Title

Formulation of a Novel HIV-Risk Algorithm for Men who have Sex with Men Visiting a Community-Based Clinic in Los Angeles, California

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Formulation of a Novel HIV-Risk Algorithm for Men who have Sex with Men Visiting a Community-Based Clinic in Los Angeles, California

A dissertation submitted in satisfaction of the requirements for

the degree of Doctor of Philosophy in Public Health

by

Matthew Beymer

2015

ABSTRACT OF THE DISSERTATION

Formulation of a Novel HIV-Risk Algorithm for Men who have Sex with Men Visiting a Community-Based Clinic in Los Angeles, California

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Matthew Beymer

Doctor of Philosophy in Public Health

University of California, Los Angeles, 2015

Professor Linda B. Bourque, Chair

Statement of the Problem: Men who have sex with men (MSM) make up only 2% of the population in the United States, but represent 60% of all HIV infections each year. Pre-exposure prophylaxis (PrEP), a once daily medication to prevent HIV infection, has emerged as a prevention tool for populations most heavily affected by HIV. However, the criteria for PrEP have only been broadly defined and lead many individuals and their medical providers to question if PrEP use is appropriate, given individual risk profile and potential drug side effects. The primary goal of this dissertation is to use risk assessment and HIV testing data to create an HIV risk score for HIV-negative MSM. The secondary goal is to use this HIV risk score to create more targeted criteria for PrEP use and subsequently inform individualized PrEP candidacy.

Methods: Behavioral risk assessment and HIV testing data were collected at the Los Angeles

LGBT Center from January 2009 to June 2014. Individuals were included in the analysis if they were MSM, had an HIV-negative test result at baseline, and returned for at least one follow-up HIV testing visit (n = 9,981). Bivariate and Multivariate Cox Proportional Hazards Models were used to determine the biological, behavioral, and substance use variables significant in HIV contraction over the 5.5 year follow-up period.

Summary of Findings: Self-reported history of gonorrhea ($p = 0.03$), chlamydia ($p < 0.0001$), and syphilis ($p = 0.01$); having receptive anal sex ($p < 0.0001$), race/ethnicity of partners ($p = 0.005$), and number of sexual partners in the last three months ($p = 0.0003$); methamphetamine ($p = 0.0008$), and nitrate use ($p = 0.002$) were all significant predictors of HIV infection during follow-up. Age of partners, intimate partner violence, and ecstasy use were not significant. Following risk score creation, approximately 45% of all individuals were above a chosen risk score, which consisted of 76% of all HIV-positives. The use of this targeted strategy is beneficial in that it more accurately outlines PrEP candidacy criteria, subsequently allowing individuals and their medical providers to make a more informed decision before use.

The dissertation of Matthew Beymer is approved.

Gilbert C. Gee

Donald E. Morisky

Suzanne B. Shu

Robert E. Weiss

Linda B. Bourque, Committee Chair

University of California, Los Angeles

2015

To Bob, Catherine and the Committee, the physician with the brilliant idea, the statistician who showed patience and kindness to a fledgling scientist, and the group who committed to completing the dream

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LIST OF ACRONYMS

AIDS	= Acquired immune deficiency syndrome
CDC	= United States Centers for Disease Control and Prevention
CI	= Confidence interval
CT	= *Chlamydia trachomatis*
ED Drugs	= Erectile dysfunction drugs
HAART	= Highly active antiretroviral therapy
HIV	= Human immunodeficiency virus
HR	= Hazard ratio
HSV	= Herpes simplex virus, type II
IDU	= Injection drug user
IH	= Internalized homophobia
IMBS	= Information-motivation-behavioral skills model
IPV	= Intimate partner violence
LA LGBT Center	= Los Angeles Lesbian, Gay, Bisexual and Transgender Center
MSM	= Men who have sex with men (also refers to MSMW in this dissertation)
MSMW	= Men who have sex with men and women
NG	= *Neisseria gonorrhoeae*
PEP	= Post-exposure prophylaxis (also called nPEP for “non-occupational”)
PI	= Pacific Islander
PrEP	= Pre-exposure prophylaxis
OR	= Odds ratio
RA	= Risk assessment
ST	= Syndemics theory
STI	= Sexually transmitted infection
UAI	= Unprotected anal intercourse
UIAI	= Unprotected insertive anal intercourse
URAI	= Unprotected receptive anal intercourse

YMSM = Young men who have sex with men (under the age of 25)
Please note: Most acronyms will be defined at first mention in each chapter to appropriately guide the reader.

SIGNIFICANCE TESTING AND DATA PRESENTATION

Unless otherwise stated,

- An alpha level of 0.05 is used for all statistical tests to determine statistical significance.
- Percentages are row percentages.

GLOSSARY

Acute HIV Infection:

1) Also known as an *early HIV infection*, an acute HIV occurs when the tests used are able to detect the virus, but are not able to detect the antibodies, since the human body takes approximately 4-6 weeks to develop an antibody response.
2) An individual with an acute HIV infection will have a positive result for the Nucleic Acid Amplification Test (NAAT, an assay that looks specifically for the virus) but a false-negative result for the HIV antibody test.

Acquired Immune Deficiency Syndrome (AIDS): A disease caused by the Human Immunodeficiency Virus (HIV) where an HIV-infected individual's immune cells (CD4) drops to less than 200 cells/mm^3. In a normal healthy adult, CD4 cell counts range from 500-1,200 cells/mm^3.

Antibody test: Blood assay that determines if HIV antibodies have been created by the body. This test is able to detect HIV as early as three weeks after infection. For earlier detection, a NAAT test can be used that tests directly for viral antigen.

Antigen: A viral antigen is a protein that is found in a particular viral genome; part of the virus.

Antiretroviral therapy:

1) Originally discovered in the early 1990s, this term represents a class of drugs that was first used to slow the progression of HIV in HIV-positive individuals.
2) In 1994, this class of drugs was then administered for 28 days to healthcare workers who had an exposure to HIV (e.g., a nurse who was accidentally stuck with a needle from an HIV-positive patient). This regimen was given the name occupational post-exposure prophylaxis or PEP.
3) In the mid-2000s, this class of drugs was then administered for 28 days to individuals who had a non-occupational exposure to HIV (e.g., through unprotected sex or injection drug use). This regimen was given the name non-occupational post-exposure prophylaxis or nPEP.

4) In early 2010, this class of drugs was then administered on a daily basis to individuals who are at high risk of exposure to HIV. Since it was administered before exposure, as opposed to after with PEP and nPEP, this regimen was given the name pre-exposure prophylaxis or PrEP.
5) Although PEP, nPEP, and PrEP are used for different purposes, the drugs that are used are the same. The only difference is the timing (PrEP vs PEP) and type (nPEP vs. PEP) of exposure.

Community Viral Load: Proportion of individuals who are HIV-positive and are adherent to treatment which is indicated by a low viral load. Lower values indicate more control of the virus in the population whereas higher values indicate less control of the virus in the population.

Homophobia: Fear of individuals who identify as gay, lesbian, or homosexual.
Infectiousness: Refers to a set of properties that influence how capable an individual is to infect another individual with a HIV.
Example: An individual with a high HIV viral load (see below) will be more infectiousness than one with a low HIV viral load.

Human Immunodeficiency Virus (HIV): The virus that will in most cases, if left untreated, lead to Acquired Immune Deficiency Syndrome (AIDS).

HIV Incidence: The number of individuals that are <u>newly</u> infected with HIV divided by the unique number susceptible to HIV infection in a population.
Example: A population with five newly infected individuals out of 100 susceptible unique individuals will have an HIV incidence of 5%.

HIV Prevalence: The number of individuals that are infected with HIV divided by the total number of unique individuals in that population.
Example: A population with twenty infected individuals out of 100 unique individuals will have an HIV prevalence of 20%.

Meth: Abbreviated version of methamphetamine.

Nucleic Acid Amplification Test (NAAT): This blood assay is an alternative to the antibody test and detects the presence of HIV antigen in the blood. This test is able to detect HIV as little as 10 days after infection.

Non-Acute Infection:
1) HIV diagnosis made after an individual has developed antibodies to HIV and therefore they are diagnosed at least 4-6 weeks after their infection was contracted.
2) In this type of HIV infection, both the NAAT assay and the antibody test are HIV-positive.

Non-Occupational Post-Exposure Prophylaxis (nPEP): Antiretroviral therapy taken for 28 days by an HIV-negative individual to avert HIV infection *after* a condomless sexual encounter

with an HIV-positive individual or *after* sharing drugs with an HIV-positive person. nPEP must be taken within 72 hours or exposure to be effective.

Occupational Post-Exposure Prophylaxis (PEP): Antiretroviral therapy taken for 28 days by an HIV-negative healthcare worker to avert HIV infection *after* a needle stick or other bloodborne exposure to an HIV-positive patient. PEP must be taken within 72 hours of exposure to be effective.

Pre-Exposure Prophylaxis (PrEP): Antiretroviral therapy taken once *daily* by an HIV-negative individual to prevent the contraction of HIV. Unlike nPEP and PEP, PrEP is taken *before* a risky exposure.

Seroconversion: Testing HIV-positive; Converting from an HIV-negative to an HIV-positive status.

Seroconvert: See *Seroconversion*.

Serodiscordant Couple: A couple where one person is HIV-negative and the other person is HIV-positive.

Seronegative: An individual who is HIV-negative.

Seropositive: An individual who is HIV-positive.

Serostatus: The HIV status of an individual.

Sexual Orientation: An identity that describes the gender(s) in which an individual is attracted.

Susceptibility: Refers to a set of properties that influence how easily an individual can contract a pathogen (e.g., HIV).
Example: An individual who only engages in receptive anal sex is more susceptible to HIV infections when compared to an individual who engages in insertive anal sex due to micro-tearing of the anal cavity.

Viral Load: The amount of HIV virus found in an individual's blood stream (high viral load increases infectiousness).

Window Period: The amount of time between becoming infected with HIV and the virus being detected by a given laboratory test. The NAAT assay has the shortest window period of 10 days and the antibody test has a window period of 20-23 days.
Example: An individual infected with HIV will test NAAT-positive 10 or more days after becoming infected with HIV.

ACKNOWLEDGEMENTS

I would like to acknowledge the funding provided by the Los Angeles LGBT Center for completing this work.

VITA/BIOGRAPHICAL SKETCH

EDUCATION

University of California, Los Angeles 2009 – 2011
- M.P.H. – Epidemiology

University of California, San Diego 2006 – 2008
- B.S. – Microbiology

United States Marine Corps, Officer Candidate School 2007
- Graduate – Class 195, Alpha Company, 4th Platoon

PROFESSIONAL EXPERIENCE

Los Angeles LGBT Center – Sexual Health and Education Program 2011 – Present
Epidemiologist
- Adaptation and presentation of the Gardner HIV Continuum of Care to the HIV testing and treatment clinics at the Los Angeles LGBT Center to inform HIV testing and treatment policy
- Project management on the formulation of risk assessments to collect data on STD and HIV screening clients, Trans* clients, and clients who are members of the House and Ball Community
- Design of an electronic registration system using iPads and SurveyMonkey software that lowered average wait time from 20 to 8 minutes, reduced missing data and streamlined clinic flow
- Creation of a SAS algorithm for nursing staff which cross-referenced STD data with treatment data to determine individuals still requiring treatment for STDs and automation of confidential morbidity reports
- Construction of a Microsoft SQL Server database to extract over 2,000 sexual health-related variables from electronic medical records for data analysis and various funder reports
- Lead author or second author on five peer-reviewed manuscripts and six conference presentations

Los Angeles County Department of Public Health – Immunization Program 2009 – 2011
Epidemiology Analyst Intern
- Completion of a study examining the risk factors influencing the complications of whooping cough in infants under two months of age
- Assisted senior epidemiologists with vaccine-preventable disease surveillance and data analysis

U.S. Agency for International Development (USAID) 2010
Bixby Fellow in Population and Reproductive Health, Africa Bureau

- Authorship of a document used to inform USAID mission leadership on women's health in Mozambique
- Grant review to ensure that all U.S. government-funded projects for HIV treatment and prevention made equal provisions across gender lines

Quintiles Transnational 2008 – 2009
Clinical Trials Assistant

- Management of clinical trial study logistics, system updates, file audits, sponsor requests and data cleaning
- Successful completion of two nephrology clinical trials ahead of the original recruitment deadline

TEACHING POSITIONS

University of California, Los Angeles Extension 2014 – 2016
Public Health XL 10 – Introduction to Public Health (Online)

- Lesson plan development and instruction to a diverse group of adult learners on topics including chronic and infectious disease epidemiology, environmental health, maternal and child health, and substance abuse
- 2016 Overall Rating of Instructor by Students (Winter): Planned for January 2016
- 2015 Overall Rating of Instructor by Students (Summer): 9 / 9
- 2014 Overall Rating of Instructor by Students (Summer): 9 / 9

University of California, Los Angeles 2013 – 2015
Community Health Sciences 212 – Advanced Social Research Methods in Health (Winter)

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- 2014 Overall Rating of Special Reader by Students: 4.5 / 5

Community Health Sciences 213 – Research in Community and Patient Health Education (Fall)

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- 2014 Overall Rating of Special Reader by Students: 4.9 / 5
- 2013 Overall Rating of Special Reader by Students: 4.9 / 5

SOFTWARE SKILLS

- Highly skilled in SAS and SPSS
- Working proficiency in STATA and R
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- Programming proficiency in Microsoft SQL and Access

Chapter 1 – Introduction

HIV Incidence in the United States

The United States (US) Centers for Disease Control and Prevention (CDC) estimates that gay, bisexual, and other men who have sex with men (MSM) represent only 2% of the US population but over 60% of all human immunodeficiency virus (HIV) cases in the US (CDC 2014a). Despite the implementation of numerous behavioral interventions since the beginning of the epidemic, the number of new HIV infections has remained at 50,000 infections per year since 2000.

While the number of new HIV infections has remained constant, there has been a shift in the people newly infected with HIV. The proportion of infections attributed to heterosexuals and injection drug users (IDU) dropped from 47% to 40% between 2008 and 2010. Conversely, the proportion of new HIV infections attributed to MSM increased from 53% to over 60% between 2008 and 2010. Therefore, the consistent number of infections overall within the past 15 years has masked worsening infection rates among MSM.

Although MSM have experienced substantially greater rates of HIV, the risk is not the same for all MSM groups. African-Americans account for an estimated 39% of all HIV infections per annum in the MSM population yet make up only 13% of the overall population in the US (US Census 2010, CDC 2014b). Furthermore, Hispanics account for 21% of all HIV infections per year among MSM but only make up 16% of the overall population in the US (US Census 2010, CDC 2014c). In contrast, Whites represent 72% of the overall population in the US but only 35% of all HIV infections (US Census 2010, CDC 2014a).

There are even greater HIV infection disparities between races by age group, especially for MSM under 35 in the African-American and Hispanic communities. An estimated 67% of all

HIV infections in Hispanic MSM occur in individuals between 13 and 35, and 75% of all HIV infections in African-American MSM occur in this age group (CDC 2014b, CDC 2014c). Therefore, rates of HIV incidence are not only increasing among MSM but are increasing most rapidly among racial/ethnic minority MSM and young MSM. The heterogeneity in incidence among these different MSM communities calls for greater surveillance of the specific risk factors that are associated with HIV in each MSM subgroup.

The purpose of this dissertation is to address these increasing HIV incidence rates by looking at specific variables that are associated with HIV infection among all MSM, racial/ethnic minority MSM, and young MSM. More specifically, the primary objective of this dissertation is to create an HIV risk score tailored to each MSM demographic subgroup through retrospective analysis of HIV testing data and self-reported behavioral risk assessment data from a large community-based organization. The secondary objective is to use this HIV risk score to triage individual MSM into the most appropriate biomedical intervention based on their HIV risk score. The next section will discuss these biomedical interventions and how expanded uptake in appropriate populations can effectively reduce the HIV burden in these MSM communities.

Biomedical Tools to Prevent HIV Infection

HIV occupational post-exposure prophylaxis (PEP) was originally pioneered in 1994 as a biomedical intervention to protect healthcare workers from contracting HIV after being exposed to the blood products of an HIV-infected individual (Beekmann et al. 1996). Early research showed that a 28-day regimen of PEP within 72 hours of HIV exposure significantly reduced the chances of HIV infection among healthcare workers exposed to the blood products of HIV-infected individuals (Beekmann et al. 1996).

In 1998, non-occupational PEP (nPEP) was proposed as a method for potentially aborting HIV infection following sexual or IDU exposure to HIV (Kalichman et al. 1998, Kinghorn et al. 1998). In 2005, the CDC released guidelines stating that nPEP was efficacious if taken correctly and consistently in line with the occupational recommendations (Smith et al. 2005).

