Department: Biology Date: May 2nd, 2023

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**THESIS/PROPOSAL TOPIC APPLICATION AND PROSPECTUS**

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**DATE SUBMITTED: May 5th, 2023**

**THESIS/PROPOSAL TITLE: Use of PrEP to reduce transmission of HIV among African American men that sleep with men.**

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**ANTICIPATED GRADUATION DATE: June 2024**

**BACKGROUND AND LITERATURE**

**INTRODUCTION**

The infection human immunodeficiency virus, also known as HIV, targets the body's immune system, particularly the CD4 cells, which are white blood cells. A person's resistance to opportunistic infections like tuberculosis and fungal infections, severe bacterial infections, and several malignancies is weakened because of HIV's destruction of these CD4 cells. Acquired immunodeficiency syndrome, also known as AIDS, occurs when the immune system is too badly damaged from the HIV infection. AIDS is normally considered the later stages of the HIV infection. According to HIV.gov, in 2020, more than half (57%) of new diagnoses were made in patients between the ages of 13 and 34. Of those newly diagnosed, 37% (11,336) were between the ages of 25 and 34. In 2021, almost 46% of HIV positive patients classified themselves as Black or African American, 27% as White, 24% as Hispanic or Latino, and fewer than 2% each as Asian, Native Hawaiian or Pacific Islander, American Indian/Alaska Native, or individuals of mixed races. In the United States in 2020, 30,635 persons were diagnosed with HIV. Around 2% (635) of the 30,635 new HIV diagnoses in 2020 were transgender people. Of the new diagnoses, transgender women made up 2% (638) of the total. 40 new diagnoses, or less than 1%, were for transgender guys. In the United States in 2020, 22% (6,626) of HIV cases were attributable to heterosexual contact. 7% of new HIV diagnoses were given to people who were born with the male sex and acquired HIV through heterosexual interaction. 15% of people with HIV who contracted it from heterosexual women were born with the gender given to them. HIV cases resulting from heterosexual contact fell overall by 13% between 2016 and 2019. In the United States and six dependent areas in 2020, people who inject drugs (PWID) were responsible for 7% of new HIV infections. 1198 new HIV diagnoses in men who inject drugs, or 4% of all new HIV diagnoses. 3% (857) of new HIV diagnoses were among women who inject drugs. Blacks/African Americans and Hispanics/Latinos continue to be disproportionately affected by HIV in terms of race and ethnicity. Blacks and African Americans made up 12% of the country's population in 2020, yet they were responsible for 42% of all new HIV diagnoses (12,827). Diagnoses among Blacks and African Americans aged 13 and over fell by 8% between 2016 and 2019. Hispanics/Latinos made up 19% of the country's population in 2020, but they were also responsible for 27% of all new HIV diagnoses (8,285). Diagnoses among Hispanics/Latinos were steady between 2016 and 2019.

Two to four weeks post-exposure to HIV, the individual will experience flu-like symptoms. Those symptoms include fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen lymph nodes, and mouth ulcers. HIV can be spread through unprotected sex with an HIV-positive individual, sharing intravenous drug needles, encountering an infected individual’s blood, or from mother to child through pregnancy, childbirth, or breastfeeding. HIV testing is a crucial step in preventing the spread of HIV in the population. There are three types of tests that are used to diagnose HIV: antibody tests, antigen/antibody tests, and nucleic acid tests (NAT). An antibody test checks your blood or oral fluid for HIV antibodies. Antibody testing are the fastest tests and the only HIV self-test authorized by the US Food and Drug Administration (FDA). In general, testing using oral fluid or blood from a finger stick can detect HIV later than tests using antibodies that use blood from a vein. HIV antigens and antibodies are both detected using an antigen/antibody test. For testing carried out in laboratories, antigen/antibody tests are advised and are popular in the US. Blood must be drawn from a vein for this laboratory test. A NAT scans the blood for the virus itself. With a NAT, your doctor will take a blood sample from your vein and send it to a lab for analysis. This test can determine whether a person has HIV or the amount of the virus in their blood (HIV viral load test). A NAT can identify HIV earlier than other testing. Those who have recently been exposed to HIV or who may have been exposed to the virus, who exhibit early HIV-related symptoms, and who tested negative on an antibody or antigen/antibody test, should think about getting this test. To prevent HIV, an individual can abstain from having sex, eliminate the use of intravenous (iv) drugs, and use condoms when having sex There is currently no vaccine for HIV, but antiviral medications can suppress HIV replication, preventing an HIV-positive individual from transmitting it to an HIV-negative partner and extending the life of HIV-infected individuals. Antiviral medications function by halting the spread of HIV, hence lowering the viral load. Less HIV cells in the body provide an opportunity for the immune system to heal and make more CD4 cells. The goal of treatment is to lower the viral load in the blood to undetectable levels (less than 50 copies/ml), and the persistent presence of detectable viral load (greater than 1000 copies/ml) in HIV-positive individuals receiving ART is a sign that treatment is not working as intended and that the regimen needs to be changed or adjusted. Examples of antiviral medications prescribed to prevent the transmission of HIV include Combivir, Trizivir, Epzicom and Truvada.

