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An Examination of the Association between HSV2 and HIV1 Serostatus Outcome and Respective Risk Behaviors and Characteristics of a Population of Male Partners and Clients of Female Sex Workers in Kampala, Uganda

Jennifer Laliberte

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by

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APPROVAL PAGE

An Examination of the Association between HSV and HIV Serostatus Outcome and Respective Risk Behaviors in a Population of Male Partners and Clients of Female Sex Workers in Kampala, Uganda

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ABSTRACT

Background:

Presently, the region that disproportionally carries the highest burden of the HIV1 and HSV2 epidemic is SSA (sub-Saharan Africa). Uganda, a country in Sub-Saharan Africa, Uganda has both high incidence of HIV1 and high prevalence of HSV2 infection. Recent statistics demonstrate a 22% increase in HIV1 incidence from 2001 to 2011 in Uganda. A segment of this population in Uganda is composed of female sex workers (FSWs) who in Uganda account for 35 percent of the nation's HIV1 prevalence. This study explores a population of male partners and clients of these female sex workers (MPCSWs) in order to identify potential risk factors that this segment of the sex work population may contribute to HIV1 and HSV2 prevalence in the sex work population in Kampala, Uganda.

Methods:

Data was obtained from the 2008/2009 Crane Survey and collection of clinical data was completed with the collaboration of Uganda Ministry of Health STD/AIDS Control Programme, Makerere University School of Public Health, and the Centers for Disease Control and Prevention. Four multiple logistic regression models were built with the ten chosen independent variables to identify associations among these variables and each of the four cross-classified serostatuses of HIV1 and HSV2. The level of significance of all analyses was $\alpha=.05$.

Results:

Having a presence of a genital ulcer/sore in the last 12 months was found to have significant association with cross-classified serostatuses HIV1-, HSV2- (OR: 0.52) and HIV1+, HSV2+ (OR: 2.29). Reporting "ever been married" was found to have significant association with cross-classified serostatuses HIV1-, HSV2- (OR: 0.52), HIV1+, HSV2- (OR: 2.90). The variable "age" was found to have significance with cross-classified serostatuses HIV1-,HSV2- (OR: 0.90), HIV1-, HSV2+ (OR: 1.06), and HIV1+, HSV2+ (OR: 1.08). Lastly, those that reported having had a circumcision had significant associations with cross-classified serostatuses HIV1+, HSV2- (OR: 0.26) and HIV1+, HSV2+ (OR: 0.48).

Conclusion:

Although significant associations were not established across all cross-classified serostatuses for all variables found to have at least one significant association with a cross-classified serostatus, previous evidence provides support for these type of observational studies with similar survey structures to have compromised statistical power and possibly explain for why within significant variables, significant associations were not found across all outcome groups. Circumcision status and the presence of a genital ulcer/sore in the last 12 months appears to have possible important implications with acquiring both these infections, especially HIV-1 for the studied population.

CHAPTER I

Introduction

1.1 Background

HIV1 (Human Immunodeficiency Virus 1) still remains a global challenge. HIV1 is found worldwide and it affects about 35.3 million individuals currently.[71] Presently, the region that disproportionally carries the highest burden of the HIV1 epidemic is SSA (sub-Saharan Africa) where it is home to 70% of new HIV1 infections and where 25 million individuals live with HIV1 according to recent statistics[71]. Another sexual transmitted infection that has been documented to have high prevalence is HSV2 (Herpes Simplex Virus type-2) infection in SSA for both the general and high risk populations.[10,13,24,26,42,45,55,59,77] HSV2 is recognized as a major cause of genital ulcerative disease where HIV1 susceptibility increases through the disruption of the mucosal barrier associated with ulceration, and genital shedding which causes increases in HIV1 infectivity.[13,26,36,39,43,51,66] Worldwide, HSV2 has been found to be associated with HIV1 infection.[13,26,36,39,43,51,66] From the documented literature, HSV2 serostatus is an important factor and may play a role in the spread of HIV1 infection.

Uganda has both high incidence of HIV1 and high prevalence of HSV2 infection. Recent statistics demonstrate a 22% increase in HIV1 incidence from 2001 to 2011 in Uganda.[28] "A study conducted among women from Zimbabwe and Uganda found that seroprevalence of HSV2 upon enrollment was 52% for Ugandan women in the study.[7] " The population attributable risk for HIV1 due to HSV2 infection was 42% among these Ugandan women.[7] A recent study conducted in Rakai, Uganda involved 176 men coinfected with HIV and HSV2 who underwent male circumcision in the study and HSV2 shedding was recorded weekly until male circumcision

wounds were certified to be cured.[23] Lavage samples were taken to record HSV2 shedding. Lavage samples before male circumcision procedures were done before any post circumcision lavage samples to serve as baseline for all men in this study. The study found that before male circumcision procedures, HSV2 shedding was detected in 9.7% of men and after male circumcision procedures HSV2 shedding was detected in 27.3% of men.[24] The median time for men to heal completely from circumcision wounds was 4 weeks. All men healed from circumcision wounds completely by 6 weeks. Although only 15 men in the study resumed sexual intercourse by week 4, 12 of them did not have a completely healed wound before resuming sexual intercourse.[23] This study demonstrated that men in Uganda, specifically in Rakai, may participate in risky sexual behavior before complete wound healing where HSV2 shedding showed in this study to have a tendency to increase, and therefore, possibly increase chances for HSV2 transmission. The study recommended that men should be counseled on the potential risk of HIV and HSV2 transmission given their serostatus and programs that conduct male circumcision procedures should promote sexual abstinence during wound healing and condom use thereafter.[23]

A population that has growing risk for HIV infection in Uganda is the population involved in sex work. A segment of this population in Uganda is composed of female sex workers (FSWs) who in Uganda account for 35 percent of the nation's HIV1 prevalence.[70] Another segment of this population is composed of the male partners and clients of these female sex workers (MPCSWs). Although, scarce literature exists demonstrating the risk factors of FSWs for HIV1, there exists even less literature of MPCSWs. Through available studies, including Uganda, researchers have found that specifically male clients of sex workers contribute disproportionally to HIV prevalence.[4,21,35,40,49,57] For Uganda, in particular, 80% of new

infections are accounted for by heterosexual transmission.[70] Because the increasing incidence of Uganda is largely accounted for by heterosexual transmission HIV1, exploring the attitudes and behaviors of both partners and clients of female sex workers may provide insight into potential risk factors that can lead to both HSV2 and HIV1 infection in the population involved in sex work.

1. 2 General Objective

The following study will explore a group of MPCSWs and the potential risk factors that this segment of the sex work population may contribute to HIV1 and HSV2 prevalence in the sex work population in Kampala, Uganda. MPCSW data for this study were obtained from data collected by the *Crane Survey* which was conducted in 2008-2009 with the collaboration of the Uganda Ministry of Health, STD/AIDS Control Programme, Makarere University School of Public Health, and the Centers for Disease Control and Prevention.

