only 27% of PrEP users self-identified as AA or H/L. In addition, AA and H/L MSM who initiated PrEP were significantly less likely to be retained in care at three months (only 44% retained) relative to Whites (72%) in our previous study[20].

To address health disparities in the PrEP care cascade among AA and H/L MSM, we propose to develop and implement a peer-driven intervention (PDI). This PDI is a "chain-referral" approach that starts with index peers who recruit members through their social networks and follows by further enrollment through referred network members. Index peers will disseminate PrEP-related knowledge and encourage at-risk members of their social networks to seek PrEP care. The PDI approach has been demonstrated to be a cost-effective way to achieve a representative sample of hard-to-reach populations21,22 and to be efficient for spreading HIV education, promoting condom use, and expanding HIV testing among MSM and other populations at high risk of HIV acquisition 23-25. However, PDI has not been studied for PrEP promotion.

In the current study, we will first conduct qualitative interviews among AA and H/L MSM to explore elements of an effective PDI for PrEP. Then, we will train AA and H/L MSM ("index

peers") to recruit members of their social network (i.e. other AA or H/L MSM) and help link these individuals to PrEP care. Given limited access to general health care is one of the most frequently documented barriers to PrEP uptake, we will also explore the effect of PDI on linkage to other services including primary care, and treatment for mental health, alcohol use and substance use. The proposed study will evaluate a novel approach to improve PrEP uptake among AA and H/L MSM who are most at-risk of HIV infection.

STUDY SITE

The study will take place at The Miriam Hospital (TMH) Immunology Center in Providence, Rhode Island. The STD Clinic at TMH Immunology Center has been offering PrEP since 2013 with over 350 individuals currently on PrEP.

The Miriam Hospital Immunology Center. The Miriam Hospital PrEP Program and STD Clinic (Director: Chan) provides routine testing for gonorrhea, chlamydia, syphilis, trichomonas, hepatitis C virus, and HIV at no cost to patients. The Miriam Hospital Immunology Center is the main outpatient HIV clinic in Rhode Island and is also the site of The Providence/Boston Center for AIDS Research (CFAR) and The Brown University AIDS Program (BRUNAP), and is a study site of the AIDS Clinical Trials Group and several other ongoing national clinical trials. The clinic is also the site of the PrEP Program. Patients are referred to the PrEP Program from the onsite STD and HIV clinics.

RESEARCH PROTOCOL

Aim1: Perform qualitative interviews among AA and H/L MSM to determine components of an effective PDI for PrEP. We will conduct individual in-depth interviews with 15 AA and 15 H/L MSM who are HIV negative and meet clinical indications for PrEP. Interviews will be conducted by the PI or research staff, under the mentorship of Dr. Nunn, who has extensive qualitative research experience and a rich history working with sexual and gender minorities [26-28].

Inclusion criteria and sampling strategy: Individuals will be considered for inclusion in the study if they: (a) are 18 years of age or older, (b) self-identify as either AA or H/L, (c) were assigned male at birth, and (d) have had sex with men in the past three months. Interpreters will be available for Spanish-speaking individuals. We plan to recruit study participants during their routine clinical visits. We will use a purposeful sampling strategy to capture diversity in the lived experiences of AA and H/L MSM [29-31].

Procedure: Semi-structured individual interviews with AA and H/L MSM will explore the following: 1) awareness and acceptability of PrEP; 2) social network characteristics (both physical and virtual interactions) and acceptability of promoting PrEP through these networks; 3) facilitators and barriers to PrEP uptake; 4) potential intervention components and related content to support PrEP initiation; 5) characteristics of potential index members

for PrEP education (e.g. leadership, responsibility, and passion and commitment to HIV prevention); 6) facilitators and barriers to other services including primary care, and treatment services for mental health, alcohol use, and substance use. Interviews will last 30-60 minutes and will take place in private rooms. Enrollment will continue until data analysis reflects saturation. We anticipate conducting approximately 30 interviews. Each participant will be compensated $25.

Qualitative data analysis: Interviews will be digitally recorded and transcribed by an outside HIPAA-certified transcription company and reviewed for accuracy by research staff. In addition to interviews, research staff will take notes, complete standardized debriefing forms immediately following the interview, and review them with study investigators during weekly team meetings. Qualitative data will be analyzed iteratively during data collection so that we may develop additional questions and adapt the interview guides as needed to address any unanticipated themes. This method will also allow us to determine when we have reached saturation in data collection. We will develop and verify a two-phase coding scheme following the basic procedures of grounded theory [29]. Interview data will be coded by two independent raters using Nvivo software. Study investigators will review and analyze data to identify themes.