While occupational PEP and nPEP are equally effective, sexual and IDU exposures for nPEP are most often self-reported and there may be difficulty in determining if the recipient had a risky exposure to an HIV-infected individual or just had a risky exposure to an individual of unknown HIV serostatus. In contrast, occupational PEP scenarios often involve prophylaxis when the source of exposure is known to be HIV-positive (e.g., as verified in the medical record), and studies have shown that PEP is highly cost-effective in such straightforward scenarios (Scheid et al. 2000). Since the HIV status of the source of exposure may be unclear for nPEP, the cost-effectiveness of nPEP may be significantly lower than occupational PEP. Thus, nPEP programs have had lower uptake across the US because of the uncertain cost-effectiveness.

In 2004, Pinkerton et al. analyzed the cost-effectiveness of nPEP across 96 metropolitan statistical areas in the US. The researchers found that nPEP was most cost-effective in areas where a large proportion of the population was MSM and the prevalence of HIV was high (Pinkerton et al. 2004). An analysis of data in France found that nPEP was cost saving (0 Euros per quality adjusted life year (QALY) saved) in only 4.4% of cases and was cost-effective in 11.3% of cases (50,000 Euros per quality adjusted life year (QALY) saved), but only 25% of recipients were classified as MSM (Herida et al. 2006). Therefore, Pinkerton and Herida independently concluded that nPEP is cost-effective in MSM populations, but the intervention has limited effectiveness when applied to IDUs and heterosexuals (Pinkerton et al. 2004, Herida et al. 2006).

While occupational PEP and nPEP have served as important prophylactic tools, researchers found certain individuals were constantly exposed to HIV-positive individuals and therefore required repeat course of nPEP. These individuals included persons in serodiscordant couples, or relationships where one partner is HIV-negative and the other is HIV-positive, and substance-using MSM that had a high number of unprotected sexual encounters with different partners. These findings led to the scientific proposal of a once daily highly active antiretroviral therapy (HAART) taken prior to a risky exposure to reduce risk of seroconversion for HIV-negative individuals. Since this intervention was administered prior to the risk event, it was appropriately named pre-exposure prophylaxis (PrEP).

The first major trial to analyze the efficacy of PrEP was conducted from 2007 to 2009 by the iPrEx international study team. The team aimed to determine if consistent daily use of HAART could lead to reduced incidence of HIV among HIV-negative men. They found a 44% overall reduction in the incidence of HIV between individuals taking HAART and those who were in the placebo arm (Grant et al. 2010). However, mathematical models have shown that PrEP can reduce lifetime HIV infection risk from 44% to 6% if the patient adheres to their medications more than 90% of the time (Paltiel et al. 2009). Similar to PEP and nPEP, PrEP has only been found to be cost-effective if delivered to the populations at highest risk for infection such as MSM (Desai et al. 2008, Gomez et al. 2013).

Despite the availability of these biomedical resources, there is poor awareness and uptake of these tools in communities across the US, especially in communities that would most benefit. In a study among San Francisco MSM, Liu et al. found that only 47% of MSM surveyed were aware of nPEP (Liu et al. 2008). In a 2011 study among New York City MSM who were surveyed at bathhouses, only 36% reported awareness of nPEP or PrEP (Mehta et al. 2011).

Given that New York and San Francisco report about 7% of all new HIV infections in the US each year, this low level of awareness shows the need for expanded education campaigns (SFPDH 2012, NYS DPH 2011). Among HIV-positive MSM, knowledge of nPEP was comparable to the San Francisco MSM sample at 49% (Joshi et al. 2013). These data show that despite the availability of a highly effective technologies like nPEP and PrEP, few individuals are aware of these regimens in protecting themselves against HIV.

In addition to a lack of awareness, there may also be a disparity in uptake of nPEP by race/ethnicity. A study by Beymer et al. (2014a) analyzed data from the largest federally-funded nPEP program in Los Angeles County and found that while African-American MSM represented 8.5% of persons accessing nPEP services, they made up 16.7% of new HIV infections during the study period. Given that African-American MSM are at the greatest risk for HIV, these individuals should be accessing these services in the highest proportions.

Therefore, while these biomedical technologies are available, the populations that need them most are either not aware of, or not accessing, these interventions commensurate with their level of risk. By creating an HIV risk score, and subsequently an HIV risk algorithm, unique to each demographic subset of MSM, an individual's level of risk will determine if they need consistent biomedical prophylaxis through PrEP or intermittent protection through nPEP. The next section will discuss the need for developing a targeted delivery system for nPEP and PrEP given the high cost to the medical system and the side effects of these technologies.

Formulation of an HIV Risk Algorithm for HIV-Negatives

In May 2014, the CDC officially recommended that "PrEP be considered for people who are HIV-negative and at substantial risk for HIV" (CDC 2014d). Individuals at substantial risk for HIV include (1) individuals in serodiscordant relationships, (2) individuals in a non-

monogamous relationship, (3) heterosexual women with inconsistent condom use with unknown HIV serostatus partners who are bisexual or IDU, and (4) gay or bisexual men who have had anal sex without a condom or been diagnosed with an sexually transmitted infection (STI) in the past six months.

While these recommendations are specific, they may not be specific enough to avert a financial overburden to the healthcare system. A 2010 report by the CDC found that implementation of PrEP to 100,000 of the most high-risk individuals would cost an estimated $1 billion annually in medication expenditures alone (CDC 2010). In the 2015 fiscal year budget for the US government, only 3% ($912 million of the $30.4 billion) of the total money allocated for HIV and AIDS related activities were allocated to HIV prevention (Kaiser 2014). Provision of PrEP to 100,000 individuals at highest risk would exceed the amount allocated to the HIV prevention budget and would not leave funds for any other prevention programs like nPEP, HIV testing, or condom distribution activities. Given that PrEP is only part of a comprehensive prevention strategy, more targeted strategies are needed.

In addition to the financial burden, there are other concerns about poor medication adherence or the effects of long-term use. Poor medication adherence makes an individual more susceptible to contracting HIV. If an individual does contract HIV and continues taking the medication, this could lead to the development of a drug-resistant infection, ultimately making the infection harder to treat. Furthermore, long-term use of the drug among HIV-negative individuals may result in unknown side effects. The provision of PrEP must be carefully considered in light of the high cost, the potential for drug resistance through poor medication adherence, and the possibility for lasting side effects among users.

Therefore, while biomedical strategies are necessary, they may need to be targeted further to ensure that nPEP and PrEP are given to MSM appropriate to their risk behavior. This dissertation will create an HIV risk algorithm to appropriately triage individuals to PrEP, nPEP, or frequent HIV testing. While this dissertation is timely, one previous study has conceptualized a similar biomedical treatment algorithm, albeit with important differences (Chen et al. 2014).

Chen et al. (2014) created a PrEP algorithm for patients to determine their risk of HIV infection with PrEP and without PrEP, considering the individual risk profile (algorithm available at: https://ictrweb.johnshopkins.edu/ictr/utility/prep.cfm). Chen et al. developed an algorithm that used four individual-level variables and one population-level variable: condom use, type of sex, frequency of sex, relationship status, and HIV prevalence. While this algorithm considers individual and population variables key to HIV contraction, it neglects to include other variables shown to be associated with HIV infection in both applied theory (Syndemics Theory) as well as the scientific literature. The algorithm for this dissertation is different from the previous study in that it also incorporates substance use, partner characteristics, and mental health variables. Furthermore, the algorithm for this dissertation does not provide an individual's chances of HIV infection directly to the client but would instead create a provider recommendation to determine PrEP candidacy or frequent HIV testing.

The next chapter will discuss the specific aims and research questions to accomplish the outlined study objectives. Chapter 3 will discuss the theoretical background for the dissertation and discuss how Syndemics Theory will be applied as the theoretical framework to guide analyses. Chapter 4 will discuss what is known about HIV transmission in the literature and outline the limitations of past research. Chapter 5 will discuss the design, variable selection, and analytical strategy for this dissertation. Chapter 6 will discuss the bivariate results for both the

entire population as well as sub-populations at greatest risk. Chapter 7 will outline the findings from multivariate analyses and risk algorithm construction. Lastly, Chapter 8 will discuss the implications of these findings, the limitations of the analyses, and future steps for implementation of the risk algorithm at the Los Angeles LGBT Center

Chapter 2 – Study Objective, Specific Aims, and Research Questions

The primary objective of this dissertation is to create an HIV risk algorithm for men who have sex with men (MSM) clients of the Los Angeles LGBT Center. This algorithm will prospectively provide a quantifiable and standardized HIV risk score using baseline behavioral data as well as HIV testing data. The second objective is to use this HIV risk score to triage MSM into one of three biomedical/behavioral interventions (PrEP, nPEP, or frequent HIV testing). This dissertation contains three aims that will be used to assess the study objectives.

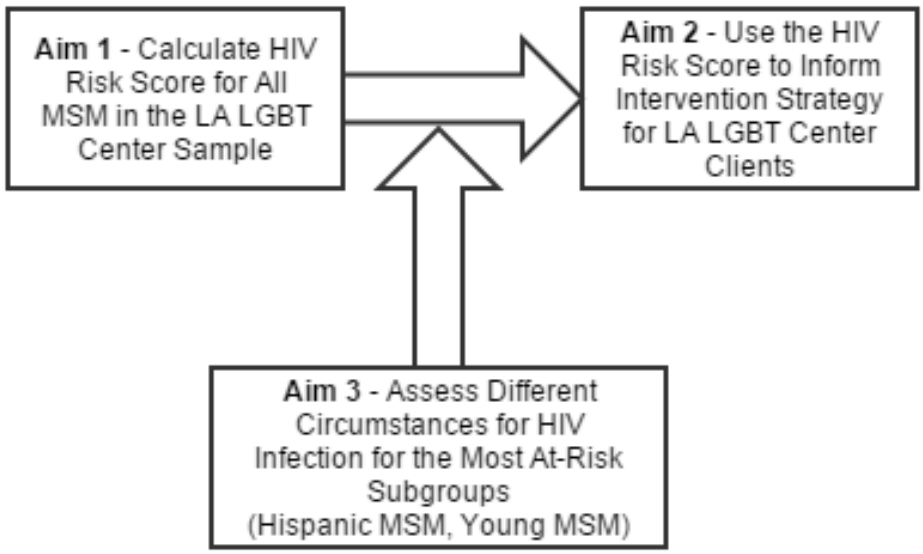
Aim 1 will use Cox proportional hazards models and survival analyses to determine what biological, sexual behavioral, and substance use variables at baseline that predict HIV seroconversion at follow-up among MSM. To be included in this analysis, MSM must have tested HIV-negative at baseline and returned for at least one follow-up HIV testing visit. This retrospective analysis will include 5.5 years of data (January 2009 to June 2014) from the LA LGBT Center and will be used to prospectively calculate HIV risk scores for MSM clients visiting the LA LGBT Center.

Aim 2 will determine the most appropriate cut points for the HIV risk scores to determine the individuals most suited for PrEP, nPEP, or frequent HIV testing. There are numerous types of interventions for HIV-negative persons, but these three interventions represent the most impactful for HIV prevention given current research. Pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (nPEP) are novel biomedical tools that can be taken either before or after a sexually risky event to reduce the chances of HIV infection. PrEP is most appropriate for individuals at consistent risk for HIV while nPEP is more appropriate for individuals at occassional risk for HIV. For individuals with low to no risk, frequent HIV testing should be employed.

Aim 3 will investigate whether different circumstances result in HIV infection for the most at-risk subgroups, particularly racial/ethnic minorities and young MSM. A majority of the new HIV infections in the US are among racial/ethnic minority MSM as well as MSM under the age of 25 (CDC 2014a). In previous HIV survival analyses, 70-80% of individuals identified as White (Menza et al. 2009, Smith et al. 2011). In contrast, 51% of the LA LGBT Center sample identifies as a racial/ethnic minority. Prior analyses have not investigated these most at-risk subgroups to determine if circumstances for HIV infection differ when compared to White MSM or older MSM.

The existing literature has primarily reported circumstances for infection among White MSM. However, there are numerous cultural and social factors that may influence HIV contraction in other subgroups of MSM. Given the dearth of literature about circumstances for infection specific to other MSM subgroups, this dissertation aims to investigate if circumstances are either similar to Whites or different among these subgroups, particularly among Hispanic MSM and young MSM.

Figure 2.1 – Graphical Depiction of Dissertation Aims



Aim 1 – Calculate HIV Risk Score

The goal of Aim 1 is to use Syndemics Theory as a framework to investigate the biological, sexual behavioral, and substance use variables at baseline that are significantly associated with HIV infection at follow-up (Halkitis et al. 2013a).

Baseline responses to risk assessment questions will serve as the predictors in this analysis. The outcome will be assessed by analyzing 5.5 years (January 2009 and June 2014) of subsequent HIV testing data to longitudinally determine if the individual became HIV infected (i.e., seroconverted) (n = 395) or remained HIV-negative at follow-up (n = 9,586). Individuals who did not return for a second HIV testing visit, or who are not MSM, will not be included in this analysis. The following research questions will be investigated to fulfill this aim:

1. What are the biological variables at baseline that are associated with HIV infection at follow-up?
2. What are the sexual behavioral variables at baseline that are associated with HIV infection at follow-up?
3. What are the substance use variables at baseline that are associated with HIV infection at follow-up?
4. How do the biological, sexual behavioral, and substance use variables at baseline, controlling for potential confounders, combine to predict HIV infection at follow-up?

Numerous behavioral interventions have been employed since the epidemic began in the 1980s. These behavioral interventions have had a limited impact as evidenced by the 50,000 new infections per year since the year 2000. Given these data, more innovative solutions are needed to ensure that MSM are triaged to an intervention reflective of their HIV risk score. Aim 1 is important because it will allow for the quantification and standardization of a risk score for each

client and systematically inform Center staff about the attributes most closely associated with HIV incidence.

Aim 2 – Use the HIV Risk Score to Inform Intervention Strategy

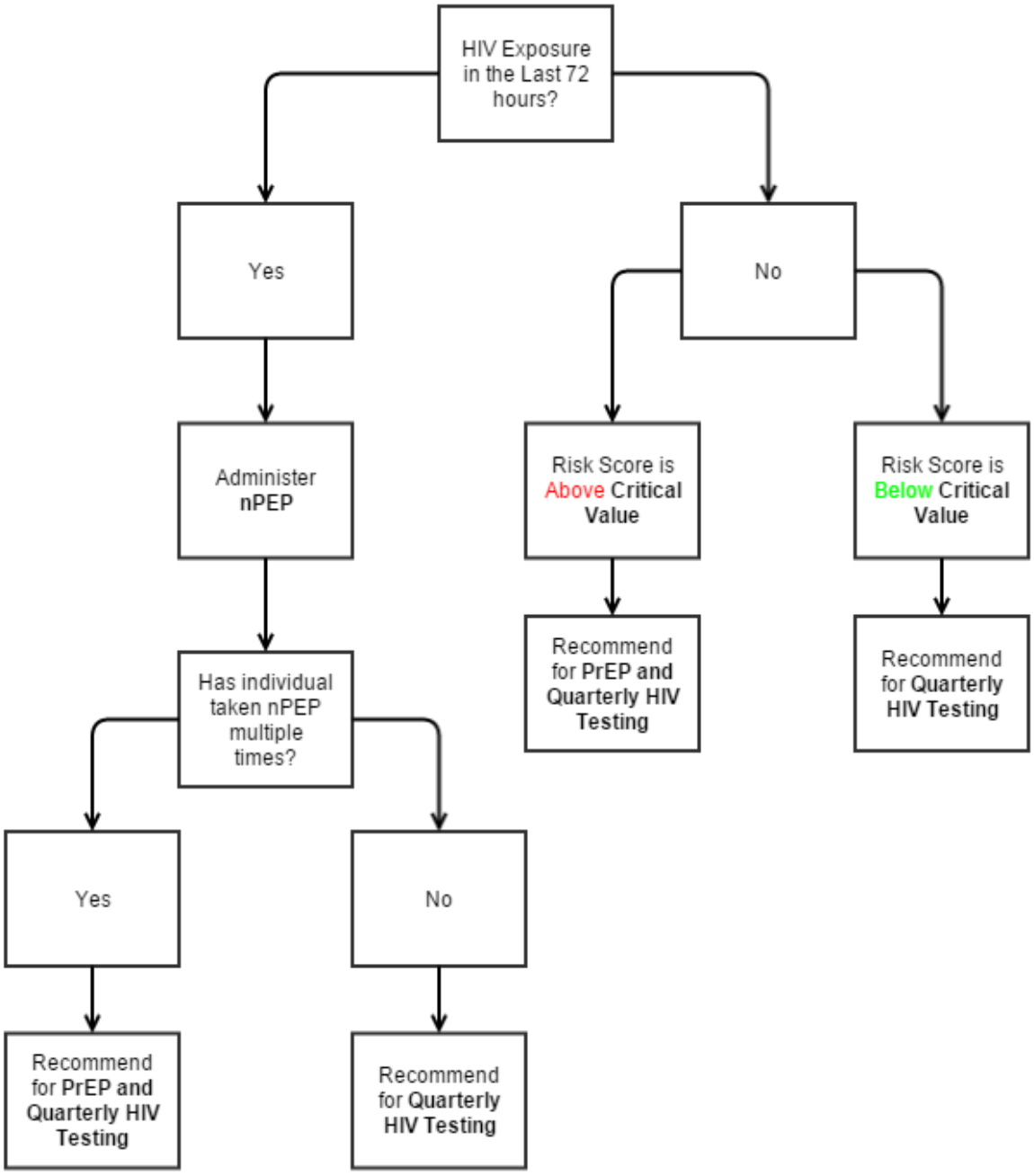
While Aim 1 provides a quantifiable and standardized HIV risk score, it does not identify appropriate interventions that the LA LGBT Center staff might recommend to each client given this HIV risk score. The goal of Aim 2 is to use this HIV risk score to identify appropriate behavioral and/or biomedical interventions for clients. The following research question will be investigated to fulfill this aim:

1. What are the most appropriate cut-points in HIV risk score to determine the differences in allocation of PrEP, nPEP, and frequent HIV testing?