SPECIFIC OBJECTIVES

1. Identify risk factors for both HSV2 and HIV1 outcomes in the *Crane* survey sample of male partners of sex workers and to then study the factors associated with the four groups of persons cross-classified by HSV2 and HIV1 serostatus, as follows.

- (HIV1+, HSV2+)
- (HIV1+, HSV2-)
- (HIV1-, HSV2+)
- (HIV1-, HSV2-)

CHAPTER II

Review of the Literature

2.1 Overview of HIV1 (Human Immunodeficiency Virus Type 1) and HSV2 (Herpes Simplex Virus Type 2)

The first case of HIV was identified in early 1959 from an adult Bantu male who lived in Kinshasa, Democratic Republic of Congo.[52,54] At the time he did not know how he was infected and research could not identify how neither.[52,54] Through many following studies since then, it has become evident that HIV was the result of virus infected primates in Africa transferring this virus to humans, zoonotic transfers.[27] The origins of HIV still remain a mystery and many theories have been argued countless times of the virus's origin. Its first discovery was made in 1984 by Luc Montagnier and colleagues at the Pasteur Institute in Paris.[75]

Today, the generally accepted theory of HIV's origin stems from the virus being a descendent of a Simian Immunodeficiency virus. HIV1 is the more virulent and the pandemic strain. HIV1's origin was determined only recently in 1999 in a subgroup of Chimpanzees (Pan troglodytes trolodyte)that were once native to west-Central Africa. This discovery was led by Paul Sharp of Nottingham University and Beatrice Hahn of the University of Alabama where after a 10- year long study they concluded that wild chimps were infected simultaneously with two different simian immunodeficiency viruses and gave rise to a third virus that could be passed on to other chimps and could have crossed species into humans and causing AIDS.[3,20]

HIV is a lentivirus meaning 'slow virus' and like all viruses of its type attacks the immune system and takes a long time to produce adverse effects.[86] HIV only affects humans and causes the weakening of the immune system by killing its important cells, namely CD4 cells.[2] By

weakening the "defense system" of the human body, the immune system, the infected body is left vulnerable to other agents of infection.[2] HIV currently has no cure, and if the infected body reaches a certain low number of viable CD4 cells there remain no way for the body to fight off infections and diseases.[2] If this occurs, a person will have progressed to the condition, AIDS.[1]

AIDS is the acronym that stands for "Acquired Immunodeficiency Syndrome" and is known as the last stage of HIV infection before death. Death usually occurs from opportunistic infections acquired during the AIDS condition. However, it is important to note that not all HIV infected individuals reach the progression of AIDS due to the help of available anti-retroviral medications.[2]

HSV (Herpes Simplex Virus) was known to be prevalent as early as in ancient Greek times.[83] Greek scholars, notably Hippocrates, defined the Greek word "herpes" to mean "to creep or crawl" in reference to the spread of the virus lesions.[83] In 1886, two French doctors, Charles-Paul Diday and Adrien Doyon published a text about herpes called "The Genital Herpes".[31] In 1893, the Herpes Simplex viruses were established by Dmitri Ivanoski in Russia and French scientist Emile Vidal proved that herpes was transmitted from person to person.[31] In 1925, an American virologist Ernest Goodpasture proves that the herpes virus travels through the nerves.[31] In 1939 Frank LacFarlane Burnet, an Australian microbiologist, developed the theory of latency where the herpes virus resides when the person affected is asymptomatic.[31] Lastly, Gertrude Elion developed in 1978 the first safe and non-toxic anti-viral drug, Acyclovir. To date there is still no cure for HSV viruses.[31]

There are two types of Herpes Simplex viruses, type 1 and type 2. Both virus types share many biological similarities based on a similar genome structure where 40% of sequence homologies reach 83% homology of their protein-coding regions.[47] Infecting the body's mucosal

surfaces/abraded skin and establishing latency in the nervous system are characteristic of both types, however, sites of infection and latency differ between the two types.[82] Herpes Simplex Type 2 (HSV2) is more associated with herpes that is sexually transmitted, where the virus infects the genital, perigenital, or anal mucosa/abraded skin and latency reside in the sacral ganglia.[82]

Certain triggers are noted to cause the virus to come out of latency or from the nerve cells and reactivate to form lesions and blisters. These reactivation triggers are commonly found to be the following: stress, fever, exposure to ultraviolet light, tissue damage, and immunosuppresion.[82] Currently, there is no cure for HSV. Medications such as Famvir, Zovirax, and Valtrex can decrease pain from blisters and decrease total number of outbreaks.[32] Warm baths are known to decrease the pain with genital sores.[14]

2.2 Burden of HIV1 and HSV2

About 34 million individuals worldwide were living with HIV/AIDS at the end of 2011.[72] Of these 34 million, only 50% know their HIV status.[74] The major risk factors of HIV infection include: unprotected sex (especially with multiple partners), having another sexual transmitted disease, use of intravenous drugs and lack of male circumcision.[34] Major groups that are termed "vulnerable" to the HIV epidemic are the following: MSM (men that have sex with men), people who inject drugs, sex workers, young women and transgender people.[28] MSM is the group that is most affected by the HIV epidemic. MSM has a high burden of HIV due to the high per-act and per-partner transmission probabilities during anal sex.[5] MSM also have higher rates of dual-variant and multiple-variant HIV infection than heterosexual people in the same setting.[5] In many parts of Africa, Asia, and Latin America, the highest rates of HIV infection in any risk

group are in these men.[6] Although data on MSM are limited and not readily comparable, global prevalence of HIV in this group appears to have increased from 2010 to 2012.[72]

It is estimated that 0.8% of adults aged 15 to 49 years old are living currently with HIV.[8] The burden of the epidemic varies greatly between countries and regions, where sub-Saharan Africa (SSA) continues to be the most affected region, where 1 in 20 adults are living with HIV and accounts for 69% of the people living with HIV globally.[12] Despite this, a decrease has been observed in HIV deaths globally since 2001. It is reported that HIV deaths decreased slightly from 1.7 million deaths in 2000 to 1.5 million deaths in 2012.[43] From the mid-2000s the number of deaths from AIDS-related causes has fallen constantly due to increasing access to antiretroviral therapy (ART) and this access is estimated to have added 14 million life-years in low-and middle-income countries since 1995.[37,43] At the end of 2011, the 8 million people who utilized ART were a 20-fold increase since 2003.[72]