A review conducted by Williams et al. (2021), was conducted to determine the prevalence of HIV among men who have sex with men (MSM) in specific geographic locations in metropolitan areas. This study extends prior work by generating HIV prevalence estimates among MSM for 86 of the largest metropolitan statistical areas (MSAs) in the United States over two decades. The prevalence estimates reported in this paper present a remarkably unified picture of increases in the prevalence rates for HIV infection among MSM from 1992–2013 across the largest MSAs in the United States. At the end of the study period, the mean prevalence of HIV infection among MSM reached approximately 20%, almost twice the estimated 11% at baseline which was 1992-2013. According to Williams et al. (2021), estimates by racial/ethnic subgroups of MSM suggest higher mean HIV prevalence among minority (Black and Hispanic/Latino) MSM than among white MSM across all years and geographic regions. Increasing HIV prevalence rates among MSM are likely driven by a combination of increased survival among HIV positive men due to improved treatment options and ongoing new HIV infections (Williams et al., 2021). The scope and persistence of these rises indicate the need to ensure that HIV prevention and care among MSM communities will remain a central focus in HIV-related public health efforts for many years to come. Increased survival among HIV-positive males as a result of better treatment options and continued new HIV infections are most likely the main causes of rising HIV prevalence rates among MSM.

Joseph et al. (2018) evaluated three HIV prevention interventions with a common protocol. Baseline data were pooled to describe sexual behavior involving transmission risk with male, female, and male-to-female transgender partners and identify factors associated with transmission risk. Black men who have sex with men and women (BMSMW) were recruited from Los Angeles, Philadelphia, and Chicago. BMSMW who reported sexual risk and bisexual behavior within the past year were recruited as participants in the research. From December 2010 to November 2012, 584 BMSMW were enrolled across the three cities. The average age of the participants was 43 and approximately 75 identified as. Only 20% of the sample had full-time jobs, 75% had yearly salaries of less than $10,000, and 39% were HIV-positive. A total of 31% were selling sex. A total of 46% of the participants reported having sex without condoms with HIV-negative or unknown male partners. Also 45% of the participants reported having sex without condoms with HIV-negative or unknown female partners. HIV diagnosis rates varied by city, with Chicago having the highest prevalence (63%). The review also indicated that 39% of the sample had HIV. The individuals diagnosed with HIV (93%) indicated receiving HIV treatment. Sixty-nine percent of individuals receiving care reported having a viral load that was undetectable. Results should be considered in light of the enrollment criteria, intentionally designed to recruit men with at least some behavioral risk for intervention studies. However, the resulting sample reflected significant risk over and above the behavioral criteria. The study population reported a high HIV prevalence as well as high prevalence of sex without condoms and multiple partners within a short time frame. The researchers concluded that there is an urgent need to address HIV among black MSMW.

The FDA approved emtricitabine-tenofovir disoproxil fumarate (FTC/TDF) for Pre-Exposure Prophylaxis (PrEP) in 2012 and it has been used in a variety of therapeutic settings across the United States. However, only a small percentage of patients with a PrEP indication have received the drugs, and there are still barriers to using FTC/TDF. To promote awareness, acceptance, and adherence to PrEP, increased education is required for both patients and clinicians. However, the long-term toxicities of tenofovir disoproxil fumarate (TDF) may dampen enthusiasm for some patients and prescribers. To date, there have been no severe unexpected drug AEs associated with the use of PrEP. Although more research is required to fully understand risk compensation and behavioral changes brought on by PrEP use, the data available today emphasize the value of patient counseling and the fact that PrEP should not be used in isolation but rather as part of an all-encompassing HIV prevention strategy. Only instances of low adherence-related drug resistance or multidrug-resistant viral transmission have been documented. Given the mounting demands on our healthcare system, the cost-effectiveness of PrEP will continue to be an important factor to take into account. Future PrEP interventions are being developed that could perhaps get around some of the drawbacks, including as long-acting medications to address adherence and acceptance issues, alternative agents with stronger barriers to HIV resistance development, and/or lower long-term toxicity. The combination of pharmaceutical services and PrEP increases accessibility and enhances adherence and retention. In conclusion, studies assessing the use of FTC/TDF as PrEP after its approval for this use show potential for reducing new cases of HIV infection when prescribed by knowledgeable physicians and given to informed and adherence-focused at-risk patients. To expand the real-world data available and improve best practices, more studies of PrEP implementation in black MSM, transgender women, heterosexual men and women, and intravenous drug users (IVDUs) are still required (Adams et al., 2019).