As discussed in Aim 1, behavioral interventions alone have had a limited impact on HIV incidence. However, novel biomedical interventions such as PrEP and nPEP have been shown to be viable alternatives. Furthermore, the acceptability and feasibility of these interventions has greatly increased over the past five years.

PrEP is a daily course of an HIV medication taken year-round by HIV-negatives to reduce their chances of contracting HIV. While this has been shown to be efficacious, it is most appropriate for individuals at consistently high risk of HIV infection (e.g., commercial sex workers, gay men with multiple partners) since it involves daily dosing. Provided an individual is adherent to the medication, the iPrEx study showed that an individual's chances of HIV infection were reduced by up to 95% (Grant et al. 2010).

Figure 2.2 - PrEP, nPEP, and Frequent HIV Testing Decision Tree



For those at lower risk of HIV but still with intermittent exposure, nPEP may be an effective alternative. nPEP, also known as the morning-after pill for HIV, is a 28-day course of an HIV medication that can be taken by an HIV-negative person after a risky sexual event to greatly reduce the chances of HIV seroconversion. Since each 28-day course is taken separately,

as opposed to year-round, this biomedical intervention may be most appropriate to those at moderate risk for HIV. As with PrEP, medication adherence is tied directly to the efficacy of the nPEP course.

Lastly, individuals who report little to no risk (e.g., individuals who report they are monogamous in a relationship) may just need frequent testing for HIV. Even if an individual reports no risk behaviors in a monogamous relationship, their partner may contract STIs or HIV from external sources (i.e., the client may be monogamous but the partner may not be faithful). Therefore, individuals in the low risk category for HIV still need to be tested intermittently, but biomedical interventions such as PrEP and nPEP may not be necessary.

In summary, PrEP and nPEP may not be ideal for each person when considering their risk profile. Aim 2 is important because it ensures that resources are used effectively and in line with an individual's actual risk for HIV.

Aim 3 – Assess Circumstances for HIV Infection among At-Risk Subgroups

Among the 50,000 new HIV infections per year in the US, the highest incidence is in African-American and Hispanic men under the age of 25 (CDC 2014a). While risk factors have been explored for White MSM, there are few studies that investigate the risk factors for HIV infection within these subgroups. The goal of Aim 3 is to determine if different circumstances lead to HIV infection among African-American MSM, Hispanic MSM, and young MSM. The following research questions will be investigated to fulfill this aim:

1. Is there a difference in the relationship between biological, sexual behavioral, and/or substance use variables and HIV infection for African-American MSM when compared to White MSM?

2. Is there a difference in the relationship between biological, sexual behavioral, and/or substance use variables and HIV infection for Hispanic MSM when compared to White MSM?
3. Is there a difference in the relationship between biological, sexual behavioral, and/or substance use variables and HIV infection for Young MSM (defined as individuals under the age of 25) when compared to Older MSM (defined as individuals 25 years of age and older)?

As outlined in the introduction, African-American and Hispanic MSM experience significant health disparities in HIV incidence in the United States. African-American individuals experience rates of HIV infection higher than any other demographic group, and Hispanics have a 50% greater incidence of HIV when compared to White, non-Hispanic MSM (Hall et al. 2005, Duran et al. 2010). Furthermore, studies by Prejean et al. (2011) and Pathela et al. (2011) have shown that HIV rates in minority MSM between the ages of 13 and 29 have increased substantially in recent years. In comparison, HIV rates have decreased among White MSM. Despite the high rates of HIV infection among these subgroups, there are few analyses focused solely on these subgroups due to sample size (Menza et al. 2009). Therefore, Aim 3 is important because it will increase understanding of HIV infection in the most heavily affected subgroups of MSM. Chapter 3 will next discuss the theoretical background for this dissertation which will ultimately inform variable selection for the aforementioned aims.

Chapter 3 – Theoretical Background

Numerous cognitive and ecological theories have been adapted and created to explain the HIV epidemic. Chapter 3 first describes the Information-Motivation-Behavioral Skills (IMBS) model, a cognitive theory which has been widely used over the past 20 years to explain HIV infection among gay, bisexual, and other men who have sex with men (MSM). The discussion of IMBS concludes with a review of the application and limitations of IMBS in the literature. These limitations will show that the use of IMBS is not appropriate for this dissertation due to its narrow focus and lack of recognition of non-cognitive constructs. While IMBS will not be used for the analysis of this dissertation, it remains the main cognitive model in the HIV literature and warrants discussion for background purposes only.

Chapter 3 then defines and discusses Syndemics Theory (ST) which has been increasingly utilized as an ecological theory to describe HIV transmission patterns within the MSM population. The application of ST in the literature is reviewed followed by the strengths and limitations of the theory. Lastly, the theoretical framework utilized for this dissertation will be discussed along with the rationale for subgroup analyses.

Information-Motivation-Behavioral Skills Model

The Information-Motivation-Behavioral Skills (IMBS) model was originally developed by Fisher & Fisher (1992) following the observation that HIV prevention interventions up to that time were atheoretical and lacked targeting of certain groups at enhanced risk for HIV infection (e.g., intravenous drug users, MSM). The model consists of three constructs that the authors argue can be used to explain HIV risk reduction in numerous populations: 1) information about how to reduce HIV risk, 2) motivation to reduce HIV risk, and 3) behavioral skills for performing HIV risk reduction (Fisher & Fisher 1992) (Figure 1).

Figure 3.1 - Information-Motivation-Behavior Skills Model (adapted from Fisher & Fisher 1992)

Information Construct

According to Fisher & Fisher (1992), the information construct refers to both knowing how HIV is transmitted (e.g., unprotected intercourse) as well as ways to prevent HIV transmission (e.g., condom use). However, they opine that "information alone is not sufficient to motivate [HIV]-preventive behavior," (Fisher & Fisher 1992), and the authors cite numerous studies among gay men that have found an ambiguous relationship between HIV information/ knowledge and prevention (Emmons et al. 1986, Kegeles et al. 1986, Kelly et al. 1990, McKusick et al. 1987). Furthermore, they cite a "ceiling effect" in which baseline knowledge of HIV is so high in certain populations that the knowledge-prevention relationship may be difficult to measure. The authors argue that information is ultimately a necessary, but not a sufficient, component of HIV prevention.

Motivation Construct

The motivation construct was adapted directly from Fishbein & Ajzen's (1975) Theory of Reasoned Action. In the context of HIV, motivation refers to both personal attitudes toward HIV

prevention behavior and perceived normative support (i.e., social norms) (Fisher & Fisher 1992). Perceived normative support can influence motivation for condom use either positively (e.g., prevention behavior is valued within a given sexual network) or negatively (e.g., suggestion of using a condom indicates that the person is sexually risky).

Fisher & Fisher (1992) hypothesize that the motivation construct influences, and is influenced by, the information construct. More specifically, an individual who has increased knowledge of HIV transmission and contraction is more likely to be motivated towards HIV prevention behavior. Conversely, an individual with heightened motivation is more likely to seek out more knowledge on how to prevent HIV. The authors also hypothesize that motivation independently influences HIV prevention behavior as well as the behavioral skills for attaining these behaviors.

Behavioral Skills Construct

Although Fisher & Fisher (1992) hypothesize that information and motivation can act independently to influence HIV prevention, these constructs mainly "activate behavioral skills" that lead to a reduction in HIV risk behavior. These behavioral skills can refer either to behaviors that occur immediately prior to sex, like self-efficacy for condom use, or to behaviors that occur more distally to the sexual encounter, like avoiding drinking or substance use prior to having sex, purchasing condoms, or screening/treatment for STIs.

However, the authors caution that "research should first be performed to ascertain those universal and group-specific behavioral skills that are both necessary for [HIV] prevention and lacking in that population." While the IMBS model is meant to span numerous populations at risk for HIV (i.e., the "universal"), the authors explicitly acknowledge that population-specific ecological factors (i.e., the "group-specific") are important to understand in the formulation of

any theoretical model. Therefore, the IMBS model is mainly individual in focus, but the authors acknowledge that additional components are needed based on the population under study to account for additional ecological factors that may influence HIV infection.

Application of Theory

Fisher & Fisher (1992) tested their results using separate structural equation models for gay men and university students. In addition to testing these models at baseline, they also tested the models at two months follow-up. Among gay men, 35% of the variance was explained by the model. Behavioral skills were significantly related to HIV prevention behavior at both baseline and two months of follow-up. However, information and motivation were not significantly related to HIV prevention, nor with each other, at two months of follow-up.

Among university students, 10% of the variance was explained by the model. Behavioral skills were significantly related to prevention behavior at both baseline and follow-up. However, motivation was not related to prevention behavior at baseline but was associated with prevention behavior at follow-up. Furthermore, information was not related to HIV prevention behavior at either baseline or follow-up.

The study had several limitations. The first limitation was a small sample size for each group under study (n = 91 for the gay sample; n = 174 for the university student sample). The second limitation was that it was not clear if the sample was randomly selected or a convenience sample. Lastly, it was unclear what proportion of the sample was sexually active and thus who was at high-risk. However, this seminal study demonstrated that the significance of each construct at both baseline and follow-up was very different based on the population under study.

In the first independent analysis of the model among gay men (n = 391), Kalichman et al. (2008) measured constructs within the IMBS model at baseline and four months follow-up for individuals who reported unprotected anal intercourse with non-primary partners. Unlike the original test of the model by Fisher & Fisher, the sample size and inclusion criteria were explicitly stated. The authors showed that while there was empirical support for the motivation and behavioral skills constructs, the information construct did not lead to a reduction in unprotected anal intercourse with non-primary partners at follow-up. The study had a key flaw in that it was not clear how information was operationalized, and thus differing modalities for operationalization may lead to different results.

Coleen Fisher (2012, no relation to Fisher & Fisher) tested the IMBS model among adolescent, gay and bisexual males (n = 156) but added alcohol, substance use, and numerous variables involved in sexual identity development to the model. The author found that 35% of the variance was explained by these predictors with information acting as a significant predictor of HIV prevention. Unlike the studies by Kalichman and Fisher & Fisher, this study included specific ecological variables relevant to adolescent, gay, and bisexual males. While ecological variables were originally proposed by Fisher & Fisher, their analyses did not actually include these variables. A second key difference was that C. Fisher found a significant relationship between information and HIV prevention. However, the information-HIV prevention relationship in this study may be overstated considering that the sample studied was between 14 and 21 years of age and still acquiring sexual knowledge. Regardless, C. Fisher showed that the relationship between the constructs may be different for adolescent MSM when compared to the previous studies that just looked at adult MSM.

The IMBS model has also been applied to the prevention of transmission by HIV-positive persons. HIV medication adherence lowers an HIV-positive person's infectiousness and is thought to be a critical component of HIV prevention. Horvath et al. (2014) showed that while the model was robust in predicting HIV medication adherence among non-substance users, information was not associated with behavioral skills among substance users. Therefore, constructs differed in importance based on if the HIV-positive person reported substance use. This finding once again suggests that the population under study is an important component to consider in evaluating construct applicability.

These studies demonstrate two key themes. First, the specific MSM group under study is important to understand given the varying importance of constructs. Second, constructs beyond information, motivation, and behavioral skills may need to be explored in evaluating HIV risk given the importance of sexual identity development variables, substance use, and alcohol use. These additional constructs may include biological constructs (e.g., prior STIs), behavioral constructs (e.g., condom use during anal sex), and demographic constructs (e.g., race/ethnicity).

Due to the limitations of IMBS, it is presented for background purposes only and will not be utilized in the analysis for this dissertation. While not explicitly based on the IMBS model, Syndemics Theory was created in order to more comprehensively address the ecological aspects that may lead to HIV and will serve as the theoretical foundation of this dissertation.

Syndemics Theory

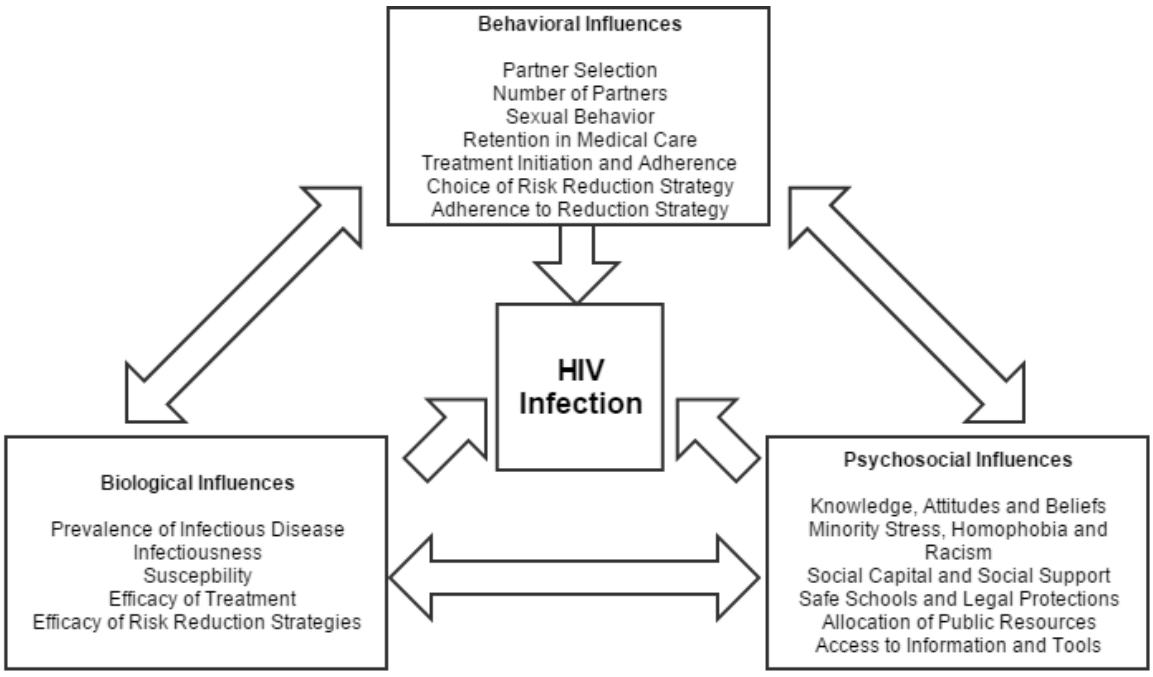
Like the IMBS model, Syndemics Theory (ST) was developed specifically to address HIV prevention. However, ST is distinct from the IMBS model in that it aims to describe HIV prevention specifically among MSM populations. Secondly, instead of claiming that the process

involved only three individual cognitive constructs as is the case with the IMBS model, Singer claimed that the HIV epidemic was both individually and ecologically driven (Singer 1994).

Singer proposed that the HIV epidemic was particularly virulent because it was reinforced by two other epidemics: mental health and substance use. More specifically, discrimination in sexual and racial minority communities leads to poor mental health resulting in elevated substance use to cope with the poor mental health outcomes. These behaviors collectively influence risky sexual behavior which lead to a greater incidence of HIV (Singer 1994). Since HIV predominantly affects the most marginalized in society, Singer argued that mental health (subsequently referred to as "psychosocial issues") and substance use epidemics were synergistically reinforcing the HIV epidemic to form a "syndemic."

Halkitis and colleagues would later use this seminal paper as the basis for the formation of Syndemics Theory (Halkitis et al. 2010). In addition to the original constructs, Halkitis would add a third biological construct to hypothesize a total of three constructs that lead to HIV contraction: 1) biological, 2) behavioral, and 3) psychosocial/structural (Figure 3.2).

Figure 3.2 – Syndemics Theory (adapted from Halkitis 2013a)



Biological Construct

The biological construct includes biological variables that lead an individual to be either more susceptible to HIV transmission or contraction depending on their HIV status. Among the biological influences, Halkitis et al. (2013a) list five variables that are biologically influential: 1) prevalence of infectious disease, 2) infectiousness, 3) susceptibility, 4) efficacy of treatment, and 5) efficacy of risk reduction strategies.

Prevalence is an intuitive way to operationalize the biological construct in that individuals are more likely to contract HIV in areas with a higher prevalence of the virus. The number of individuals infected with HIV is directly proportional to the risk for HIV contraction within a given sexual network (Hall et al. 2013).