Although a decline in HIV deaths is observed, when observing age-standardized death rates between 1990 and 2010 for AIDS, there was a decline of 21.5% in all cause death rates compared to a 258% increase in the age-standardized death rates for AIDS.[48] Also, years lived with disability per 100,000 increased 2.5% for all cause death rates in comparison to 109.4% for HIV during the same years.[76] HIV and AIDS are still the fifth leading cause of global disability-adjusted life years (DALYs). HIV/AIDS was ranked as the leading DALY cause for ages 30-44 years in both sexes and for 21 countries that fall in the following four regions: Eastern and Southern Africa, Central Africa, the Caribbean and Thailand. Also, 20% of the global HIV/AIDS burden was accounted in countries where HIV/AIDS was not one of the ten leading causes of burden.[56] Worldwide, the rate of HSV infection, including both HSV-1 and HSV2 is about 90%.[78] HSV2 is more common in Sub-Saharan Africa than in Europe or North America.[81] This

region is home to highest levels of HSV2 infection where up to 82% of women and 53% of men are seropositive.[45] In most African countries, HSV2 prevalence increases with age.[36] However, age-associated decreases in HSV2 have been reported in Uganda, Zambia, and Benin.[65]

Those that pose of highest risk are "asymptomatic" individuals which causes for individuals infected to not be detected and pose a risk to those who are vulnerable.[9] Vulnerable populations of HSV2 are cancer chemotherapy patients and children being born to mother who have HSV2 who aren't treated.[11] HSV2 can be passed vertically from mother to child during birth. Most children being born to a mother with HSV2 die 80% of the time if they do not receive treatment.[8] Those that do survive often acquire brain damage.[8] HSV2 can also be passed horizontally and infect sexual partners. HSV2 is found to be associated with an increased risk of two-to threefold for HIV acquisition.[80]

2. 3 Prevention and Control of HIV1 and HSV2

By the mid-2000's the main form of prevention and control of HIV started as a combination of interventions. These interventions' purpose are to be effective in controlling and preventing the spread of HIV. These combination interventions take into account underlying socio-cultural, economic, political, legal and many other factors in people's lives. This strategy is more of a holistic approach where behavioral, biomedical and structural prevention strategies to the spread on HIV are implemented. These interventions consider factors such as levels of infrastructure, local culture and traditions as well as populations most affected by HIV. These programs can be implemented at all population levels. UNAIDS has called for these approaches to HIV prevention to be scaled up and to reinvigorate the global response in order to create an impact on global HIV incidence rates.[73]

Another plan, held in the United States, is called Division of HIV/AIDS Prevention's Strategic Plan 2011-2015. The purpose of the plan is to lessen the burden of HIV as much as possible from the years 2011 through 2015. The plan allows for new opportunities and imperatives for HIV prevention created by large changes in the national, state, and local economic and policy environments, including the July 2010 release of the National HIV/AIDS Strategy for the United States (NHAS). DHAP strives for high-impact prevention using scalable, cost-effective interventions with the benefit of reducing the HIV epidemic impact.[85]

HSV2 does not have a plan of its own globally, but can be controlled and prevented like many other sexually transmitted diseases. Knowing the numerous and apparent problems concerning the spread of HSV2 makes knowing the correct steps and history in regards to preventing and controlling it of principal importance. According to the CDC, the correct and consistent use of latex condoms can reduce the risk of genital herpes however; outbreaks can occur in areas that are not covered by a condom which makes it prevention extremely problematic as stated in the former section. Furthermore; the best course of action to take in its prevention is to abstain from sexual contact or to be in a long-term mutually monogamous relationship with a partner who has been tested and is known to be uninfected . Knowing when to refrain from sexual acts with individuals who have the *classic* ulcerations around their genitalia goes a long way in the first steps of its prevention. Next, it's important to know that even if a person does not have any symptoms that he or she can still infect sex partners. Sex partners of infected persons should be advised that they may become infected and they should use condoms to reduce the risk. Sex partners can seek testing to determine if they are infected with HSV2.[67]

Screening and testing for the existence of HSV2 antibodies in one's bloodstream remains the best way to prevent giving the disease to another person.[38] Prevention starts with knowledge

because everything one does in prevention, management and control depends upon it. Knowing what not to do is just as important as knowing what do to in this aspect. One facet to the decreased spreading of HSV2 is using suppressive antiviral therapy because these types of drugs can diminish risks of transmission by up to 50%.[44] Antivirals also help thwart the development of symptomatic HSV2 infections. Condom are of course another form of prevention like we mentioned above; but it is much more effective at foiling male-to-female transmission than the other way around.[79] Consequentially; the use of the condoms combined with antiviral drugs increases the chances of not acquiring HSV2 by more than 75%. Individuals with an already existing HSV-1 infection diminish the risk of obtaining HSV2 infection among women by a factor of three.[85] In addition; each time the anti-HIV drug *tenoforvir* was used within a topically microbicide vaginal gel it was described to lessen HSV2 sexual transmission by more than 50 percent.[2]

2.4 HIV1 and HSV2 in Uganda

Uganda is located in East-Central Africa, west of Kenya, and has a population of about 36 million.[43] Currently, about 7.2 percent of Uganda's population is living with HIV, which encompasses about 1.4 million people including 190,000 children.[45,47] Recent estimates demonstrate that 62,000 people died from AIDS in 2011 and 1.1 million children have been orphaned by Uganda's epidemic.[72] The first Ugandan case of AIDS was diagnosed in 1982.[62] In the mid 1980's, AIDS became a visible issue in Uganda and efforts to combat this problem began shortly after its discovery.[14] In Uganda, AIDS originated in rural Uganda in the area of Lake Victoria and was termed "Slim Disease".[62] AIDS during this time spread along urban sexual network and major highways.[62]

By the implementation of the A B C prevention strategy in 1992, there was strong

leadership, open communication and involvement of numerous grassroots organizations like TASO (The Aids Support Organization), expanded condom distribution, HIV testing and treatment of sexually transmitted infections.[16,42,44] The message that was disseminated through these efforts started with President Musevini starting in 1986 with his message to maintain fidelity in relationships in Uganda.[33] Filipino Secretary of Health, Dr. Juan Flavier, is credited with being the first to articulate the " A B C" approach. The early history of the " A B C" approach started when the United States Agency for International Development (USAID) during the high onset of HIV/AIDS in the mid 1980's undertook two large scale projects called the AIDS Public Health Communication Project (AIDSCOM) and the AIDS Technical Support (AIDSTECH) Project in response to the increase of HIV/AIDS.[29] Of these two programs, AIDSCOM was directly involved in strategically targeting campaigns for behavior change involved in HIV/AIDS.[16] AIDSCOM ran from 1982 to 1992.[16] AIDSCOM is recognized as the program that gave way to the first ideas to the " A B C" approach by using an applied behavior change (ABC) framework, which integrated behavioral and social psychology, social marketing and communication.[15] AIDSCOM's early work was conducted in the following countries: the Philippines, the Eastern Caribbean, Jamaica, the Dominican Republic, and Ghana.[21] The major focus in these nations via AIDSCOM's behavior change communication campaigns were either abstinence, fidelity or condom use.[29] These campaigns advocated for one or two of these behavior changes, but never all three behavior changes together comprehensively.[29]