**BACKGROUND**

The failure of several vaccination trials in the race to defeat HIV-1 illustrates the challenges involved in combating the diseases that plague our planet, particularly the poor countries. Since AIDS was identified as a serious threat to human health 25 years ago, a cure for the disease or a vaccine to prevent HIV have not been found, despite the scientific community's best efforts. There is scientific evidence in various areas, that suggests current efforts to find a vaccine that travels along traditional immunity routes will not be successful. Some of those reasons include scientific research occasionally yields data that is difficult to reconcile with accepted theories, there have been long-standing indications of successful therapies and vaccines, yet popular thinking has frequently led researchers astray during scientific research, the reality is that retroviruses are a special type of infectious agent with direct access to the host species' genome. Classical immunity seemed reasonable as the main paradigm for an HIV-1 vaccine as recently as 10 years ago, but by the close of the previous century, immunity theory that relied on tiny double-stranded RNA arose. This particular type of immunity, which deals with RNA interference and miRNAs, checks viruses in plants by gene silencing, and acts abundantly in eukaryotic life, is based on research into worms and plants. Two American scientists, Andrew Fire and Craig Mello, were awarded the Noble Prize in 2006 for their ground-breaking research that led to the identification of RNAi. In the meantime, the usual methods that had proved so effective failed to stop the AIDS pandemic (Bagasra, 2010).

Many people think that the first life on earth, along with the early parasitic life forms (also known as retroelements) that invaded them, was RNA in nature. In their roles as genomes and ribozymes, RNA molecules carried out enzymatic reactions and stored bioinformation. Retrotransposons, which are primitive retroelements, infiltrated early RNAs and used their ribozymes as a polymerase for self-replication. RNA transformed into more durable DNA genetic storage molecules as evolution progressed, while proteins took on complex enzymatic activities when several structure components evolved. RNA split off into specialized molecules that act as a gene regulator and biodefense network. Most of the human intracellular defenses produced by miRNAs, which are supported by current research, are thought to have evolved from transposable elements (TEs) and retrotransposons. The present understanding of how retroelements were incorporated into higher life forms during evolution is still in its infancy. Retroelements, which provided intracellular protection for survival, appear to have been integrated into the host genome prior to the development of Archaea. Many retroelements went extinct as evolution advanced because they were unable to locate compatible hosts, which strengthened the host's miRNA-based defenses against invasion and infection. The integrated retroelements now act as a first line defense against any retrovirus or lentivirus with a distinct genetic signature in the host genome. Higher animals are frequently exposed to lentiviruses and retroviruses, yet they do not get sick from them, as we will demonstrate later. One of the reasons for this is that pieces of integrated retroelements, which in higher life forms include retroviruses and lentiviruses, are strategically expressed as miRNAs, introns, and other small anti-sense RNAs that search for homologous sequences in the invasive viruses or microorganisms and disable them using a variety of mechanisms (Bagasra, 2014).

**SPECIFIC AIMS**

The proposed experiment will investigate the use of PEP to reduce the transmission of HIV among African American men that sex with other men in Orangeburg, SC. The study will also investigate if condoms are more effective at preventing HIV than PEP, and if it is necessary to use PEP if the individual’s sex partner is also HIV positive.

Aim #1: Submit an IRB application for the use of PEP to reduce HIV transmission.

Aim #2: Conduct a study for HIV-positive men who have sex with men (MSM) after receiving approval.

Aim #3: Provide the participants with the 28 day treatment of PEP that will be used to reduce their risk of transmitting HIV.

**REFERENCES**

HIV and AIDS resources. 2017 Jun 28. HIVgov; [accessed 2023 January 17]. <https://www.hiv.gov>.

Williams, LD, Stall, R, Tempalski, B, Jefferson, K, Smith, J, Ibragimov, U, Hall, HI, Satcher, Johnson, A, Wang, G, Purcell, DW, et al. 2020 Sep. Trajectories of and Disparities in HIV Prevalence among Black, White, and Hispanic/Latino Men who Have Sex with Men in 86 Large U.S. Metropolitan Statistical Areas, 1992-2013. Annals of Epidemiology. [accessed 2022 December 4]; (54):52-63.

doi:https://doi.org/10.1016/j.annepidem.2020.09.004.

Joseph, HA, Pan, Y, Mendoza, M, Harawa, NT, Lauby, J, Hosek, SG, Bluthenthal, RN, Milnamow, M, Fernandez, MI, Jeffries, WL, et al. 2017. HIV Acquisition and Transmission Potential Among African American Men Who Have Sex with Men and Women in Three U.S. Cities. Archives of Sexual Behavior. [accessed 2022 December 4];47(1):183–194.

doi:https://doi.org/10.1007/s10508-017-1052-z.

Adams JL, Shelley, K, Nicol, MR. 2019. Review of Real‐World Implementation Data on Emtricitabine‐Tenofovir Disoproxil Fumarate as HIV Pre‐exposure Prophylaxis in the United States. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. [accessed 2022 December 4]; 39(4):486–500.

doi:https://doi.org/10.1002/phar.2240.

Bagasra O, Pace D. 2010. A new perspective on HIV vaccine design: A viewpoint. Ibnosina Journal of Medicine and Biomedical Sciences. [accessed 2023 March 28]; 02(01):1–13.

doi:https://doi.org/10.4103/1947-489x.210963.

Bagasra O, Pace DG. 2014. Reassessing HIV Vaccine Strategies. Austin J Vaccines and Immunother. [accessed 2023 March 28]; 1(1):10.