Susceptibility is equally important and can be operationalized through either the type of sex act or the infection with STIs. Studies have shown that those who exclusively assume the receptive anal role are at a greater risk for HIV than those who exclusively assume the insertive

anal role due to micro-tearing of the anal cavity (Baggaley et al. 2010). Micro-tearing causes local inflammation which leads to the migration of immune cells to the area. These immune cells then serve as convenient hosts for HIV to infect. Secondly, HIV-negative individuals with sexually transmitted infections (STIs) other than HIV (e.g., gonorrhea, chlamydia, and syphilis) are more likely to contract HIV due to local inflammation caused by the STIs per the aforementioned rationale (Fleming et al. 1999, Millett et al. 2006, Millett et al. 2007, Pathela et al. 2011). Therefore, susceptibility can be operationalized through two events that lead to inflammation: the type of sex act in assuming the receptive or insertive role (e.g., microtearing of the anus causing inflammation) as well as the presence of gonorrhea, chlamydia, syphilis, and/or another STI.

Efficacy of treatment is a recent phenomenon and can refer to post-exposure prophylaxis (nPEP) or pre-exposure prophylaxis (PrEP) for HIV-negatives. Studies have shown that these medications either before the sex act (in the case of PrEP) or after the sex act (in the case of nPEP) can reduce the chances of HIV acquisition by up to 95% provided adequate medication adherence (Smith et al. 2005, Grant et al. 2010). Efficacy of treatment can thus be operationalized as use of either nPEP or PrEP for HIV-negatives.

Efficacy of treatment can also refer to the treatments used by HIV-positives to lower their infectiousness. More specifically, HIV-positive individuals are more successful at halting transmission of HIV biologically if they are adherent to their treatment regimen and therefore have a suppressed viral load leading to lower infectivity. Therefore, efficacy of treatment can refer to either treatments that keep an individual HIV-negative or treatments that suppress the infectiousness of an HIV-positive person.

Behavioral Construct

The behavioral construct includes variables like substance use, condom use, and other behavioral risks that have been associated with HIV contraction in this population. Halkitis et al. (2013a) specifically outline the following behavioral variables that make up the behavioral construct in HIV infection: 1) partner selection, 2) number of partners, 3) sexual behavior, 4) retention in medical care, 5) treatment initiation and adherence, 5) choice of risk reduction strategy, and 6) adherence to risk reduction strategy.

Partner selection can refer to many different characteristics of the sex partner from their demographic profile (e.g., race, age) to their HIV status (e.g., serosorting) to where the partner is found (e.g., through a bar or a geosocial networking phone app like *Grindr*).

Recent research has begun to explore how sexual networks may influence contraction of HIV. For example, numerous authors have argued that African-American individuals who have sex with other African-Americans exclusively (referred to as racially homophilous partnerships) are more likely to contract HIV due to the higher prevalence of HIV within that segment of the population (Harawa et al. 2004, Newcomb et al. 2013, Sullivan et al. 2014).

Partner selection also refers to the practice of "serosorting" where HIV-positive persons seek out other HIV-positive persons for sex and HIV-negatives seek out HIV-negatives. This concept has been proposed since the beginning of the epidemic, but the lack of frequent testing and honesty in serostatus disclosure has caused numerous researchers to be skeptical of the effectiveness of this practice (Parsons et al. 2005, Golden et al. 2008).

Lastly, partner selection could refer to the type of venue that an individual locates their sexual partners (e.g., through a bar, internet site or mobile phone app). Studies in the early 2000s found that those who use the internet to find partners were more at risk for HIV than those who met in person (Liau et al. 2006, Ng et al. 2013), and recent analyses have found that those who

use mobile phone apps may be at greater risk than other venues for partner selection (Beymer et al. 2014b). Therefore, partner selection can be operationalized through demographic profile of previous partners, serostatus of previous partners, or venue for finding previous partners.

Partner selection only refers to the *type* of partner selected and does not refer to the *frequency* of partners. It is logical to assume that the frequency of exposure is just as important as the partner type chosen as more frequent exposure may lead to greater chances for infection. Intuitively, the number of sexual partners has been shown to be an important predictor of HIV contraction (Buchbinder et al. 2005). Previous studies have most commonly operationalized the number or sexual partners by looking at both the number of partners in the last thirty days as well as the last three months.

The type of sexual behavior can refer to behaviors both prior to sex (e.g., substance use) as well as behaviors during sex (e.g., condom use). For example, individuals who use drugs like methamphetamine (meth) prior to sex are at a higher risk for HIV than individuals who abstain from meth use (Buchacz et al. 2005, Plankey et al. 2007). Furthermore, Mansergh et al. (2001) have shown that the number of drugs is just as important as the type of drugs used (Plankey et al. 2007, Ostrow et al. 2009). Condom use displays an individual's choice/adherence to a risk reduction strategy. While condoms may be used with one type of sex act, they may not be used with another. Therefore, consistency of condom use is important to analyze for each type of sex act. In summary, type of sexual behavior can therefore be operationalized through multiple variables: type of substances used, number of substances used, and condom use for each type of sex act.

Retention in medical care, treatment initiation, and medication adherence collectively refer to characteristics that apply mainly to HIV-positive persons. Both HIV treatment initiation

and medication adherence lower an HIV-positive person's viral load and decreases their level of infectivity to HIV-negative partners. Retention in care ensures that their viral load is monitored and medications are adjusted as needed. Medication adherence can also refer to individuals who take nPEP or PrEP. As stated in Chapter 1, medication adherence is important as it directly impacts the success of the interventions. Therefore, while retention in medical care and treatment initiation refer to HIV-positive persons, medication adherence can refer to either HIV-positive or HIV-negative persons.

Psychosocial and Structural Construct

The psychosocial construct contains numerous variables from national legal protections (structural) to internalized homophobia (psychosocial). These variables include: 1) knowledge, attitudes, and beliefs; 2) minority stress, homophobia, and racism; 3) social capital and social support; 4) safe schools and legal protections; 5) allocation of public resources; and 6) access to information and tools.

Knowledge, attitudes, and beliefs closely mirror the IMBS model's cognitive constructs. More specifically, the ST's knowledge construct resembles the IMBS model's information construct and the ST's attitudes construct resembles the IMBS model's attitudes construct which is nested within the information construct. Knowledge refers to how much someone knows about HIV prevention and can be operationalized in numerous ways including knowing how HIV is transmitted and the physical presentation of an HIV-positive person (e.g., "men who look clean don't have HIV"). Attitudes and beliefs can refer to attitudes/beliefs about physical prevention methods like condoms, biomedical prevention methods like PEP/PrEP, or behaviors linked to risky sex like drug and alcohol use.

For predictors like discrimination and internalized homophobia, Halkitis et al. (2013a) openly admit "the literature on the association between HIV risk and discrimination and internalized homophobia has yielded a complex and contradictory pattern of findings." Other variables within this construct such as minority stress have yielded much more consistent findings (Meyer et al. 2003, Meyer et al. 2010). There may be different circumstances for HIV infection between different racial/ethnic groups as well as different age groups among MSM. For example, African-American MSM are more likely to report condom use and less likely to report substance use when compared to their White counterparts (Koblin et al. 2006, Millett et al. 2006, Millett et al. 2007). Similar to the IMBS, each risk may have a different relationship with HIV prevention given the racial/ethnic group or age group under study.

Social capital and social support literature has been evolving and shows important associations across an array of health behaviors, but a meta-analysis published in 2014 revealed mixed results among MSM at risk for HIV (Qiao et al. 2014). Safe schools, legal protections, allocation of public resources, and access to information and tools are macro-level variables that also intuitively contribute to the contraction of HIV, but the public health literature on these variables is less robust.

Application of Theory

Syndemics Theory has been successfully applied to numerous groups within the gay and bisexual populations including MSM across the US (Stall et al. 2003), young MSM (Mustanski et al. 2007), African-American MSM (Ayala et al. 2012), and MSM in China (Jie et al. 2012). A majority of these studies have been cross-sectional in nature, but cohort (Koblin et al. 2006) and latent class modeling (Halkitis et al. 2013b) studies have also been conducted.

In one of the seminal studies of Syndemics Theory, Stall et al. (2003) showed that substance use (OR: 2.2; 95% CI: 1.7-2.8) and intimate partner violence (OR: 1.5; 95% CI: 1.2-1.9) had a significant association with, and an additive effect on, HIV seroconversion. In addition, the number of psychosocial health problems had a significant relationship with HIV. However, the relationships between HIV infection and either depression or childhood sexual abuse were not statistically significant.

Mustanski et al. (2007) showed that the number of psychosocial problems also additively increased the risk for HIV infection among young MSM. Among 310 young MSM, each additional psychosocial problem increased the odds of an HIV-positive status by 42%. In addition, multiple anal sex partners (OR: 4.46; 95% CI: 1.91-10.37), unprotected anal sex (OR: 3.52; 95% CI: 1.82-6.82), substance use (OR: 2.33; 95% CI: 1.19-4.59), and intimate partner violence (OR: 2.11; 95% CI: 1.06-4.21) showed strong relationships with HIV infection. Therefore, this study further verified the findings of Stall et al. (2003) in young MSM but also showed the importance of multiple partners and unprotected sex.

Koblin et al. (2004) found similar results in their longitudinal analysis, showing that number of sexual partners (attributable risk (AR): 32%) as well as alcohol and substance use prior to sex (29%) had the highest levels of attributable risk. Furthermore, their sample was heterogeneous enough to detect differences based on race, showing that African-American men were less likely to report unprotected anal intercourse (hazard ratio (HR): 0.5; 95% CI: 0.4-0.62) and four or more partners (HR: 0.73; 95% CI: 0.6-0.88).

While numerous variables have shown a consistent relationship with HIV incidence (e.g., substance use prior to sex and intimate partner violence), other variables have differing importance based on the population studied (e.g., unprotected intercourse is more prevalent in

Whites than African-Americans). Similar to the IMBS model, the constructs within the ST have differing influences based on the group under study. While each model presented has strengths, there are numerous limitations to consider.

Limitations to Presented Theories

The IMBS model and ST both present key constructs involved in the contraction or prevention of HIV within the MSM community, but each has important limitations. The IMBS mainly focuses on the individual cognitive variables that lead to HIV prevention. While these constructs may all show a relationship to HIV prevention at baseline, results at follow-up have shown conflicting results. In the original study by Fisher & Fisher (1992), neither information nor motivation was significantly related to HIV prevention behavior at follow-up. In the study by Kalichman et al. (2008), motivation and behavioral skills were significantly related to HIV prevention behavior at follow-up but information was not significantly related to HIV prevention behavior. The lack of a relationship between information and HIV prevention may be because there is a ceiling effect with information or there may be "prevention burnout" where individuals hear messages so many times that the intent no longer resonates. The first limitation is that the behavioral skills construct is the only construct that has been shown to be consistently related to HIV prevention behavior at follow-up.

The second limitation of the IMBS model is that variables beyond these three constructs (e.g., substance use) have been incorporated into this model and shown robust results (Fisher C. 2012). Given these findings, the three constructs in the original model may be too narrow in focus. Therefore, the utility of both information and motivation constructs are limited and ecological variables beyond the original three constructs may be important.

In contrast to the IMBS model's cognitive focus, the ST has an ecological focus. While the focus may be more comprehensive, the model still has numerous limitations. These limitations include 1) the psychosocial category is ambiguous in its operationalization in the original model, 2) many variables explicitly mentioned in the original model have been unsupported or inconsistently supported by the literature, 3) the relationships between the three constructs are poorly defined in the original model, and 4) the relationship between the three constructs and the five "Syndemic Health Problems" in the Venn diagram are also not clear.

Despite the limitations of Syndemics Theory, the "Knowledge, Attitudes, and Beliefs" component of the Syndemics Theory closely mirrors the constructs within IMBS. Therefore, although Syndemics Theory has an ecological focus, it also has a cognitive component.

Although both theories have limitations, IMBS is much narrower and does not incorporate many predictors of HIV infection among MSM such as substance use, number of partners, or the networks of sexual partners. In contrast, Syndemics Theory acknowledges both the cognitive and ecological aspects of HIV infection. Syndemics Theory will be exclusively used as the theoretical framework for this dissertation, and IMBS will not be referenced in subsequent sections. Chapter 4 will next discuss the background literature of HIV among MSM and outline the variables that have been shown to be significantly related to HIV seroconversion.

Chapter 4 – Background and Literature Review

Numerous risk factors contribute to HIV infection within the MSM communities of the United States (US). This chapter will review the existing research on the three constructs (biological, sexual behavioral, and substance use) outlined by Syndemics Theory as relating to HIV infection among MSM. Chapter 4 will then discuss the limitations of the variables studied in the literature as well as summarize the overall findings.

Biological Variables

Biological variables make up the first construct that affect an individual's chance of being infected with HIV. The following section demonstrates how the presence of sexually transmitted infections (STIs), type of sex act, and serosorting correlate with contracting HIV.

Current Diagnosis or History of Sexually Transmitted Infections

Both ulcerative and non-ulcerative STIs are associated with the contraction of HIV. Ulcerative STIs (e.g., syphilis) are characterized by open lesions on the genitals and/or anus whereas non-ulcerative STIs (e.g., gonorrhea and chlamydia) are not as damaging to the outer skin layer but lead to tissue sensitivity. This sensitivity leads to increased susceptibility to tearing and bleeding. If infected with either type of STI, an inflammatory response is initiated by the body, and T cells from the immune system migrate to the area of infection. These T cells then become prime targets for HIV to infect (AIDSMap 2014). The inflammatory response caused by STI infection increases an individual's chances for HIV infection.

A meta-analysis by Fleming et al. (1999) found that MSM with infections of *Treponema pallidum* (syphilis) and/or *Neisseria gonorrhoeae* (gonorrhea, NG) had 2.3 to 5.2 greater odds of HIV infection than MSM without these STIs. When analyzing rectal infection with NG or *Chlamydia trachomatis* (chlamydia, CT), Bernstein et al. (2010) found an eight-fold increased

risk of HIV infection among MSM who had a history of two or more instances of either NG or CT. Another study by Pathela et al. (2013) found that the HIV incidence of MSM in New York with either an NG or CT rectal infection was 6.7%, a rate significantly higher than the 2.5% HIV incidence rate among MSM who did not contract either an NG or CT rectal infection. An association has also been proposed between Herpes Simplex Virus Type 2 (HSV2) and HIV, but in three of four studies that analyzed this association in this meta-analysis, the confidence interval straddled the null, indicating a non-significant relationship between HSV2 and HIV. However, a 2010 study by Jin et al. (2010) found a 7-fold greater odds of HIV contraction for MSM with rectal NG and 3-fold greater odds of HIV contraction for MSM with HSV2. Therefore, there seems to be a consistent association between HIV and syphilis, NG, and CT. However, the link between HIV and HSV2 may be more tenuous given the different study findings presented.

Presence of STIs is one of two consistent links to HIV among African-American MSM. In two meta-analyses by Millett et al. (2006, 2007), STIs and delayed diagnosis of HIV infection were the only consistent variables that contributed to the higher incidence of HIV in African-American MSM when compared to White MSM. While the prevalence of STIs is important to consider in a sexual network, susceptibility to STIs and HIV can largely depend on sexual positioning and the type of sex act.

Type of Sex Act

Sexual positioning plays an important role in chances for HIV infection. MSM who exclusively engage in unprotected receptive anal sex (URAI), known as "bottoms," are at the highest risk for HIV contraction when compared to MSM who exclusively engage in unprotected

insertive anal sex (UIAI, MSM known as "tops"), MSM who engage in both bottom and top roles ("versatile"), and/or MSM who only engage in oral sex.

A meta-analysis by Baggaley et al. (2010) of 16 studies determined the per-act risk of sexually transmitting HIV through anal intercourse. Researchers found that the overall per-act chance of transmission was 1.4%. This analysis also presented estimates on a per partner basis over a span of 1,000 sex acts. The authors found that individuals who participated in UIAI exclusively had a risk of 21.7% over 1,000 sex acts versus those who participated in URAI exclusively had a risk of 40.4%.

Although MSM who engage in URAI exclusively are at greater risk of HIV contraction than MSM who engage in UIAI exclusively, the prevalence of each type of sexual act differs with certain factors. In the EXPLORE study, Hong-Van et al. (2013) found that 9.6% of HIV-negative MSM in their sample were exclusively anal receptive partners, 16.7% were exclusive insertive partners and 73.7% practiced both insertive and receptive sex with partners. Researchers also found that MSM with an exclusive receptive role were most common among substance users and younger men. Therefore, while receptive anal sex carries the greatest risk, this study demonstrates that only a small proportion of MSM assume an exclusively receptive role. The last biological factor that may bear impact on an individual's chances of HIV infection is a process known as serosorting.