The Philippines experienced their first case of HIV in 1984. During the early 1990's, Philippines had increasing numbers of HIV and at this time started to face tension about issues of sexuality between the Philippine Department of Health (DOH) and the Catholic church. During the same time, Secretary of Health, Dr. Juan Flavier, a Catholic physician who dealt with both

DOH and the Catholic church with a family planning program, undertook a nation-wide, important campaign.[18] The goals of this campaign were to increase awareness of HIV/AIDS and promote HIV prevention behaviors through public discussion of condom use.[18] Dr. Juan Flavier during this time continued to pursue the goals of the campaign by doing activities such as giving members of the media condoms during the preparation for a presidential trip to Thailand in 1992 where the DOH proclaimed that December to be "National AIDS awareness month" and implemented a range of AIDS education and activities due to increasing HIV prevalence in Thailand.[46] Through this act , Dr, Juan Flavier, won the allocation of money for HIV prevention programs by the Philippines Congress.[29]

Through this achievement, Dr. Juan Flavier, continued his close work with HIV prevention programs with the church where he was always careful to use scientific evidence as the basis for future programs to avoid debates of morality. Dr. Juan Flavier always believed that AIDS was avoidable, however, crucial steps had to take place to do so. Dr. Juan Flavier then was the first to articulate the " A B C" approach, where denoted it to be the following: A represented abstain from sex, B represented be faithful if you cannot abstain, keep one partner and C represented be careful and use a condom if you cannot be faithful.[29]

Dr. Juan Flavier's "A B C" constructed approach at this time gained popularity worldwide. Dr. Juan Flavier took advantage of media and public speaking opportunities to spread messages about HIV prevention. Examples of these opportunities included: international presentations, International AIDS conferences, meeting of health ministers, and at the 1994 International conference on Population and Development.[65]

The A B C strategy to combat HIV/AIDS in Uganda is the main intervention that is thought to be responsible for the decrease in HIV prevalence in Uganda from 1991 at about 15%

to about 5% in 2001 from analysis of surveys conducted in both 1988 (women only), 1995 (women and men) and 2000 (women and men) from Uganda's Demographic and Health Survey (DHS) and Global Programme for AIDS (GPA) surveys conducted in 1989 (women and men) and 1995 (women and men).[64] It is still unclear as to what segment of the A B C intervention sexual behavior changes that led to the decline in HIV prevalence during these times.[25] Key roles that have led to the decline include: changes in sexual debut, casual and commercial sex trends, partner reduction and condom use.[25]

The President's Emergency Plan for AIDS relief (PEPFAR) and Prevention of Mother to Child Transmission (PMTCT) are two prevention interventions that followed in 2004 and 2002, respectively, and that also provided assistance with antiviral medication access to those infected by HIV/AIDS globally. Despite the onset of these new interventions, HIV prevalence has failed to decline much further and has been pretty stable between 6 and 7 percent.[84] Additionally, there has been an observed increase in prevalence rates in Uganda since 2006.[50]

Critics argue that the reason for the incline may be due to the strict abstinence approach PEPFAR has taken in their efforts in 2003.[19] Critics have also argued that the A B C intervention, has had efforts concentrated around A and B. The intervention has focused on individual behaviors.[53] The A B C approach fails to acknowledge factors that make people vulnerable to HIV/AIDS. The intervention dismisses the real social, political and economic causes of the epidemic.[53] Infected people are then blamed because they didn't adopt the A B C intervention. Further, the ABC intervention ignores vulnerable populations such as sex workers and those who lack the ability to negotiate safe sex.[53] Presently, in Uganda this abstinence program is still in effect today.

Little is known about HSV2 in Uganda, and even less so of programs implemented for HSV2 control and prevention despite studies that demonstrate high prevalence of HSV2 in the population, among them women.[7]

2.5 HIV1 Risk Factors Involved amongst Female Sex Workers (FSWs) and their Male Partners and Clients of Female Sex Workers (MPCSWs)

The relationships between FSWs and their MPCSWs is a notable one since factors that pose FSWs at higher risk for HIV are interrelated with the behavior and attitudes of their MPCSWs. These behaviors include: homosexual behaviors of MPCSWs, gender-based expectations, violence, drugs for pleasure and condom use with multiple partners. Gay and bisexual men of all ages and races are disproportionally the more severe affected group by HIV.[2] These men, including those men that are transgender are termed MSM (men that have sex with men). Statistics demonstrate that MSM are 19 times more likely to be living to be living with HIV than the general population in low-and middle-income countries. Also, it has been found that in MSM populations that proportions of these men display bisexual behaviors. These bisexual behaviors have been extensively documented in Kenya. A study conducted in Nairobi found that 23% of MSM reported being bisexual although 69% reported ever having sex with a woman. It was also found that 14% of these MSM were currently married or had ever been married to a woman.[6] In another study from Kenya it was found that 60% of 285 MSM reported having female sexual partners.[60] These studies demonstrate that MSM may be a bridge population for HIV infection between MPCSWs and FSWs.

Gender-based expectations can also pose as a risk factor for HIV infection. In many countries women are expected to display more submissive behavior when it comes to sexual acts.

This may deter women from feeling empowered to access sexual health information and services.[33] Men, on the other hand, may link masculinity with taking risks and demonstrating toughness. This behavior could also deter men from seeking HIV testing and treatment.[4]

MPCSWs can also play a part in perpetuating violence when coming into contact with an FSW. FSWs are usually stigmatized and criminalized in many societies and worldwide there is scarce legislation and policies implemented to protecting sex workers.[60] The lack of protective infrastructure for sex workers can make FSWs be more susceptible to being vulnerable to acquiring HIV infection.[63] A recent systematic review determined that lifetime prevalence of any or combined workplace violence that sex workers encountered ranged from 45% to 75%.[17] Particularly in Uganda, a study found that FSWs were aware of HIV knowledge and risk, however, due to the fear of violence and the financial need to survive these women viewed HIV as being less of a risk than the violence they faced for them to survive.[61]

It is known that proper condom use is effective at preventing STIs, including HIV.[1,37] Sex workers have more sex partners when compared to the general population. Although, increasing the number of sex partners poses a risk to HIV acquisition, it has been found that if condoms are used properly and consistently the number of partners does not increase the likelihood of HIV acquisition.[67] There are few studies that have surveyed PSWs and their condom use with female sex workers. One study, conducted in Kenya with a population of truck drivers as MPCSWs determined that MPCSWs had a high HIV1 seroprevalence rate upon entry and release from the study and risk factors determined from this group included low condom use and uncircumcised status to contribute to HIV infection.[53]

Lastly, drugs for pleasure such as alcohol is well documented to be associated with HIV prevalence.[13] Alcohol consumption has been long recognized as an important aspect of

commercial sex.[58] Studies have found that alcohol use in commercial sex has led to FSWs being victimized during violent acts by their partners and have also led to higher number of unprotected sex.[11,22,41]

CHAPTER III

METHODS AND PROCEDURES

3.1 Data Source

Data obtained for this thesis analysis was provided by The Centers for Disease Control and Prevention in Atlanta, Georgia. Specifically, the data provided is a subset of the data collected that originated from The Crane Survey 2008/2009 and clinical data that were obtained for this survey. This survey and obtained clinical data was used as a tool to monitor HIV occurrence and prevention with its concerns and parameters being focused to most at risk populations from May 2008 until April 2009 in Kampala, Uganda. The Crane Survey and collection of clinical data was completed with the collaboration of Uganda Ministry of Health STD/AIDS Control Programme, Makerere University School of Public Health, and the Centers for Disease Control and Prevention. In this study, I have limited analysis to the most-at-risk population from the original collected data:male partners and clients of female sex workers (MPCSWs).