Aim 2: Evaluate the feasibility and efficacy of a PDI on promoting PrEP uptake among AA and H/L MSM. PDI is a "chain-referral" outreach method with two main components: "index peers" and "peers." Index peers will be chosen from our study population (i.e. AA and H/L MSM). They will undergo training about PrEP and other HIV prevention approaches and will be asked to refer members of their social network ("peers"). Our primary outcome is PrEP uptake that will be evaluated by three methods: (a) receiving a prescription for the medication, (b) filling a prescription at a pharmacy, and (c) self-reported adherence at three months. We will assess the feasibility and efficacy of the PDI on PrEP uptake. The comparison group will be AA and H/L MSM who present to our STD clinic naturally (no intervention, Figure 1). Our secondary outcome is linkage to other health care services, and will be measured by self-reported referral and linkage to care, such as primary care and treatment services for mental health, alcohol use, and substance use.

Initial peer recruitment. The inclusion criteria of index peers will be men who: (a) are 18 years of age or older, (b) are AA or H/L, (c) have had sex with men in the past three months, and (d) are willing to receive training about PrEP and disseminate it through their social networks. We will recruit index peers among AA and H/L MSM who are currently in our PrEP program as well as through the STD clinic, and community-based outreach.

PrEP and general health care education for index peers. Drs. Chan and Tao will design a 2-hour comprehensive training about PrEP and health care services. This program will include general information of HIV, PrEP, prevention approaches, and access to other health care

services, as well as 1-on-1 practice counseling sessions. The two-hour in-person or virtual training will be given one-on-one or as a group training with our research staff. Dr. Chan currently runs the statewide HIV testing and counseling course which provides certification by the Rhode Island Department of health. At the end of the program, individuals will complete a written test to demonstrate that they retained the required knowledge. Index peers will be given five (5) referral cards each and asked to refer their peers at risk of HIV acquisition. Each referral card will include a unique number that is linked to a particular index peer. The referred peers will be required to repeat the same procedures as index peers.

Recruitment for PrEP promotion and linkage to general health care. The initial seeds are encouraged to use their social networks to circulate PrEP and health care education and to motivate their eligible peers to visit our clinic. They could either give the hard copy or a digital copy of the referral card to their peers. The referred MSM will call research staff who will explain the purpose and nature of the study. If interested, peers will present for an in-person or virtual research visit where they will undergo informed consent, present their referral card, and complete a short survey. Individuals who are interested will also be referred for clinical services including PrEP. Those referred individuals who meet the same inclusion criteria as above for index peers will serve as recruiters for a second wave of recruitment. We expect to observe a 25% increase in PrEP uptake in the PDI group. To have an 80% of power (Type I error [α] =0.05), we will recruit 60 participants in each group.

PrEP uptake and linkage to other health care services. All peer participants will be referred for clinical services regardless of whether or not they participate in the study. Clinical care may include laboratory testing for HIV and other STDs, PrEP, and other education and counseling. We will also ask study participants for permission to review pharmacy information. **All clinical related services involved in this study are part of routine clinical care and not research.** MSM who are HIV positive will be linked to HIV care. Referred peers will also be linked to other health care services as needed such as primary care and treatment services for mental health, alcohol use and substance use. PrEP uptake and linkage to care will be assessed by research staff at the time of the clinical visits and by review of pharmacy and clinical electronic medical records.

Incentives mechanism. Each index peer will be compensated $50 for undergoing the PrEP training. For each referred study participant, they will receive a $50 gift card (an additional $250) up to a maximum of five (maximum $300). Peers who only participate in our study without any recruitment will receive a $50 gift card.

Data collection. Each referred peer will have a unique research ID number at their initial clinic visit linking them to the index peer who referred them. All referred peers will be offered enrollment into the study, but will be provided appropriate clinical care regardless of whether or not they consent. All study participants will complete a self-administrated

questionnaire to collect demographic and behaviors information at their initial visits and follow-up visits at three months. Demographics, including age, race, ethnicity, sex at birth, gender identity, sexual orientation, employment, income and highest education level completed will be evaluated. Validated or modified scales will be used to measure PrEP acceptability[33], HIV risk behaviors[34], perceived HIV risk[35], PrEP adherence[36], and medication taking self-efficacy[37]. We will also assess engagement in primary care services[38], depression and anxiety[39], unhealthy alcohol use[40], and substance use[41].