Serosorting

HIV serosorting is a risk reduction technique where MSM have UAI only with partners of the same serostatus (e.g., HIV-positive MSM only have sex with other HIV-positive MSM). In a study by Truong et al. (2006) among San Francisco MSM between 1998 and 2004, researchers found that while rates of STIs increased each year, the HIV epidemic stabilized from

2000 to 2004. Researchers claimed that serosorting may account for the trend of stable HIV incidence and increasing STI incidence among MSM in San Francisco.

Other studies have attempted to debunk serosorting as an effective HIV prevention tool. Golden et al. (2008) analyzed STI data from 2001 to 2007 at a Seattle clinic and defined the percentage of visits where an HIV diagnosis was given and serosorting was reported. Researchers found that 32% of new infections occurred among HIV-negative MSM who claimed they were serosorting. Golden et al. (2012) conducted another serosorting study comparing White, African-American, and Hispanic MSM using data from 2001 to 2010. Researchers found that there was no difference in HIV infection between MSM who claimed they were serosorting and those who reporting no serosorting behavior for African-American and Hispanic MSM. However, there was a difference among Whites with individuals who reported serosorting having a lower HIV incidence than individuals who did not report the behavior. Given these cultural differences, there may be other serosorting differences by age, acculturation, and other factors that should be studied further in the MSM context.

It is easy to understand why the findings between Truong and Golden are mixed. The first reason is that people may be dishonest to potential sexual partners about their HIV status. The second reason is that MSM may regularly be tested for HIV, but they were infected in an encounter between HIV testing visits or may have received a false negative HIV result during the window period (i.e., where they were actually HIV-positive, but the test was not able to detect the virus since they were recently infected). As Eaton et al. (2009) opines, "[it] is nearly impossible for persons who engage in high risk behaviors to ever be certain of their HIV status in part because they do not test often enough." Therefore, the practice of serosorting can be flawed for these reasons and partially explains the differences in findings.

Sexual Behavioral Variables

Just as important as the biological components of HIV infections are the behaviors that contribute to HIV infection. *Where* an individual finds sexual partners, *who* an individual has sex with, and *how many times* they have sex with these partners are all important behaviors to consider in correlation with HIV infection. Lastly, the physical and emotional power dynamics within a sexual relationship can further determine an individual's sexual positioning, whether or not condoms are used, and can have significant effects on mental health. These predictors collectively form an individual's sexual network and play an important role in HIV contraction.

Venue for Finding Sex Partners

The first component of an individual's sexual network is the method they use to find sexual partners. Due to the high level of stigmatization historically experienced by the MSM community, the nature of sexual encounters has often trended towards anonymous liaisons in furtive locations designed specifically for sexual encounters. These meeting places included public cruising areas (PCAs), T rooms, and bathhouses and were initially treated equally as a proxy for risk behavior (McKusick 1985). Binson et al. (2001) found that individuals who reported illicit substance use and had frequent unprotected anal intercourse (UAI) were more likely to visit sex venues than individuals who did not use drugs or report frequent UAI.

However, PCAs, T rooms and bathhouses do not necessarily carry the same amount of risk. Binson showed that MSM who went to PCAs were less likely to have risky sex when compared to MSM who frequented bathhouses. A study among bathhouse attendees by Van Beneden et al. (2002) found that individuals who reported UAI were more likely to be HIV-positive and have more than four sex partners in the past 30 days than individuals who did not report UAI.

In the last ten years, the high-risk trends associated with these venues have slightly waned. A more recent study by Binson et al. (2010) showed that although 14% of bathhouse attendees admitted to unprotected anal intercourse (UAI) during their last visit, a majority of these individuals did not ejaculate inside their partners, a possible risk reduction strategy for HIV prevention. While it may seem that risky behaviors are less prevalent, the unwavering HIV rate may indicate that the risk for HIV has merely shifted to other venues.

In the mid to late 1990s, MSM began to utilize the internet to locate anonymous partners. Gauthier and Forsyth (1999) explained a concept known as "barebacking" where HIV-negative individuals use the internet to actively look for intentional unsafe sex with HIV-positive partners. A study by Halkitis et al. (2010) among a convenience sample of individuals who used a popular barebacking site found that over 43% of the HIV-positive MSM surveyed had sex with a partner of unknown serostatus in the past three months. Researchers argue that the internet has provided the forum for like-minded individuals to meet, thus creating a concentrated number of those looking for sexual adventurism. This sexual adventurism may have shifted from communal bathhouses to individual encounters facilitated via niche internet sites.

In addition to sexual adventurism niches, the internet also affords MSM the opportunity to increase their *frequency* of sexual encounters. Websites like *Adam4Adam*, *Manhunt*, *Dudesnude*, and even *Cragislist* are specifically tailored to obtaining a high frequency of geographically-convenient sexual partners. A meta-analysis by Liau et al. (2006) showed that MSM who used the internet to locate sexual partners were more likely to have UAI with partners when compared to individuals who used offline methods (OR: 1.68; CI: 1.18–2.40). Another study by Ng et al. (2013) found that among 5,925 MSM cases of syphilis diagnosed between 2004 and 2008, 36% used the internet to locate sexual partners, and MSM who used the internet

to meet sexual partners had an average of 9.8 partners in the past six months compared with an average of five partners for MSM who met partners via other methods.

In 2009, Rosser et al. (2009a) used results from the Men's Internet Sex Study (MINTS) to show that risk of UAI substantially increased for online partners when compared to offline partners. In an analysis of Hispanic MSM within the MINTS cohort, Rosser (2009b) reported that Hispanics had UAI with almost twice as many men first met online compared to offline. Rosser concluded, "…efficiency appears the primary risk associated with meeting partners online" (Page 746).

In the past five years, MSM have increasingly turned to geosocial networking apps like *Grindr, Scruff, Jack'd,* and *Recon* to increase their number and efficiency of sexual liaisons. In a study of HIV-negative sexual health clinic attendees, Beymer et al. (2014b) showed that individuals who used geosocial networking apps had increased odds of gonorrhea and chlamydia when compared to those who met partners in person, but no association was shown with use of these apps and HIV. However, this is only one study and future studies need to examine the longitudinal risk of using these apps with HIV.

Just as important as *how* an MSM finds a prospective sexual partner is *who* the individual ends up finding for a sexual liaison. As discussed in the introduction, HIV disproportionately affects MSM compared to the general population. However, there are further disparities by demographic factors such as race/ethnicity and age group.

Race/Ethnicity of Sexual Partners

According to the CDC (2014a), the rate of HIV infection is eight times higher in African-Americans and three times higher in Hispanics when compared to Whites. Furthermore, there are higher rates of infection among young MSM when compared to older MSM which may be

accounted for by increased social vulnerability and fewer safe sex negotiation skills when compared to older peers. Due to higher incidence and prevalence of HIV within these racial and age subsets of MSM, researchers have posited that the age and race of an individual's sexual partner may be an important determinant in HIV infection.

In a seminal study of Los Angeles MSM, Bingham et al. (2003) found that partner age and partner race partially accounted for differences in HIV incidence between African-American and White MSM. In a study of young African-American MSM, Newcomb et al. (2013) found that there was a significant interaction between subject's age and having risky sex with older partners. Mustanski et al. (2013) opined that this subject deserved greater attention in studying these associations given the paucity of current evidence. Few studies have looked at this association, and it may provide useful insights into comprehensively addressing the HIV epidemic among MSM. In addition to the venue for locating partners as well as the demographic attributes of partners, the *frequency* of exposure is another important component in HIV incidence.

Number of Sexual Partners

Numerous studies have found that the number of sexual partners is an important predictor of HIV infection among MSM. Buchbinder et al. (2005) reported that the number of sexual partners had one of the highest population attributable risks of all predictors evaluated for HIV infection. Subsequent studies have verified this finding and shown that the number of sexual partners is an important predictor of HIV infection (Koblin et al. 2006, Plankey et al. 2007, Ostrow et al. 2009, Li et al. 2012, Marcus et al. 2015).

The first three sexual behavioral variables discussed have covered an individual's sexual network, but power dynamics within that network have also been explored. The last sexual

behavioral variable that will be discussed is an individual's experience of intimate partner violence (IPV) and how those experiences many impact HIV risk.

Intimate Partner Violence

IPV has only recently been studied as a potential contributor to HIV and other health disparities among MSM. Recent studies have linked IPV to substance use among White MSM (Li et al. 2012), Hispanic MSM (De Santis et al. 2014), Asian/Pacific Islander MSM (Tran et al. 2014) and African-American MSM (Dyer et al. 2012, Wu et al. 2015). IPV has also been associated with having unprotected sex in MSM (Buller et al. 2014). However, few studies have analyzed the specific link between IPV and HIV seroconversion.

Stall et al. (2003) conducted a cross-sectional study in 2003 to determine if psychological traumas like depression, IPV, and childhood sexual abuse increased likelihood of HIV seropositivity. The researchers found neither depression nor childhood sexual abuse were associated with HIV seroconversion; only IPV was significantly associated with HIV contraction (OR: 1.5; CI: 1.2-1.9). In contrast, Li et al. (2012) analyzed HIV testing data from 2000 to 2007 and found that although IPV was significantly associated with HIV in bivariate models (OR: 1.67; CI: 1.14-2.45), it was not statistically significant after controlling for other known HIV risk behaviors. Lastly, a study by Parsons et al. (2012) found a significant positive relationship between IPV and HIV. However, a meta-analysis by Finneran and Stephenson (2013) revealed that the operationalization of IPV has been inconsistent across studies.

Substance Use Variables

Substance use does not directly increase an individual's biological susceptibility to HIV. However, like the sexual network variables discussed previously, substance use can contribute to the riskiness of each sexual encounter. This section discusses how commonly-used drugs such as

methamphetamine (meth) and nitrates have often been associated with HIV infection through greater odds of unprotected intercourse following use. In addition to the biological and sexual behavioral constructs outlined above, substance use plays a major role in HIV contraction among MSM in the US.

Substance Use and Number of Substances Used

In a study of over 400 MSM in Chicago and Los Angeles, Carey et al. (2009) compared substance users and non-users to determine if certain substances led to risky behavior which increased the likelihood for HIV infection. Within the sample, 28.8% of individuals reported use of inhaled nitrates, 15.8% reported meth use, and 15.3% reported un-prescribed use of erectile dysfunction drugs (EDDs). Multivariate models showed that use of either EDDs and/or nitrates was significantly associated with HIV seroconversion. Carey reinforced the idea first proposed by Merrill Singer (1994) in stating that the overlapping substance use and HIV epidemics collectively formed a "syndemic" within the MSM communities (Page 1093).

In a study by Buchacz et al. (2005) in San Francisco from 2001 to 2002, 2,991 MSM were interviewed anonymously and 9.7% reported the use of amphetamines in the past 12 months. Of the 290 who reported use in the past 12 months, over 80% also reported having sex while taking the drug. Researchers found that amphetamine users were more likely to report unprotected anal intercourse (UAI) (OR: 2.3; CI: 1.8-3.0) and to have ten or more sex partners (OR: 2.5; CI: 2.0-3.3) when compared to non-users. Most strikingly, the HIV incidence within the amphetamine using subset was 6.3% per year, three times the 2.1% HIV incidence found in the non-amphetamine using population of MSM.

Buchbinder et al. (2005) found a similarly deleterious association between inhaled nitrates and HIV. In a multivariate analysis, researchers found that nitrate use and number of

sexual partners had the greatest population-attributable risk of all the significant factors, with nitrate users having a greater odds (OR: 2.2; CI: 1.4–3.7) of HIV contraction when compared to similar individuals who did not report nitrate use.

In addition to the type of substance used, the *number* of substances used is an important predictor of HIV acquisition. In a study conducted among circuit party attendees in the MSM community, Mansergh et al. (2001) were able to show that as the number of drugs increased, so did the odds of UAI (OR: 1.25; CI: 1.06-1.47). Compared to MSM who abstained from using either EDD drugs or meth, Fisher et al. (2011) found that users who took either drug alone or both in concert had a higher risk for syphilis, Hepatitis C, and HIV.

In a study of MSM enrolled in the Multicenter AIDS Cohort Study (MACS), researchers found that after adjusting for covariates, the relative hazard of meth use on HIV seroconversion was 1.46 (CI: 1.12-1.92), and the relative hazard of nitrate use on HIV seroconversion was 2.1 (CI: 1.63-2.70). The joint relative hazard for meth *and* nitrates was 3.05 (CI: 2.12-4.37) (Plankey et al. 2007).

In another MACS study, researchers found that individuals who used all three drug types studied (nitrates, stimulants, and EDDs) had the greatest risk of acquiring HIV (Hazard Ratio: 8.45; CI: 2.67-26.7) when compared to individuals who used only one substance or those who identified as drugs abstainers (Ostrow et al. 2009). As Ostrow opines, "any combination of these drugs dramatically raise[s] risk of HIV seroconversion over use of 1 drug alone" (Page 352).

Control Variables

The three main constructs of HIV infection have been discussed, but control variables are also necessary to rule out spuriousness between these predictors and HIV infection. The "MSM" term encompasses numerous different sexual identities including gay, bisexual, and heterosexual.

This section will discuss how risk behaviors may differ between MSM with different sexual orientations. Furthermore, the circumstances for HIV infection may be different between age and racial/ethnic subgroups of MSM given the disparate HIV burden among these groups. This section will discuss the differences in HIV infection among each subset to demonstrate the differences between these populations.

Sexual Orientation

Lyons et al. (2012) found that bisexual-identified MSM were more likely to have sex with a partner who was serodiscordant, or whose serostatus was unknown at the time of sex, when compared to gay-identified MSM. Furthermore, Brennan-Ing et al. (2014) found that bisexual men reported lower rates of unprotected sex and lower use of drugs commonly associated with HIV seroconversion (e.g., nitrates, methampethamine). Given these differences in sexual and substance use behavior, sexual orientation may be an important variable to control for in analyzing predictors of HIV infection.

Age Group

Over the past fifteen years, age of seroconversion (i.e., initially testing positive for HIV) has garnered significant attention due to increasing rates of infection among young MSM (YMSM). Prejean et al. (2011) reported that there was a 34% increase between 2006 and 2009 in rates of HIV contraction for MSM aged 13 to 29. A study by Whitmore et al. (2012) reported that individuals 13 to 24 years old accounted for nearly 26% of new cases of HIV, but this age group only accounted for 21% of the total US population.

HIV incidence disparities are further compounded in racial/ethnic minority YMSM. In a study conducted between 1994 and 1998, Valleroy et al. (2000) found that African-American YMSM (OR: 6.3; CI: 4.1-9.8) and Hispanic YMSM (OR: 4.8; CI: 3-7.6) were more likely to be

HIV infected than their White YMSM peers. In a study among YMSM by Harawa et al. (2004), researchers found that HIV prevalence was 16% for African-American YMSM, 6.9% for Hispanic YMSM, and 3.3% for Whites YMSM.

The rates of HIV in minority YMSM have only increased since these two studies were conducted. In a study by Prejean et al. (2011), the number of new HIV cases among African-American MSM increased by over 48% between 2006 and 2009. In a study among YMSM in New York City, the rates of HIV more than doubled between 2005 and 2008 (Pathela et al. 2011).

Although there are significant disparities by age group, these studies show that the HIV disparities are further compounded in racial/ethnic minority YMSM and continue to get worse. The next section will discuss how these racial/ethnic disparities in HIV infection are not necessarily confined to YMSM.

Race/Ethnicity

African-Americans bear a disproportionate number of HIV infections in the MSM community, accounting for 39% of all HIV infections per annum in MSM (CDCb, 2014). In a study of all HIV cases diagnosed throughout 29 states in 2000, Hall et al. (2005) found that, in all regions, African-Americans had the highest rates of HIV diagnoses followed by Hispanics and Whites.

African-Americans are not the only minority group that suffers a disproportionate burden of the HIV infections in the US. In a study of all CDC-funded testing sites in 2007, Duran et al. (2010) found that Hispanics had a 50% greater incidence of HIV when compared to Whites. In 2010, the CDC reported even greater disparities stating that the rates of infection among Hispanic men were more than three times the rate experienced by White men (CDCc 2014). This

disparity has been attributed to a cultural concept known as *Simpatía* which loosely translates to agreeableness in social relationships (Wilson et al. 2009). This agreeable attitude may prevent Hispanic MSM from discussing condom use with potential sex partners, potentially leading to higher rates of UAI and subsequent HIV infection when compared to their White counterparts (Lo et al. 2011).

The cultural differences between Hispanic and White MSM may lead to either differing circumstances for infection or a different effect of certain risk behaviors on HIV seroconversion. Furthermore, differences in age group may impact the focal relationship in a similar way. Therefore, potential interactions between age group and race/ethnicity may act as important predictors of HIV and have yet to be extensively explored in the literature.

Limitations to the Literature Findings

The first limitation in the literature is that studies can only reveal what variables are linked to HIV diagnosis, and not necessarily HIV infection. While HIV diagnosis and infection are similar, these two terms have an important distinction. It is estimated that about 16% of all individuals infected with HIV in the US are not aware of their HIV infection (Hall et al. 2013), but studies are not able to analyze the precursors for infection in this population since cases have not yet been identified. Therefore, the literature can only comment on the association (and not causality) between precursor variables and HIV diagnosis, and not HIV infection, despite the interchangeability of terms that may have been used in this chapter as well as throughout the dissertation.