3.2 Study Sample in Analysis

The analysis conducted for this thesis was a secondary analysis of survey responses and clinical data obtained, as previously described, from a sample of 520 men who were male partners and clients of female sex workers in Kampala, Uganda.

3.3 Independent and Dependent Variables

Scientifically relevant independent variables that had 10% missing or less that were used for this analysis are displayed in Table 1 in the Results section of this thesis. Ten independent

variables were chosen for this study to compare their influences in the population cross-classified by serostatus of HIV1 and HSV2. Eight of these ten predictors were dichotomous categorical variables and two of these categorical variables were modified. The six unmodified variables were: circumcision status, ever had anal intercourse with a man, ever used a male condom, had casual intercourse in the last 6 months, presence of genital ulcer/sore in the past 12 months and ever married status. The two categorical predictors that were modified due to low counts in cells were "drank alcohol in the last 30 days" and "sexual orientation." "Drank alcohol in the past 30 days" had original levels: about every day, at least once a week, less than a week, none. These levels were modified by collapsing original levels dichotomously to None and At least Once a week for analysis. "Sexual Orientation" had original levels: Homosexual, Bi-sexual, and Heterosexual. These levels were modified by collapsing them dichotomously to Hetero and Homo/Bi. The remaining two predictors used in analysis were continuous variables that were not modified. These were "age" and "# lifetime female sexual partners".

The four dependent variables used for this analysis were created from the clinical data that provided serostatus of HSV2 and HIV1 for male partners and clients of female sex workers. Using these data four dependent dichotomous variables were constructed to represent the cross-classification of serostatus for the population understudy.

3.4 Statistical Analysis

All analyses were conducted using SAS 9.4. Descriptive statistics for the study were conducted by identifying frequency distributions of categorical variables (including modified variables) and distributions of continuous variables. Missing data were discovered during the development of frequencies and distributions of study variables. This information is reported in Table 2 of the results section.

Multiple logistic regression models were used to determine associations between each independent variable and each cross-classified serostatus outcome. The level of significance of all analyses was α=.05. With logistic regression, the dependent variable is dichotomous. The log odds of the outcome of interest is a linear function of the independent variables. The regression coefficients measure change in log odds associated with a one unit change in the independent variable. In SAS, logistic regression is conducted using the PROC LOGISTIC procedure.

Four logistic regression models were constructed in this study where each model consisted of the same 10 independent variables chosen for analysis and a cross-classified serostatus of the population represented the dependent variable. Once significant associations of independent variables with their respective cross-classified serostatus outcomes were obtained, these findings were then compared among the four cross-classified outcomes for this population. Statistics of associations found can be observed in Tables 3-6 and Table 7 in the Results section.

CHAPTER IV

RESULTS

4.1 Descriptive Statistics of HSV2, HIV1 Serostatus within Chosen Study Variables

Table 1 lists the independent variables of interest that will be used for multiple logistic regression analysis and their respective values. Table 2 depicts descriptive statistics of each independent variable for each of the four cross-classified HSV/HIV serostatus outcome groups. As mentioned previously the four cross-classified serostatus outcome groups are the following: (HIV1+, HSV2+), (HIV1+, HSV2-), (HIV1-, HSV2+), (HIV1-, HSV2-). As Table 2 displays, there were a total of 520 male partners and clients of sex workers (MPCSWs) that were included in analysis. While obtaining descriptive statistics of independent variables it was discovered that some of these variables contained missing observations. Missingness is reported in the footnote to Table 2. The two continuous independent variables used in analysis were found to have skewed distributions when observing their histograms, therefore, median and interquartile range (IQR) were reported as the descriptive statistics for each of the four serostatus outcome groups in Table 2.

The following frequencies were observed in each of the cross-classified serostatus groups: (HIV1+, HSV2+) n=74, (HIV1+, HSV2-) n=24, (HIV1-, HSV2+) n=113, (HIV1-, HSV2-) n=309. About double the amount of men were found to have cross-classified serostatus (HIV1-, HSV2-), (42.1%) when compared to those men that had cross-classified serostatus (HIV1+, HSV2-), (20.8%) and (HIV1+, HSV2+), (20.3%) for those men that reported having been circumcised. Also, about double the amount of men were found to have cross-classified serostatus (HIV1+, HSV2-), (70.8%) and (HIV1+, HSV2+), (78.2%) when compared to those men that had cross-classified serostatus (HIV1-, HSV2-), (35.8%) for those men reporting ever

been married. Lastly, a difference was observed in frequencies of cross-classified serostatus in the population understudy was observed in those men that reported having a genital ulcer/sore. Almost double the amount of men were found to have cross-classified serostatus (HIV1+, HSV2-), (58.3%) and (HIV1+, HSV2+), (61.1%) when compared to those men that had cross-classified serostatus (HIV1-, HSV2-), (32.3%).

4.2 Multiple Logistic Regression Analysis

Multiple logistic regression analysis was implemented to build models using the ten independent variables with each of the four cross-classified serostatus outcomes in order to discover associations between the study variables and the serostatus outcomes in each model. Tables 3 through 6 display the findings of significant associations for each of the four models. Table 7 provides a comparison of odds ratios of cross-classified serostatus for each of the ten study variables from collected data from Tables 3 through 6. Below is reported significant findings of all cross-classified serostatus outcomes.

Table 3 presents the statistics for the model that contains (HIV1-, HSV2-) cross-classified serostatus outcome. In this model 3 of the 10 study variables were found to be significant. These significant predictors were: "presence of a genital ulcer/sore in the last 12 months", "ever been married", and "age". For those men that reported having had a presence of a genital ulcer/sore in the last 12 months, holding all other independent variables constant, were found to have an odds ratio of 0.52 compared to those men that reported having not had a genital ulcer/ sore in the last 12 months for those men who were cross-classified serostatus (HIV1-, HSV2-). This odds ratio demonstrates a protective effect where men that reported having had a genital ulcer/sore in the past 12 months are 48% less likely to have this cross classified serostatus. For those that have

ever been married, holding all other independent variables constant, men who reported ever been married were found to have an odds ratio of 0.52 compared to those men that reported having not ever been married for those men who were cross-classified serostatus (HIV1-, HSV2-). This odds ratio also demonstrates a protective effect where men that reported having ever been married are 48% less likely to have this cross classified serostatus. For the independent variable "age", holding all other independent variables constant, the odds of men obtaining a (HIV1-,HSV2-) cross-classified serostatus decreases by 10% for every one unit (year) increase in age. This independent variable was found to have an odds ratio of 0.90 and also reflects a protective effect against (HIV1-, HSV2-) whereas age increases this serostatus is less likely.