Quantitative analysis plan. Bivariate analyses will be used to examine any differences in demographics, behaviors, attitudes, and medical indicators between groups. Multivariate Cox proportional hazard model will be used to assess PrEP uptake. Multivariate logistic regression will be performed to assess the efficacy of the PDI on PrEP adherence. Logistic ANCOVA will be used for the pretest-posttest linkage to health care. Confounding variables will be identified by a priori and directed acyclic graphs (DAGs). Additional variables could be adjusted to control biases introduced by the non-randomized control study design.

PROTECTION OF HUMAN SUBJECTS

The goal of this research study is to use a mixed-methods approach to evaluate the feasibility and efficacy of a PDI approach on promoting PrEP uptake. Important ethical considerations in this study include confidentiality and privacy, as well as the considerations associated with working with stigmatized populations such as MSM of color. This section seeks to address these issues.

Human Subjects Involvement, Characteristics, and Design: Specific Aim 1 involves individual interviews to further examine knowledge of components of an effective PDI and barriers to PrEP initiation. Because of the potentially uncomfortable or stigmatized nature of this information, sensitivity toward participants and the confidentiality of their responses during both aims will be of the utmost concern. Specific Aim 2 involves a survey that collects information on HIV-risk behaviors, facilitators and barriers to PrEP use, knowledge of and attitudes toward non-oral PrEP formulations, potential for non-oral PREP formulations to promote adherence to the intervention, and interest in initiating alternate formulations in the future.

Sources of Materials

The qualitative interview (Specific Aim 1) and quantitative survey (Specific Aim 2) will serve as the material sources for this study.

Potential Risks

Protected Health Information: This study will obtain data on sexual practices, sexual partners, PrEP use, and attitudes regarding sexuality and PrEP. During the course of the

study, preservation of confidentiality and safeguarding of PHI will be a paramount concern. A potential risk is breach of confidentiality and privacy.

Psychological Consequences: Another potential risk of the study is the possibility that participants could become upset, uncomfortable, or have other serious emotional responses to discussing sexual health information and risk behaviors during the study.

Recruitment and Informed Consent

Subjects will be recruited through routine clinical care and peer referral. Potential participants will be offered enrollment in the study by research personnel. Participants will be told that the study is being conducted to evaluate whether a PDI approach can significantly improve PrEP uptake among AA and H/L MSM at greater risk of HIV infection. Conversations will be held in closed and private areas. Participants who agree to enter the study will sign a statement of informed consent. Participants will be informed that they do not have to answer any of the questions if they choose not to.

Adequacy of Protection against Risks

Protected Health Information: For all components of the research plan, the study team will clearly identify themselves as being research personnel. During the course of informed consent, strict confidentially will be assured to all subjects and will be stated on the informed consent form. Only the PI and immediate study personnel performing the study will have access to PHI and other sensitive data. All data including names and identifying information will be kept behind locked doors in locked cabinets or on password-protected hospital computers. Data obtained over web survey will be collected in a secure and encrypted format available only to research staff. Data emailed over the Internet will be avoided, but if essential will be using standard encryption browser technology. All persons involved in this research project will undergo human subjects and HIPAA training. In the event that confidentiality is breached, the PI, mentoring team, and IRB will immediately be notified. All conversations with study subjects will be behind closed doors in confidential settings to address privacy.

Psychological Consequences: Any psychological or other mental health consequences as a result of this study will be immediately referred to the study PI and will be addressed by the study team and by trained clinical psychologists that currently provide support services at the clinic, free of charge. Participants will be able to stop the assessment or interview at any point and may discontinue their involvement in the study at any time.

Additional Protections for Children

The prospective component of this proposal will only enroll individuals aged 18 years or older and is not pertinent to children.

Potential Benefits of the Proposed Research to Human Subjects and Others

There will be no direct benefit from participating in this study to the participating subjects. The knowledge and public health benefits gained in this study will help in promoting PrEP uptake and adherence among high-risk populations. Subjects' access to regular PrEP or STD care will not be affected by study participation.

Timeline

The expected timeline of the study is one year. Reviews and updates will be provided to the IRB as necessary.

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