The second limitation is how the number of sexual partners is measured. Most of the studies discussed ask about the number of partners but do not ask about the condom use with those partners. If a condom is correctly and consistently used, the number of sexual partners has

no bearing on HIV incidence. In addition, if an individual only had one sexual partner, but had sex with the individual thirty times, the number of sexual encounters instead of sexual partners becomes more important. Lastly, the number of unprotected sexual encounters should be further stratified by the type of sex act. As discussed in the section covering type of sex act, MSM who engage only in oral sex will have a risk for HIV that is virtually zero. In contrast, MSM who engage exclusively in unprotected, receptive anal sex will have the highest risk for HIV. Therefore, the literature on the number of sexual partners is limited in that it asks 1) about all sex as opposed to just unprotected sex, 2) asks about number of sex partners instead of number of sexual encounters, and 3) does not distinguish between the type of unprotected sexual act during each sexual encounter (e.g., anal sex may have been protected but oral sex was not).

The third limitation is the paucity of studies among racial, ethnic, and age group strata within the MSM community. Epidemiological evidence (CDC 2014a) shows that young MSM, and young Hispanic and African-American MSM in particular, are at the highest risk for HIV. Risk factors for HIV infection may therefore be different than for White MSM in their 30s and 40s. While the highest risk groups have been identified, there need to be further studies on what specific factors affect these groups. There needs to be further study on how age group and race/ethnicity impact the associations between the biological, behavioral, and substance use constructs and HIV infection.

The fourth limitation is the lack of studies to incorporate questions on use of biomedical interventions that impact the HIV epidemic. From a biomedical perspective, non-occupational post-exposure prophlyaxis (nPEP) began implementation in communities in 1999 (Kahn et al. 2001). Pre-exposure prophylaxis (PrEP) began implementation in 2010 (Grant et al. 2010). Both of these seminal studies showed that appropriate use of these biomedical tools will greatly reduce

HIV infection. However, few studies exist on how nPEP and PrEP impact overall HIV risk when accounting for other demographic, sexual behavioral, and substance use variables (Jain et al. 2015).

The fifth limitation is the lack of consideration of how policy changes may affect the HIV epidemic. Halkitis et al. (2012) argued that marriage equality in the US would usher in an end to the HIV epidemic among MSM when he states, "If gay men were allowed to get married, this disease would go away." Although the marriage equality movement has only occurred over the past fifteen years, studies should look at how policy changes in different jurisdictions have affected the HIV epidemic within those areas. More specifically, studies should examine how internalized and institutional homophobia has changed over time in different areas and determine if there is any association with a decrease in HIV infection. Furthermore, studies should analyze how marriage may impact multiple partnerships and determine if marriage equality is associated with greater monogamy and lower rates of HIV transmission.

Summary of Literature Findings

This chapter outlined the literature findings on the predictors that have consistently been associated with HIV infection. The literature shows three overall constructs that lead to HIV: biological, behavioral, and substance use. In addition, sexual orientation, race/ethnicity, and age groups have been explored as important control variables. Infection with STIs, type of sex act, sexual network attributes, meth use, and nitrate use, were just a few of the many variables that show a consistent link with HIV. While other variables may be linked to HIV infection beyond the variables discussed, the evidence has been either mixed or insufficient to warrant further discussion.

In addition to the discussion of key variables, numerous limitations were highlighted. These limitations include inconsistency in how the number of sexual partners is measured, the lack of specificity for risk among minority communities, and the failure of recent studies to incorporate variables on use of biological interventions like nPEP and PrEP.

While this dissertation cannot address all of these limitations, it plans to more accurately determine the circumstances for HIV within different racial/ethnic and age subsets. Furthermore, the dissertation plans to address how these risk factors can be used as a tool to determine an individual's candidacy for interventions such as nPEP and PrEP. The next chapter will discuss how data is collected at the Los Angeles LGBT Center and how the data will be analyzed to accomplish the aims of this dissertation.

Chapter 5 – Research Design and Methods

The dataset analyzed in this dissertation contains HIV testing and risk assessment data from the Los Angeles LGBT Center (LA LGBT Center). This chapter will first describe how the raw LA LGBT Center dataset is restricted to only include the study population of interest. Second, this chapter will discuss how the constructs within Sydnemics Theory are operationalized using LA LGBT Center HIV testing and risk assessment data. Lastly, the chapter will discuss the analytical strategy for measuring Syndemics Theory constructs and HIV infection in the study population.

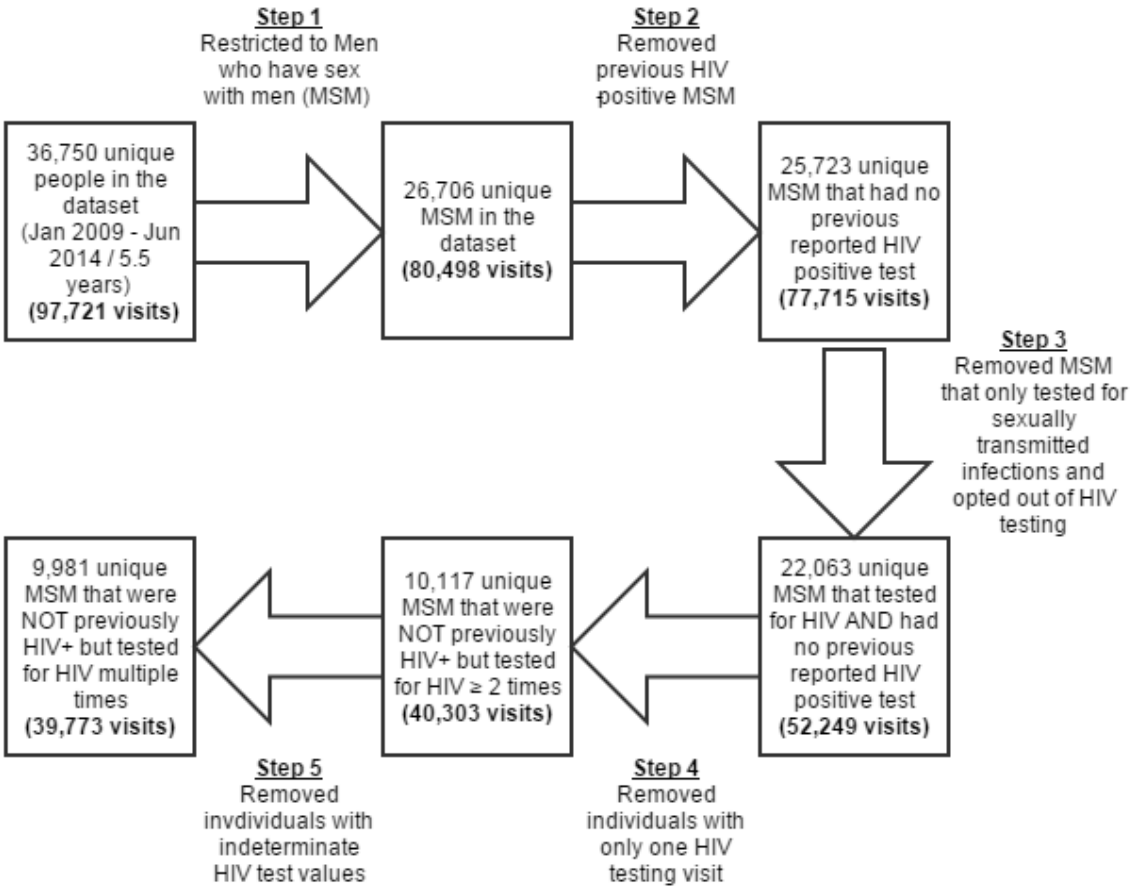
Study Population

The dataset for this dissertation contains HIV and sexually transmitted infection (STI) testing data as well as risk assessment data from individuals presenting to the LA LGBT Center for HIV/STI screening services from January 2009 to June 2014 (5.5 years of data). This dissertation uses these data to predict HIV risk for men who have sex with men (MSM) (Step 1), who did not report a previous HIV-positive result (Step 2), tested for HIV two or more times during the study window (Steps 3 and 4), and had a conclusive HIV result, either positive or negative, at follow-up (Step 5) (Figure 5.1). Given the inclusion criteria, numerous steps were needed to refine the raw dataset to meet these criteria.

In the first step, only MSM were included in the dataset. An MSM was defined as an individual who reported a male gender identity and sex with another man at least once in the past year. This definition also includes men who have sex with men and women (MSMW). In the second step, individuals who reported a prior HIV-positive result were removed in order to only include MSM who were HIV-negative at baseline. In the third step, MSM were removed who only tested for STIs and opted out of HIV testing at the LA LGBT Center during baseline and

follow-up visits since their true HIV status could not be determined at any time point. In the fourth step, MSM were removed who only tested once for HIV within the study window. In the fifth step, MSM who initially tested HIV-negative at baseline were removed if their last HIV test was either inconclusive or indeterminate. There were 9,981 unique MSM who met the inclusion criteria for analysis.

Figure 5.1 – Procedure for Selecting the Study Population



Dependent Variable

The dependent variable for this dissertation is the last recorded, valid HIV test result within the study window. Individuals who tested HIV-positive at any time in the follow-up window were considered HIV-positive and were right-censored at their positivity date.

Individuals who tested HIV-negative at their last visit will be treated as HIV negative and were right-censored at their last visit date.

HIV infection is measured at the LA LGBT Center in two different ways. The first method of measurement is through an HIV antibody test. Following HIV infection, the human body takes approximately four to six weeks to develop antibodies to the virus. Thus, a newly HIV-positive individual will have a false negative HIV antibody test result if they test for HIV before the body develops an antibody response. Therefore, there is a possibility that an individual is actually HIV-positive even if they test HIV antibody negative within this four to six week period. Individuals who test HIV antibody positive are known as non-acute HIV infections.

To account for this window period, the LA LGBT Center also administers nucleic acid amplification testing (NAAT) in concert with each HIV antibody test. NAAT assays specifically test for viral antigen and can detect virus as early as ten days after infection. As with the antibody test, an individual that tests less than ten days after the initial infection will have a false negative NAAT result and the infection will go undetected until their next HIV screening visit. Despite the potential for false negative tests, these technologies used together are capable of detecting the vast majority of HIV infections in the population with a sensitivity of 99.76% (Masciotra 2011). Individuals who are HIV antibody negative and NAAT positive are known as acute HIV infections, since the virus is detected soon after infection.

Independent Variables

MSM who receive HIV testing services from the LA LGBT Center are given a risk assessment at intake that contains questions on STI history, sexual behaviors, intimate partner violence, substance use, and demographics. This 82-item risk assessment is administered to each client at their initial/baseline visit and then administered at subsequent visits where the time

elapsed between visits has been greater than or equal to three months. While the risk assessment contains numerous important variables, only the variables outlined by Syndemics Theory (Chapter 3) and the literature search (Chapter 4) will be consider for inclusion into the overall model. Furthermore, only risk assessment responses at baseline will be used since the goal of the analysis is to predict future HIV infection given baseline behavior.

Syndemics theory outlines three constructs that are associated with HIV infection: biological, behavioral, and substance use. Chapter 4 discussed how these constructs have been operationalized in previous studies, and this section will discuss how each of these constructs is operationalized using data from the LA LGBT Center. The biological variables are discussed first followed by discussions of the behavioral variables and then substance use variables.

Biological Variables

Current Diagnosis or History of Sexually Transmitted Infections

The LA LGBT Center administers STI and HIV testing to all clients receiving sexual health screening services. Laboratory staff members draw blood samples for HIV and syphilis testing and administer a throat swab for pharyngeal gonorrhea (NG) testing. Clients are subsequently asked to self-collect urine samples and rectal swabs for NG and chlamydia (CT) testing. Individuals who do not want comprehensive STI and HIV screening must explicitly opt out of this service. Therefore, the dataset for this analysis contains the biomedical results of STIs for each individual client visit in all cases where a client did not opt out of a particular STI test. At baseline, approximately 640 individuals opted out of chlamydia or gonorrhea testing and 1,100 individuals opted out of syphilis testing. These individuals are still included in the analysis, they just have missing values at baseline for one or more of these STI variables.

In addition to the biomedical STI measures, the LA LGBT Center also collects data on self-reported STI history during the risk assessment interview. More specifically, counselors ask if clients have been diagnosed with any of the following STIs "never," "ever," or in the "past year": CT, NG, herpes, warts, Hepatitis B, Hepatitis C, and/or syphilis. The literature has only shown a definitive link between HIV and NG, CT, and syphilis, and a possible link between HIV and HSV2. Furthermore, the LA LGBT Center does not do routine testing for warts, Hepatitis B or Hepatitis C, and thus only self-reports are available. Based on the literature findings, only CT, NG, syphilis, and HSV2 will be evaluated. There were very few missing values for the self-reported STI history variables: 65 (0.7%) for CT, 77 (0.8%) for NG, and 106 (1.1%) for syphilis.

In addition to measuring each individual infection, this analysis will also explore a composite variable for each measure. More specifically, if an individual tested positive at baseline for NG, CT, and/or syphilis, they would be assigned a yes response for the composite "Testing positive for any STI" variable. Likewise, if an individual reported a history at baseline of NG, CT, and/or syphilis, they will be assigned a "yes" response for the composite "History of any STI."

Therefore, current diagnosis and history of sexually transmitted infections will be measured with nine variables: history of chlamydia, history of gonorrhea, history of syphilis, history of HSV, history of any STI (chlamydia, gonorrhea, syphilis, and/or HSV), diagnosis of chlamydia, diagnosis of gonorrhea, diagnosis of syphilis, and diagnosis of any STI (chlamydia, gonorrhea, and/or syphilis). This dissertation will examine the relationship between HIV contraction and these nine variables in bivariate survival analyses. Following the results of bivariate analyses, the suitability of the biomedical tests and self-reported history of STIs will be compared to determine which is most appropriate for the multivariate survival analyses.

Type of Sex Act and Condom Use

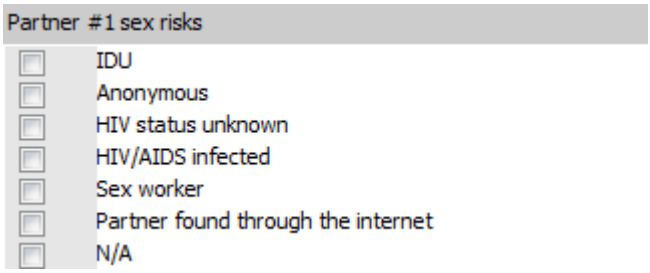
To measure HIV risk from unprotected anal intercourse, the LA LGBT Center asks clients to report if they engaged in insertive anal sex, receptive anal sex, or vaginal sex during their last sexual encounter. If they report "yes" to any of the aforementioned questions, they are then asked about their condom use behavior during each act to measure unprotected receptive anal sex, unprotected insertive anal sex, and unprotected vaginal sex. The three levels for each variable are as follows: "No," "Yes with condom," and "Yes without condom." The no response indicates that they did not engage in this type of sex at the last sexual encounter, and the remaining two responses are self-explanatory.

Serosorting

The LA LGBT Center risk assessment asks the client if the HIV serostatus of their last sexual partner was either HIV-positive and/or unknown to the client. This question has been presented due to its complexity in Figure 5.2 (see next page). For a full list of the risk assessment questions, please see Appendix I.

If the client reports that the partner was either "HIV/AIDS infected" or "HIV status unknown," then the individual could be classified as *not* engaging in serosorting since all clients are HIV-negative at baseline. However, there is no option for "HIV status negative" for their partner's HIV status which would indicate that the client was either engaging in serosorting or just happened to have an HIV-negative partner. It is unreasonable to assume that an individual is serosorting if they did not indicate "HIV/AIDS infected" or "HIV status unknown." As the option for "HIV status negative" is not available, we determined it would be methodologically flawed to include this as a variable in the overall analysis.

*Figure 5.2 – Graphical Depiction of "Partner #1 Sex Risks" Question**



**The question asks counselors to check all that apply*

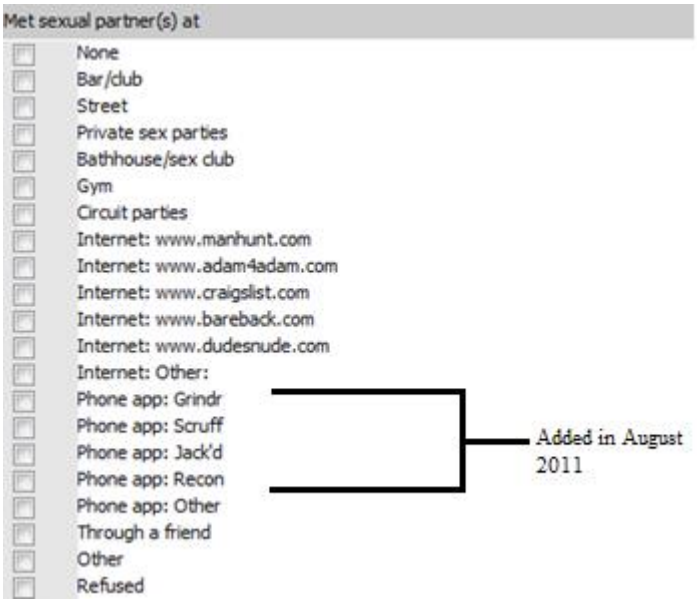
Overall, the biological construct using LA LGBT Center data is operationalized using the following variables at baseline: infection with STIs, history of infection with STIs, the types of sex acts, and condom use for each of those sex acts. The operationalization of the sexual behavioral construct will be discussed in the next four sub-sections.