Table 4 presents the statistics for the model that contains (HIV1-, HSV2+) cross-classified serostatus outcome. In this model 1 of the 10 study variables was found to be significant. For the independent variable "age", holding all other independent variables constant, the odds of men obtaining a (HIV1-,HSV2+) cross-classified serostatus outcome increases by 6% for every one unit (year) increase in age. This independent variable was found to have an odds ratio of 1.06 and reflects a risk effect for (HIV1-, HSV2+) whereas age increases this serostatus is more likely.

Table 5 presents the statistics for the model that contains (HIV1+, HSV2-) cross-classified serostatus outcome. In this model 2 of the 10 study variables were found to be significant. These significant predictors were "ever been married status" and "circumcision status". For those that have ever been married, holding all other independent variables constant, men who reported ever been married were found to have an odds ratio of 2.90 compared to those men that reported having not ever been married for those men who were cross-classified serostatus (HIV1+, HSV2-). This odds ratio also demonstrates a risk effect where men that

reported having ever been married are 190% more likely to have (HIV1+, HSV2-). For those men that reported having been circumcised, holding all other independent variables constant, were found to have an odds ratio of 0.26 compared to those men that reported having not been circumcised who were cross-classified serostatus (HIV1+, HSV2-). This odds ratio demonstrates a protective effect where men that reported having been circumcised are 74% less likely to have this cross classified serostatus.

Table 6 presents the statistics for the model that contains the (HIV1+, HSV2+) cross-classified serostatus outcome. In this model 3 of the 10 study variables were found to be significant. These significant predictors were: "presence of genital ulcer/sore in the last 12 months", "circumcision status", and "age". For those men that reported having had a presence of a genital ulcer/sore in the last 12 months, holding all other independent variables constant, were found to have an odds ratio of 2.29 compared to those men that reported having not had a genital ulcer/ sore in the last 12 months for those men who were cross-classified serostatus (HIV1+, HSV2+). This odds ratio demonstrates a risk effect where men that reported having had a genital ulcer/sore in the past 12 months are 129% more likely to have this cross classified serostatus. For those men that reported having been circumcised, holding all other independent variables constant, were found to have an odds ratio of 0.48 compared to those men that reported having not been circumcised who were cross-classified serostatus (HIV1+, HSV2+). This odds ratio demonstrates a protective effect where men that reported having been circumcised are 52% less likely to have (HIV1+, HSV2+). For the independent variable "age", holding all other independent variables constant, the odds of men obtaining a (HIV1+,HSV2+) cross-classified serostatus outcome increases by 8% for every one unit (year) increase in age. This independent

variable was found to have an odds ratio of 1.08 and reflects a risk effect for (HIV1+, HSV2+) whereas age increases this serostatus is more likely.

CHAPTER V

DISCUSSION AND CONCLUSION

Discussion

Findings from this study discovered significant associations between certain independent variables studied and one or more cross-classified serostatus of HIV1 and HSV2 as stated previously. As noted before, these independent variables included: "presence of genital ulcer/sore," "ever married status," "age" and "circumcision status". Although these variables were found to have a significant association with at least one of the cross-classified serostatus groups, significant associations were not detected across all cross-classified serostatus groups for any of these given variables. A possible explanation for this discovery is found in a study where researchers reviewed the available literature involving male circumcision and sexually transmitted effects, including HIV1 and HSV2, in adulthood. [69] The researchers found that many of the studies they reviewed were observational studies that contained limited statistical power, were vulnerable to confounding, and contained limitations of self-reporting. [69]

The nature of this study involves sexually transmitted effects, is also observational, specifically cross-sectional, and responses for independent variables studied were limited to self-reporting. Since the nature of this study is closely related to what the researchers in the study discovered of other related observational studies, it is possible that this study may also contain limited statistical power and can possibly explain and provide insight into why all the cross-classified serostatus groups were not found to be significant given that an independent variable was found to have a significant association with at least one of these cross-classified serostatus groups. The following discussion will take into consideration a possible statistical power issue

and will describe observed differences in obtained odds ratios across cross-classified serostatus groups for independent variables that were found to have at least one significant association with a cross-classified serostatus group and based on these differences describe possible implications. Table 7 displays the odds ratio results of each cross-classified serostatus for each study variable used in analysis. Significant results are depicted in bold.

For the independent variable, "presence of genital ulcer/sore in the last 12 months", an important comparison exists between (HIV1-, HSV2+) and (HIV+, HSV2+). As depicted in Table 7, the odds ratios for these cross-classification serostatus are 1.08 and 2.29 respectively. These two odds ratios demonstrate a large difference and this difference indicates that the presence of HIV1 may be important in acquiring HSV2 when a genital ulcer is present within the last 12 months. Another odds ratio comparison between (HIV1-, HSV2+) and (HIV1+, HSV2-) has odds ratios 1.08 and 2.50 respectively. These odds ratios demonstrate a large difference as well and further support the presence of HIV1 being an important factor when a genital ulcer is present in the last 12 months. Specifically, the presence of HIV1 in the absence of HSV2 is more likely when a genital ulcer is present in the last 6 months than in the absence of HIV1 and the presence of HSV2. Lastly, when comparing these odds ratios to the odds ratio of (HIV1-, HSV2-), 0.52, a large difference is also observed and as stated before the presence of a genital ulcer in the last 12 months is protective against (HIV1-, HSV2-). These odds ratios collectively reflect that presence of HIV1 has influence in the presence and absence of HSV2 when a genital ulcer is present in the last 12 months.