Sexual Behavioral Variables

Venue for Finding Sex Partners

The LA LGBT Center staff asks clients if they met sexual partners in one or more of 19 different ways (Figure 5.3). Responses will be collapsed into in-person venues (e.g., bar/club, party), online venues (e.g., *manhunt.com*, *adam4adam.com*), and both in person and online. Please note that data collection on geosocial phone apps (e.g., *Grindr*, *Scruff*) began in 2011, and thus these options are not available for all individuals and will not be included in the analysis.

*Figure 5.3 – Graphical Depiction of "Met sexual partner(s) at" Question**



**The question asks counselors to check all that apply*

Race/Ethnicity of Sexual Partners

The risk assessment asks clients about the last two partners' perceived race/ethnicity. To better conceptualize these variables in line with present social network research, three levels will be created: Both Partners Different Race; Both Partners Same Race; One Partner Same Race, One Different. For example, if an individual identified as Hispanic and the last two partners were Hispanic, they would be classified as "Both Partners Same Race." In contrast, if an individual identified as White and the last partner was White and the partner before was Asian, they would be classified as "One Partner Same Race, One Different."

Age of Sexual Partners

The LA LGBT Center risk assessment also asks clients about the last two partners' ages. Although a partners' age has not been extensively explored in the literature, this dissertation analysis will test how partner age is associated with HIV infection by adding the last two partner ages and then dividing by two to obtain and average. Lastly, this average will be subtracted from

the client's age to create an overall age difference (Client's Age – ((Partner 1 Age + Partner 2 Age) / 2)).

Number of Sexual Partners

The LA LGBT Center asks clients how many different sexual partners they have had both in the past 30 days as well as the past three months. Both variables will be analyzed in bivariate analyses to determine if there is a difference between these variables in their association with HIV infection.

Intimate Partner Violence

Clients are also asked if they have been a victim of intimate partner violence (IPV). Responses are coded as "never," "ever," "past year," or "past 3 months." This is the only mental health variable that is included in this analysis.

Thus, the sexual behavioral construct is operationalized by asking about the four questions pertaining to an individual's sexual network (venue for finding partners, race/ethnicity of sexual partners, age of sexual partners, and number of sexual partners) as well as this fifth mental health variable which measures IPV among LA LGBT Center clients. The last construct outlined by Syndemics theory is the substance use construct and variables contributing to this construct will be discussed in the next sub-section.

Substance Use and Number of Substances Used

The LA LGBT Center collects substance use history in the past year for the following substances: ecstasy, methamphetamine (meth), nitrates/poppers, cocaine, crack, heroin, gamma-Hydroxybutyric acid (GHB), and un-prescribed use of Viagra/Cialis/Levitra (also known as erectile dysfunction drugs or EDDs). However, not all of these drugs have been shown to be related to HIV incidence. Therefore, history of ecstasy, meth, nitrates, and EDDs will be

analyzed in the HIV risk algorithm. Since the number of drugs used has also been shown in the literature to be an important predictor in HIV acquisition, a count of the number of illicit drugs used will be included as another predictor.

The biological, sexual behavioral, and substance use variables have been shown to be primary variables that predict HIV acquisition. However, other variables need to be considered as control variables and will be discussed in the next section.

Control Variables

Sexual Orientation

Clients at the LA LGBT Center are asked to identify their sexual orientation on their registration packet with the options of "gay," "bisexual," "heterosexual," "lesbian," "questioning," and "other" with a write-in option. As the study population is MSM, individuals will be put into one of three strata based on their responses: "gay," "bisexual," or "other."

Race/Ethnicity

Clients of the LA LGBT Center are asked to report their race/ethnicity while registering for services. Clients are asked a multi-select question to determine if they identify with one or more of the following races/ethnicities: "White," "Black/African-American," "Asian," "Native Hawaiian or Other Pacific Islander," "American Indian or Alaskan Native," "Hispanic," and lastly a write-in option for "Other." Due to sample size considerations, these categories will be collapsed into the following four racial/ethnic categories: White, Black, Hispanic, and Other. The "Other" category includes "Asian," "Native Hawaiian or Other Pacific Islander," "American Indian or Alaskan Native," and the write-in options that clients provide.

Age Group

Age is calculated by subtracting the date of birth reported on the registration form from the visit date. As with the independent and control variables, baseline age will be used for all participants.

Summary of Variable Relationships

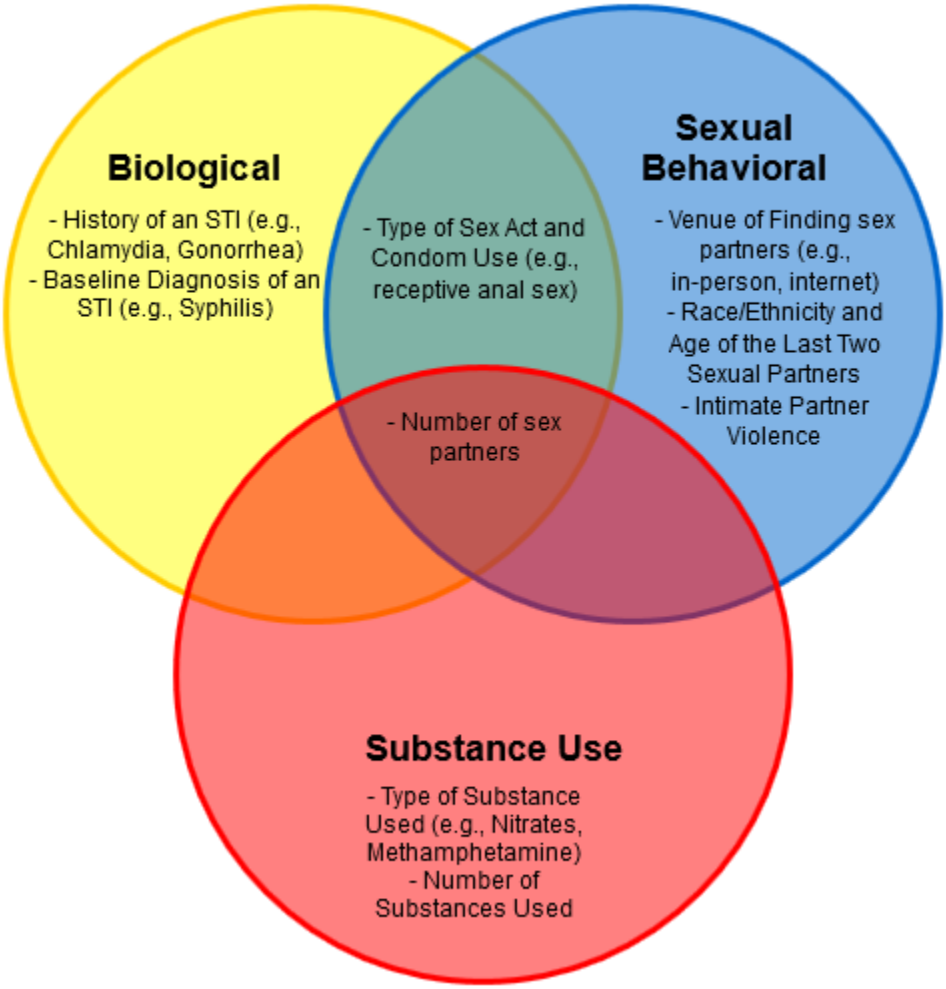
The three main constructs of Syndemics Theory were operationalized using the variables discussed in previous sections in order to show the overlap between constructs in predicting HIV infection (Figure 5.4). In summary, the biological construct was operationalized using History of STIs as well as baseline diagnosis of an STI. The sexual behavioral construct was operationalized through venue for meeting sexual partners, race/ethnicity of the last two sexual partners, and age of the last two sexual partners. The substance use construct was operationalized through type of drugs used (ecstasy, methamphetamine, nitrates, EDDs, cocaine, and alcohol use) as well as number of drugs used.

There were also variables that spanned two or three constructs. For example, the condom use variables refer to both a sexual behavior (e.g., the act of using condoms) as well as the biological risk associated with each type of sexual behavior (e.g., a higher risk to engage in receptive anal sex when compared to insertive anal sex). The variable representing the number of sexual partners fit into all three constructs in the figure. The rationale for this variable being placed in all three constructs is that the number of sexual partners is a behavioral choice leading to higher biological exposure which is a choice that may be fueled by the use of substances.

Similar to Syndemics Theory, we hypothesize that not all variables fit discretely into one construct. As stated previously, both age group and race/ethnicity will be controlled as potential

confounders in these analyses. Sexual orientation may be controlled for depending on the bivariate results in Chapter 6.

Figure 5.4 –Theoretical Model with Operationalized Constructs and Associated Variables



Analytical Procedures

The study population consists of 9,981 unique MSM who tested HIV-negative at baseline and returned for at least one subsequent visit for HIV testing within the testing period. Among the 9,981 unique individuals, 395 MSM seroconverted to HIV-positive during the study period for an incidence rate of 3.96%.

Aim 1 will use the log-rank results of bivariate Cox proportional hazards models (also known as *survival analyses*) to determine the variables at baseline that are predictive of HIV infection at follow-up within the entire study population. Cox proportional hazards models are most commonly used to determine what variables influence the occurrence of a particular event over time (IDRE 2015). Individuals have attributes assessed at the baseline visit and are then followed over time to determine who develops the event of interest and thus determine if there are any differences in baseline characteristics. Since individuals develop an HIV infection prior to diagnosis, the midpoint between the diagnosis date and the previous testing date will be imputed as the day of HIV infection.

Individuals are right-censored when they test HIV-negative at their last observable visit in the follow-up. The follow-up time ends at the time of right-censoring. For example, if an individual first tested HIV-negative on January 1st, 2011, had three more testing visits, and tested HIV-negative on with their last visit on January 1st, 2012, they would contribute 365 days to the analysis.

There are numerous advantages of survival analysis over ordinary least squares regression. In ordinary least squares regression, censoring bias is introduced in cases where the event did not occur (i.e., the individuals who remain HIV-negative). This bias is appropriately dealt with by survival analyses by ensuring that the length of time in the analysis is accounted for by the model. Furthermore, survival analyses also account for differing entry points by clients into the study. Although the study window spans from January 1st, 2009 to June 30th, 2014, not all individuals had their first visit on the first day of the study window. Therefore, proportional hazards models correct for bias that is not normally corrected for in ordinary least squares models.

For a proportional hazards model to be used, the proportional hazards assumption must be met for each continuous variable. This assumption states that the hazard ratio between levels of continuous covariates is consistent over time as indicated by a p-value exceeding 0.05. Although most variables for the analysis are discrete, there are three candidate variables with continuous outcomes: sexual partners in the last 30 days, sexual partners in the last three months, and the age of the last two sexual partners. The Supremum Test for Functional Form shows that each of these variables exceed 0.05 as evidenced by $p = 0.2$ for sexual partners in the last 30 days, $p = 0.07$ for sexual partners in the last three months, and $p = 0.55$ for the age of the last sexual partner.

Following the bivariate tests, numerous multivariate Cox proportional hazard models will be constructed using the significant variables determined by log-rank tests in the bivariate analyses. To empirically test the theory, all variables that are proposed by Syndemics Theory will be added to the multivariate model for both the entire population and each subgroup of interest (e.g., Hispanic MSM, young MSM).

To accomplish Aim 2, the overall Hazard Ratio scores of the HIV-positives will be compared to the HIV-negatives to determine what cut-points are most appropriate for post-exposure prophylaxis (nPEP), pre-exposure prophylaxis (PrEP), and frequent HIV testing given each risk level.

Aim 3 will be accomplished by first adding interaction terms between the client's race/ethnicity (NOT the race/ethnicity of the last two sexual partners) and all available HIV predictors to determine what interactions are significant for subsets of MSM. Second, interactions between age group and the HIV predictors will also be considered to determine how age group impacts different predictors. Lastly, bivariate and multivariate analyses will be run for

subgroups of MSM including White MSM, Hispanic MSM, young MSM, and older MSM. All analyses will be conducted using SAS Version 9.3 (Cary, NC).

Imputation of STI and HIV Data

Between January 2009 and July 2011, a counselor was not required to ask a client all risk assessment questions in order to sign off on the risk assessment. Therefore, there is a number of missing data points within this 31-month period. Starting in August 2011, all of the questions analyzed became required as part of the risk assessment and the amount of missing data dropped precipitously. While most data points regarding the last sexual experiences as well as substance use cannot be imputed prior to August 2011, STI history can be imputed based on analysis of baseline STI results.

If an individual had a missing value for self-reported chlamydia history, self-reported gonorrhea history, or self-reported syphilis history, the value could be imputed provided the individual tested positive for that given bacterium at baseline. For example, if an individual had a missing value for self-reported gonorrhea history but tested positive for gonorrhea at baseline, the self-reported gonorrhea history value could be imputed to "Diagnosed Less than One Year Ago" since they were positive the day of the visit. This imputation was performed for the self-reported chlamydia history, self-reported gonorrhea history, and self-reported syphilis history variables.

In addition, HIV test results were recorded in an auxiliary system up to July 31st, 2011 for the satellite clinic. While the HIV lab testing data were not stored in the medical record for this satellite site, it was possible to see that an individual presented and received an HIV test. If patient had a test type of "STD and HIV" between January 1st, 2009 and July 31st, 2011 AND had subsequent visits with an HIV-negative test AFTER August 1st, 2011, these original values

were imputed as HIV-negative. A total of 636 visits met these criteria, and 620 of these visits could be single imputed based on subsequent testing results. The remaining 16 did not have subsequent HIV testing after July 31st, 2011 and therefore it could not be determined if they were HIV-positive or HIV-negative.

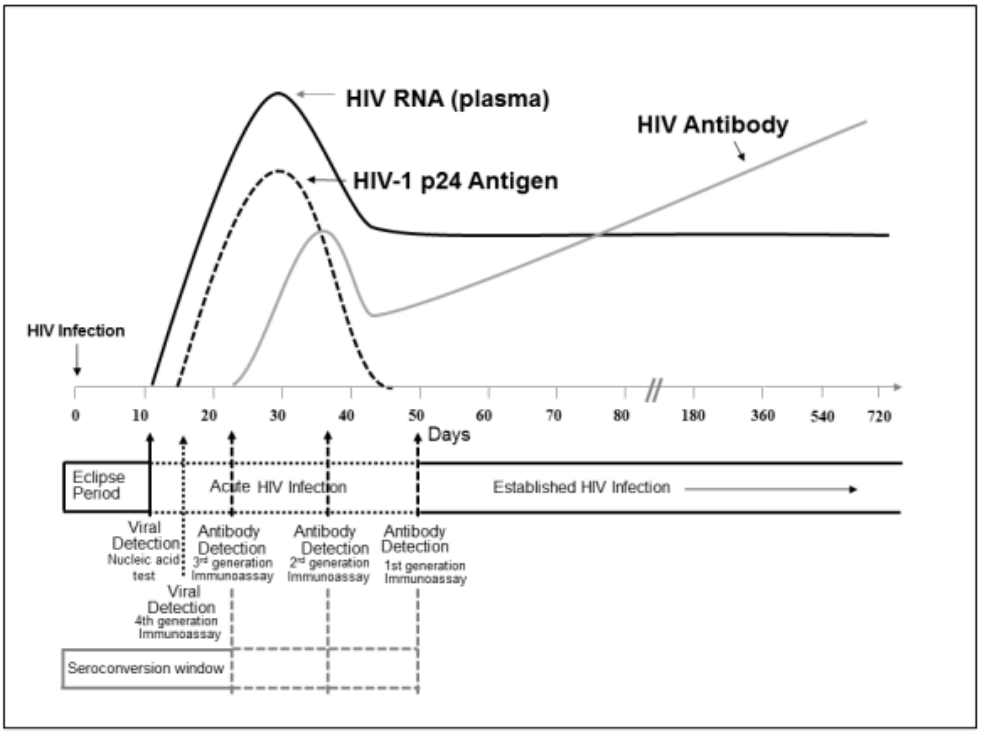
The third variable imputed was that actual day of HIV infection. As discussed previously, individuals may test HIV-positive through either an acute HIV infection (NAAT positive and antibody negative) or a non-acute HIV infection (NAAT positive and antibody positive). Since there is a lag time between infection and testing positive for HIV, the actual day of infection could be imputed based on literature findings. For acute infections, the NAAT assay can detect HIV approximately 10 days after infection (Figure 5.5, CDC 2014e). For non-acute infections, current research shows that 3rd and 4th generation antibody tests can detect antibodies within 10-13 days after the NAAT assay detects viral material in the blood (or approximately 20-23 days after infection).