Evidence from the literature has found that genital ulcerative disease usually caused by HSV2, allows for HIV1 susceptibility to increase through the disruption of the mucosal barrier associated with ulceration, and genital shedding which causes increases in HIV1 infectivity.[13,26,36,39,43,51,66]

For the independent variable ,"ever been married", the comparison between (HIV1-, HSV2+) and (HIV+, HSV2+) is similar, 1.38 and 1.74 respectively. However, this difference indicates that the presence of HIV1 may be an influence in acquiring HSV2 when the person has ever been married. The comparison between (HIV1-, HSV2+) and (HIV1+, HSV-) which has odds ratio 2.90 reflects a large difference and demonstrates that a person who has ever been married is more likely to have a presence of HIV1 in the absence of HSV2 than is to have a presence of HSV2 and an absence of HIV1. This comparison reflects the influence of the presence of HIV1 when a person has ever been married. Lastly, the comparison of these odds ratios compared to the odds ratio of (HIV1-, HSV2-), 0.52, once more shows a protective effect against this cross-classified serostatus when a person has ever been married. Evidence from the literature provide evidence for the influence of the presence of HIV1 when a person has ever been married. The 2004 Behavioral Surveillance survey indicated that the highest rates of HIV1 infection occur among married men and unmarried women.[30] Researchers believe these high rates are due to cultural and societal expectations of gender roles in Uganda.[49] Researchers have found that in Uganda, "men generally have more power in sexual relationships, and not expected to be faithful, often use violence as a way to resolve conflicts, and are not involved in reproductive health matters, including HIV testing and disclosure." [49] In addition, a 2006 study conducted by the Uganda AIDS commission determined that controlling for these gender role imbalances would play a large role in HIV prevention.[10]

For the independent variable,"age", the odds ratio comparison between (HIV1-, HSV2+) and (HIV+, HSV2+) is also similar, 1.06 and 1.08 respectively. However, this slight difference indicates that the presence of HIV1 may be a slight influence in acquiring HSV2 with increasing age. When comparing these odds ratios to the odds ratio of (HIV1-, HSV2-), a protective effect against this cross-classified serostatus is observed with odds ratio 0.90 is observed. Evidence from the literature reflects both presence of HIV1 and presence of HSV2 as an implication as age increases. A study from Rakai, Uganda determined that HSV2 prevalence in men increased with older age.[68] Another study conducted in rural Rakai, Uganda where among girls aged 15-19, the adjusted relative risk of HIV1 infection doubled among those reporting a most recent sexual male partner that was 10 or more years older.[44]

Lastly, for the independent variable "circumcision status", the odds ratio comparison between (HIV1-, HSV2+) and (HIV1+, HSV2+) is very large, 1.35 and 0.48 respectively. These findings indicate that the presence of HIV1 may be important in acquiring HSV2 when a person is not circumcised and the presence of HIV1 when HSV2 is also present allows for a protective effect for those that are circumcised. The influence of HIV1 is also reflected when these odd ratio findings are compared to the odds ratio of (HIV1+, HSV2-), 0.26. The presence of HIV1 still demonstrates a protective effect in the absence of HSV2 for those that reported being circumcised. Lastly, comparing the odds ratio of (HIV1-, HSV2-), 1.53, to the odds ratios of (HIV1+, HSV2+) and (HIV1+, HSV2-) the absence of HIV1 and HSV2 is more likely when circumcision has taken place. Evidence from the literature provide evidence for the absence of HIV1 when a person is circumcised. Findings were supported by a study that reviewed the available literature regarding male circumcision and sexually transmitted infection effects in

adulthood and reported significant effects based on randomized controlled trials. The study found from 3 randomized controlled trials conducted in South Africa, Kenya and Uganda that discovered that circumcision decreases the acquisition of HIV1 by 53% to 60% among heterosexual men.[69] The study also discovered two randomized controlled trials conducted in Uganda and South Africa whose findings indicated that circumcision decreases the acquisition of HSV2 by 28% to 34%.[69]

Limitations

Despite the statistical results agreeing with literature findings, limitations were faced through this analysis. The quality of survey questions constructed from the primary investigators were poor and could have been constructed in a more tailored method for the population studied. Another limitation to this study is missing data. The data that was missing if was made available could have allowed for a more accurate characterization of these men in the study. Lastly, another limitation is that, with the exception of HIV1 and HSV2 serostatus data, the data was self-reported.

Conclusion

Findings from this study discovered that reporting the presence of a genital ulcer/sore in the past 6 months, reporting ever been married, and increased age give higher odds for HSV2+, HIV+ and HIV+ and HSV2+ respectively. Similar findings have also been discovered previously in the literature. Given the evidence presented in this study and findings from previous studies of these identified risk factors, more tailored surveys and studies must be implemented to precisely understand the sexual risk behaviors of MPCSWs and other marginalized populations. With a

more favorable method of survey methodology tailored to MPCSWs and that account for documented risk factors, a clearer picture can be achieved to understand the prevention methods needed in the MPCSWs.

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Table 1. All study variables.

Variable	Values
Ever used a male condom	Yes/No
Ever had anal intercourse with a man	Yes/No
Drank alcohol in the past 30 days	None/At least once per week
Sexual Orientation	Hetero/ Homo, Bi
Circumcised	Yes/No
Genital ulcer in the past 12 months	Yes/No
Casual intercourse in the last 6 months	Yes/No
Ever married	Yes/No
# of lifetime female sexual partners	Continuous
Age	Continuous

*Decided a priori

Table 2. Descriptive Statistics of serostatus outcome of HIV1, HSV2 for study variables.

Variable	HSV-, HIV- (n=309)	HSV-,HIV+ (n=24)	HSV+,HIV- (n=113)	HSV+,HIV+ (n=74)	Total* (n=520)
Continuous Median (IQR)					
Age	25 (8)	31 (7)	32 (14)	36 (12)	28 (12)
# of lifetime female sexual partners	21 (51)	26 (66)	30 (81)	34 (271)	25 (71)
Categorical n (%)					
Ever used a male condom**	254 (82.7)	22 (91.7)	91 (81.3)	61 (82.4)	428 (82.8)
Ever had anal intercourse with a man**	22 (7.1)	1 (4.2)	9 (8.0)	7 (9.6)	39 (7.5)
Drank alcohol in the past 30 days ***	82 (26.8)	7 (29.2)	41 (36.6)	20 (27.8)	150 (29.2)
Sexual Orientation****	41 (13.6)	1 (4.4)	12 (10.6)	6 (8.2)	60 (11.7)
Casual intercourse in the last 6 months**	209 (68.8)	16 (66.7)	70 (62.5)	38 (52.8)	333 (65.0)
Circumcised**	130 (42.1)	5 (20.8)	49 (43.4)	15 (20.3)	199 (38.3)
Ever married**	110 (35.8)	17 (70.8)	70 (62.5)	57 (78.1)	254 (49.2)
Genital ulcer in the past 12 months**	99 (32.3)	14 (58.3)	48 (42.5)	44 (61.1)	205 (39.7)

*Missing (counts): Ever used a male condom 3, Ever had anal intercourse with a man 2, Drank alcohol in the past 30 days 6, Sexual Orientation 9, Casual intercourse in the last 6 months 8, Ever married 4, Genital ulcer in the past twelve months 4

**Category of variable reflecting descriptive statistics is "Yes"

***Category of variable reflecting descriptive statistics is "At least once per week"

****Category of variable reflecting descriptive statistics is "Homo, Bi"

Table 3. Multiple Logistic Regression Model for HIV1-, HSV2-; model includes 10 independent variables.

Variable	Level	Adjusted Odds Ratio	95% Confidence Interval		p-value*
			Lower	Upper	
Sexual Orientation	Homo, Bi	1.27	0.586	2.771	0.541
	Hetero (Reference)	**1.00**	-	-	-
Drank alcohol in the past 30 days	At least once per week	0.83	0.834	0.510	0.468
	None (Reference)	**1.00**	-	-	-
Circumcised	Yes	1.53	0.954	2.446	0.078
	No (Reference)	**1.00**	-	-	-
Ever had anal intercourse with a man	Yes	1.04	0.426	2.511	0.940
	No (Reference)	**1.00**	-	-	-
Ever used a male condom	Yes	0.98	0.536	1.792	0.948
	No (Reference)	**1.00**	-	-	-
Casual intercourse in the last 6 months	Yes	1.20	0.751	1.907	0.451
	No (Reference)	**1.00**	-	-	-
# of lifetime female sexual partner**	Continuous	1.00	0.997	1.001	0.323
Genital ulcer/sore in the past 12 months	Yes	0.52	0.329	0.809	**0.004**
	No (Reference)	**1.00**	-	-	-
Ever married	Yes	0.52	0.323	0.826	**0.006**
	No (Reference)	**1.00**	-	-	-
Age**	Continuous	0.90	0.869	0.932	**<.0001**

*Statistically significant results in bold (α=.05)

** Reference level to continuous variable odds ratios are 1.00

Table 4. Multiple Logistic Regression Model for HIV1-, HSV2+; model includes 10 independent variables.

Variable	Level	Adjusted Odds Ratio	95% Confidence Interval		p-value*
			Lower	Upper	
Sexual Orientation	Homo, Bi	1.07	0.471	2.421	0.874
	Hetero (Reference)	**1.00**	-	-	-
Drank alcohol in the past 30 days	At least once per week	1.43	0.850	2.406	0.117
	None (Reference)	**1.00**	-	-	-
Circumcised	Yes	1.35	0.823	2.208	0.236
	No (Reference)	**1.00**	-	-	-
Ever had anal intercourse with a man	Yes	1.04	0.402	2.699	0.934
	No (Reference)	**1.00**	-	-	-
Ever used a male condom	Yes	1.24	0.633	2.415	0.534
	No (Reference)	**1.00**	-	-	-
Casual intercourse in the last 6 months	Yes	1.07	0.646	1.788	0.782
	No (Reference)	**1.00**	-	-	-
# of lifetime female sexual partners**	Continuous	1.00	0.998	1.002	0.895
Genital ulcer/sore in the past 12 months	Yes	1.08	0.660	1.759	0.764
	No (Reference)	**1.00**	-	-	-
Ever married	Yes	1.38	0.806	2.349	0.242
	No (Reference)	**1.00**	-	-	-
Age**	Continuous	1.06	1.027	1.094	**0.0004**

*Statistically significant results in bold (α=.05)

** Reference level to continuous variable odds ratios are 1.00

Table 5. Multiple Logistic Regression Model for HIV1+, HSV2-; model includes 10 independent variables.

Variable	Level	Adjusted Odds Ratio	95% Confidence Interval		p-value*
			Lower	Upper	
Sexual Orientation	Homo, Bi	0.64	0.072	5.685	0.689
	Hetero (Reference)	**1.00**	-	-	-
Drank alcohol in the past 30 days	At least once per week	1.03	0.392	2.692	0.956
	None (Reference)	**1.00**	-	-	-
Age**	Continuous	0.99	0.932	1.052	0.748
Ever had anal intercourse with a man	Yes	0.55	0.059	5.204	0.605
	No (Reference)	**1.00**	-	-	-
Ever used a male condom	Yes	1.79	0.395	8.136	0.449
	No (Reference)	**1.00**	-	-	-
Casual intercourse in the last 6 months	Yes	0.97	0.386	2.457	0.955
	No (Reference)	**1.00**	-	-	-
# of lifetime female sexual partners**	Continuous	1.00	0.995	1.004	0.910
Genital ulcer/sore in the past 12 months	Yes	2.50	0.983	6.192	0.055
	No (Reference)	**1.00**	-	-	-
Ever married	Yes	2.90	1.008	8.308	**0.048**
	No (Reference)	**1.00**	-	-	-
Circumcised	Yes	0.26	0.073	0.898	**0.033**
	No (Reference)	**1.00**	-	-	**-**

*Statistically significant results in bold (α=.05)

** Reference level to continuous variable odds ratios are 1.00

Table 6. Multiple Logistic Regression Model for HIV1+, HSV2+; model includes 10 independent variables.

Variable	Level	Adjusted Odds Ratio	95% Confidence Interval		p-value*
			Lower	Upper	
Sexual Orientation	Homo, Bi	0.49	0.125	1.886	0.297
	Hetero (Reference)	**1.00**	-	-	-
Drank alcohol in the past 30 days	At least once per week	0.99	0.511	1.929	0.983
	None (Reference)	**1.00**	-	-	-
Ever Married	Yes	1.74	0.855	3.548	0.126
	No (Reference)	**1.00**	-	-	-
Ever had anal intercourse with a man	Yes	1.18	0.354	3.899	0.793
	No (Reference)	**1.00**	-	-	-
Ever used a male condom	Yes	0.62	0.277	1.380	0.241
	No (Reference)	**1.00**	-	-	-
Casual intercourse in the last 6 months	Yes	0.66	0.346	1.240	0.194
	No (Reference)	**1.00**	-	-	-
# of lifetime female sexual partners**	Continuous	1.00	1.000	1.005	0.042
Genital ulcer/sore in the past 12 months	Yes	2.29	1.217	4.302	**0.010**
	No (Reference)	**1.00**	-	-	-
Circumcised	Yes	0.48	0.234	0.954	**0.037**
	No (Reference)	**1.00**	-	-	-
Age**	Continuous	1.08	1.041	1.124	**<.0001**

*Statistically significant results in bold (α=.05)

** Reference level to continuous variable odds ratios are 1.00

Table 7. Comparisons of odds ratios of cross-classified serostatus outcomes in study variables. *Odds ratio ref=**1.00,** **Level of Categorical Variable

Variable	**Cross-Classified Serostatus Odds Ratios***			
	(HIV1-, HSV2-)	(HIV1-, HSV2+)	(HIV1+, HSV2-)	(HIV1+, HSV2+)
Sexual Orientation *Homo, Bi***	1.27	1.07	0.64	0.49
Drank alcohol in the past 30 days *At least once per week***	0.83	1.43	1.03	0.99
Ever Married *Yes***	**0.52**	1.38	**2.90**	1.74
Ever had anal intercourse with a man *Yes***	1.04	1.04	0.55	1.18
Ever used a male condom *Yes***	0.98	1.24	1.79	0.62
Casual intercourse in the last 6 months *Yes***	1.20	1.07	0.97	0.66
# of lifetime female sexual partners	1.00	1.00	1.00	1.00
Genital ulcer/sore in the past 12 months *Yes***	**0.52**	1.08	2.50	**2.29**
Circumcised *Yes***	1.53	1.35	**0.26**	**0.48**
Age	**0.90**	**1.06**	0.99	**1.08**