Based on these literature findings, an acute HIV infection that is NAAT positive and antibody negative has been infected between 10 days and 20-23 days prior to their HIV-positive test date. To account for this uncertainty, the midpoint between 10 and 23 days, 17, will be subtracted from the visit date to impute the date of positivity for acute HIV infections. For example, if John Doe tested acute HIV positive on January 30th, 2014, his date of HIV infection will be imputed as January 13th, 2014.

For individuals who are non-acute HIV infections, we can assume that they were infected as least 20-23 days prior to the HIV-positive test date based on the literature. Therefore, an individual may have become positive at any time between 20-23 days prior to their visit and the last date they tested HIV-negative. If James Doe tested HIV-negative on January 1st, 2014 and

then tests HIV-positive on July 23rd, then we would know that he contracted the infection between January 2nd, 2014 and June 30th, 2014, since June 30th is 23 days prior to his HIV-positive test date. To impute the date of HIV infection, we would take the midpoint of this 180 day interval (i.e., 180 days between January 2nd, 2014 and June 30th, 2014) and impute the date of infection as April 1st, 2014.

Figure 5.5 – HIV Detection by Test Type (CDC 2014e)



For values that could not be imputed, listwise deletion (i.e., deleting the entire observation if an individual had a value missing for one or more of the covariates) was used in the survival analyses equations.

Individuals who had a missing value for history of STIs but had a positive result for gonorrhea, chlamydia, or syphilis (n = 97) had value of "Past Year" imputed for the history of STIs. No other imputations were made for this variable.

Individuals who reported a discordant result for race/ethnicity on their registration form and their visit were investigated and rectified. Scanned registration forms were used to determine an individual's true race/ethnicity.

Chapter 6 – Bivariate Results

Chapter 6 will discuss the findings of the bivariate analyses for the biological, sexual behavioral, substance use, and demographic variables. Chapter 6 will conclude with a discussion about potential interactions for these variables.

Bivariate Survival Analyses – Biological Predictors

Nine biological predictors were analyzed in bivariate survival analyses: history of chlamydia (Figure 6.1), history of gonorrhea (Figure 6.2), history of syphilis (Figure 6.3), history of Herpes Simplex Type II (HSV2) (Figure 6.4), history of any STI (Figure 6.5), diagnosed chlamydia infection at baseline (Figure 6.6), diagnosed gonorrhea infection at baseline (Figure 6.7), diagnosed syphilis infection at baseline (Figure 6.8), and any STI infection at baseline (Figure 6.9).

History of chlamydia, gonorrhea, syphilis, or any STI at baseline were all significantly related to HIV infection at follow-up ($p < 0.0001$) (Table 6.1). Approximately 8.6% of all individuals who reported a diagnosis of chlamydia within one year prior to their baseline visit tested HIV-positive over the follow-up period versus only 3.5% of individuals never diagnosed with a chlamydia infection. An even greater disparity existed with gonorrhea with 10.4% of individuals with a recent gonorrhea infection seroconverting compared with only 3.4% of individuals seroconverting who had never been diagnosed with gonorrhea. However, the greatest disparity was found with syphilis infection: 11.2% of individuals diagnosed less than one year prior to the baseline visit seroconverted compared to only 3.7% who had never been diagnosed with syphilis. For the composite STI history variable, 7.6% of those who were diagnosed in the year prior to the baseline visit seroconverted compared to only 3.1% of individuals who were never diagnosed with any of these STIs.

In contrast to these findings, there was no difference in HIV incidence between individuals who reported a history of HSV2 at baseline and those who did not report a history of infection ($p = 0.26$).

When analyzing diagnosis of an STI at baseline, chlamydia ($p < 0.0001$), gonorrhea ($p < 0.0001$), syphilis ($p = 0.0004$), and any STI diagnoses ($p < 0.0001$) were each associated with eventually testing positive for HIV. Overall, 7.1% of individuals who tested positive for chlamydia at baseline eventually tested HIV-positive compared to only 3.6% of individuals who initially tested negative for chlamydia. The rates were also nearly double for gonorrhea and almost triple for syphilis. Lastly, 6.4% of individuals testing positive for any STI at baseline would seroconvert compared to only 3.1% of individuals who tested negative for all STIs.

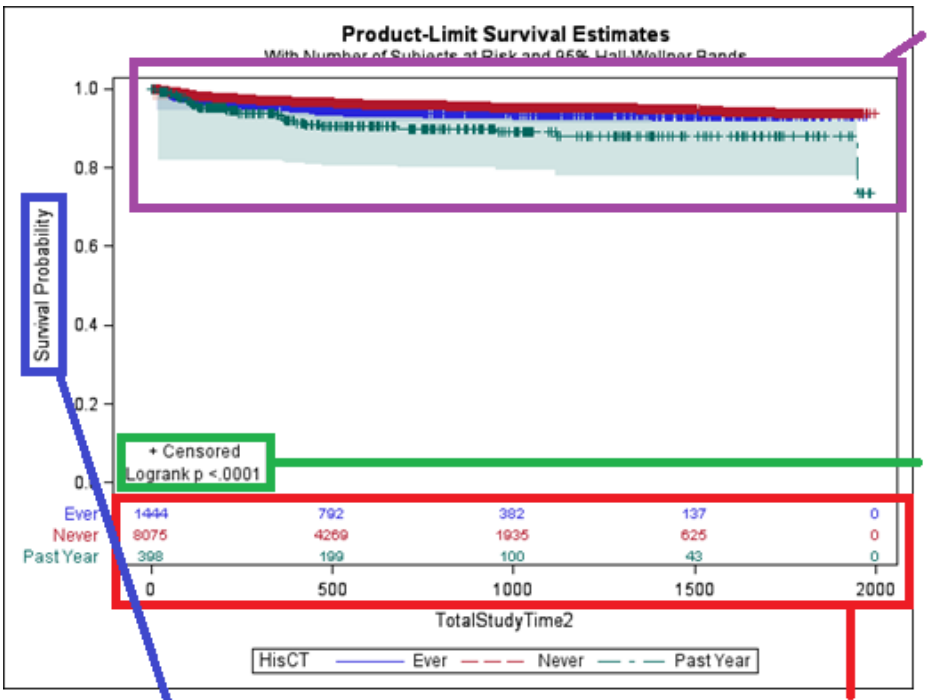
Table 6.1 - Bivariate Survival Analyses of Biological Risk Behaviors at Baseline by Final HIV Serostatus (n = 9,981), January 2009 - June 2014.

	HIV-negatives (n = 9,586)		HIV-positives (n = 395)		Total (n = 9,981)
	n	%	n	%	n
History of Chlamydia					$p < 0.0001$
Never Diagnosed	7,793	96.5%	285	3.5%	8,078
Diagnosed More than One Year Ago	1,370	94.9%	74	5.1%	1,444
Diagnosed Less than One Year Ago	360	91.4%	34	8.6%	394
Missing	63	96.9%	2	3.1%	65
History of Gonorrhea					$p < 0.0001$
Never Diagnosed	7,197	96.6%	257	3.4%	7,454
Diagnosed More than One Year Ago	1,883	95.7%	85	4.3%	1,968
Diagnosed Less than One Year Ago	432	89.6%	50	10.4%	482
Missing	74	96.1%	3	3.9%	77
History of Syphilis					$p < 0.0001$
Never Diagnosed	8,916	96.3%	344	3.7%	9,260
Diagnosed More than One Year Ago	393	94.0%	25	6.0%	418
Diagnosed Less than One Year Ago	175	88.8%	22	11.2%	197
Missing	102	96.2%	4	3.8%	106
History of Herpes Simplex Type II					$p = 0.26$
Never Diagnosed	8,341	95.9%	355	4.1%	8,696
Diagnosed More than One Year Ago	417	97.4%	11	2.6%	428
Diagnosed Less than One Year Ago	146	94.8%	8	5.2%	154
Missing	682	97.0%	21	3.0%	703
History of any STI					$p < 0.0001$
Never Diagnosed	5,305	96.9%	170	3.1%	5,475
Diagnosed More than One Year Ago	2,839	95.7%	129	4.3%	2,968
Diagnosed Less than One Year Ago	1,045	92.4%	86	7.6%	1,131
Missing	397	97.5%	10	2.5%	407
Chlamydia Testing Result					$p < 0.0001$
Negative	7,865	96.4%	297	3.6%	8,162
Positive	1,079	92.9%	82	7.1%	1,161
Missing	642	97.6%	16	2.4%	658
Gonorrhea Testing Result					$p < 0.0001$
Negative	7,668	96.4%	289	3.6%	7,957
Positive	1,297	93.4%	91	6.6%	1,388
Missing	621	97.6%	15	2.4%	636
Syphilis Testing Result					$p = 0.0004$
Negative	8,389	96.3%	322	3.7%	8,711
Positive	87	89.7%	10	10.3%	97
Missing	1,110	94.6%	63	5.4%	1,173
Tested Positive for any STI					$p < 0.0001$
Negative	6,369	96.9%	201	3.1%	6,570
Positive	2,207	93.6%	150	6.4%	2,357
Missing	1,010	95.8%	44	4.2%	1,054
Total	9,586	100.0%	395	100.0%	9,981

Figure 6.1 displays the first of 30 Kaplan-Meier plots to be shown in Chapter 6. This first figure will be described to provide the reader with familiarity in interpreting this type of plot. The y-axis ("Survival Probability") gives the percent that "survive" or do not develop the event over time for each stratum (in this case, HIV infection). The higher a given stratum is at the end of the follow-up period, the lower the hazard of contracting HIV and thus the higher the rate of "survival." For Figure 6.1, individuals who reported never having chlamydia (red line) at baseline have the highest survival probability over time, but it is not much different than individuals who reported ever having chlamydia (blue line). The survival probability over time is roughly 95% for both groups, indicating that 5% who report either "never" or "ever" getting chlamydia will eventually contract HIV. In contrast, individuals who have had chlamydia over the past year (green line) have a much lower survival rate (approximately 75%) and thus a higher probability of getting HIV over the follow-up period.

The x-axis represents the time in days from the baseline visit to either HIV infection or the time of right censoring (i.e., the HIV-positive visit or the last date an individual was seen in the clinic during the study window), and the table represents the number of individuals that remained in that stratum at each given number of days. The lines represent each stratum of the predictor variable with the shading indicating the confidence interval for each, and the "+" icons representing an event that was right-censored. The log-rank p-value indicates if the groups are significantly different at follow-up as indicated by a p-value of less than 0.05 and greater line separation indicates more significant differences between groups. For Figure 6.1, we see that at least two of the groups are significantly different as indicated by a log-rank $p < 0.0001$.

Figure 6.1 - Kaplan-Meier Survival Analysis for History of Chlamydia



Represents the number of individuals in each group of the predictor (e.g., individuals diagnosed with chlamydia in the past year) that survive (e.g., don't test positive for HIV) at each time point. The + icon indicates a right censoring event (see red text for description); the shading indicates the confidence interval.

Indicates if at least two of the groups are significantly different at follow-up as indicated by a p-value less than 0.05.

Gives the percent that "survive" or do not develop the event over the follow-up period for each group. A steeper decline over time indicates a lower survival and thus a higher rate of HIV contraction.

Represents the time in days from the baseline visit to the last visit where an HIV test was performed, or the time an individual is right-censored. The table above the x-axis shows the number of individuals that remained in each group at each time point (500 days, 1000 days, etc.).

Figure 6.2 - Kaplan-Meier Survival Analysis for History of Gonorrhea

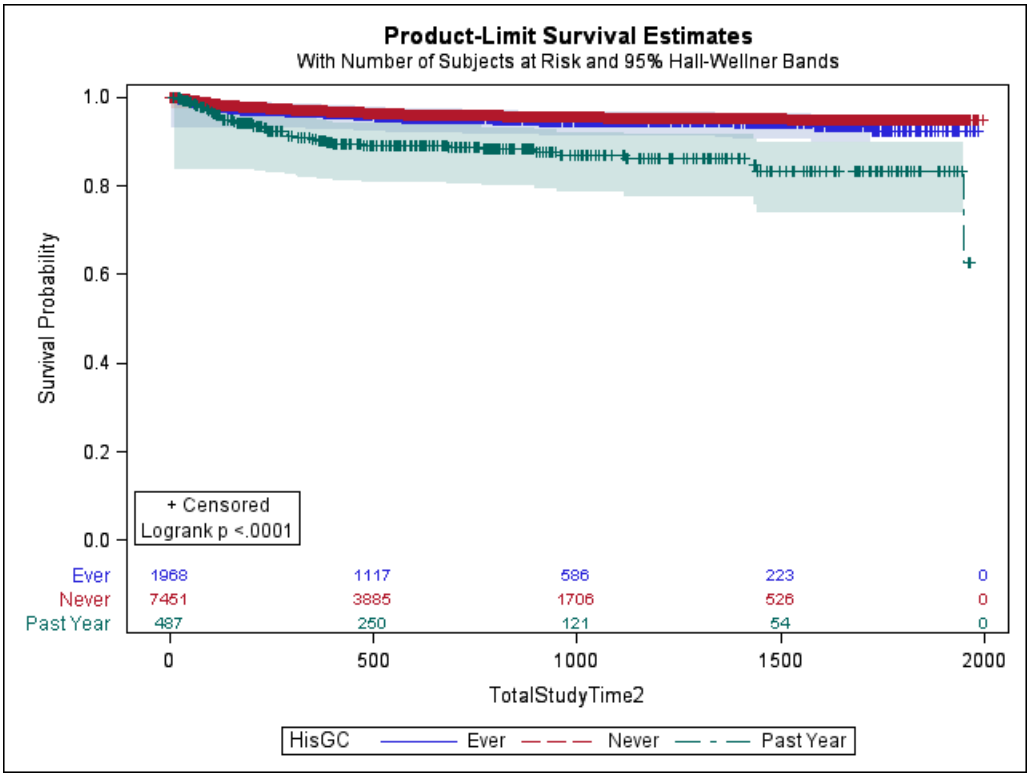


Figure 6.3 - Kaplan-Meier Survival Analysis for History of Syphilis

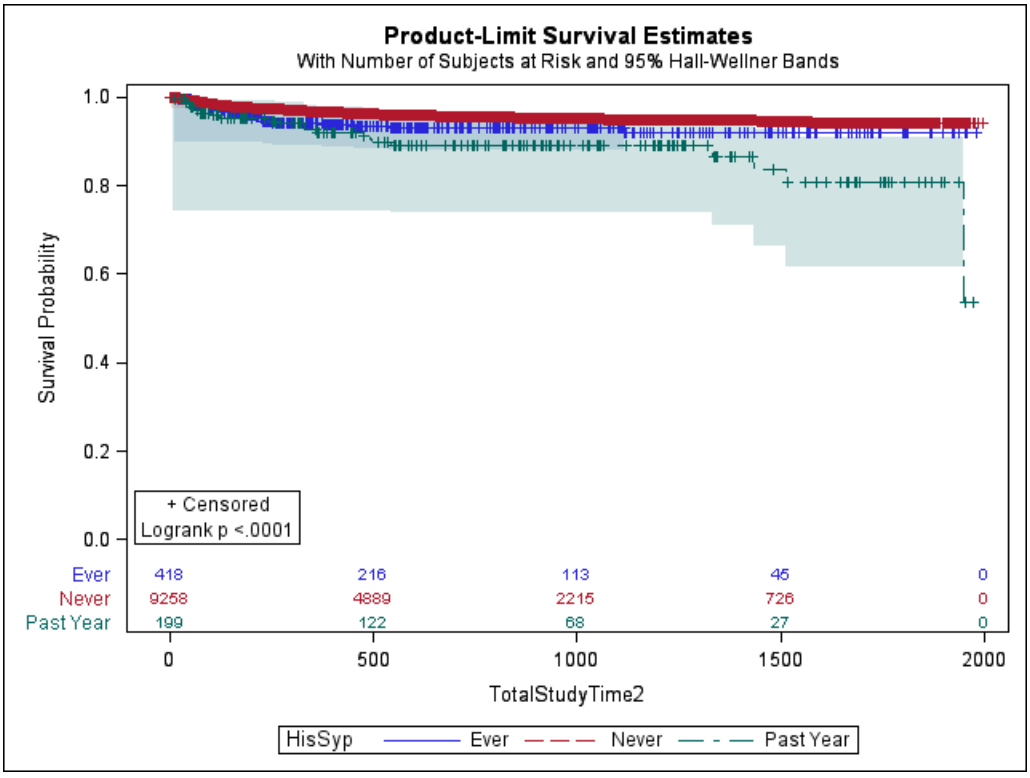


Figure 6.4 - Kaplan-Meier Survival Analysis for History of Herpes Simplex, Type II

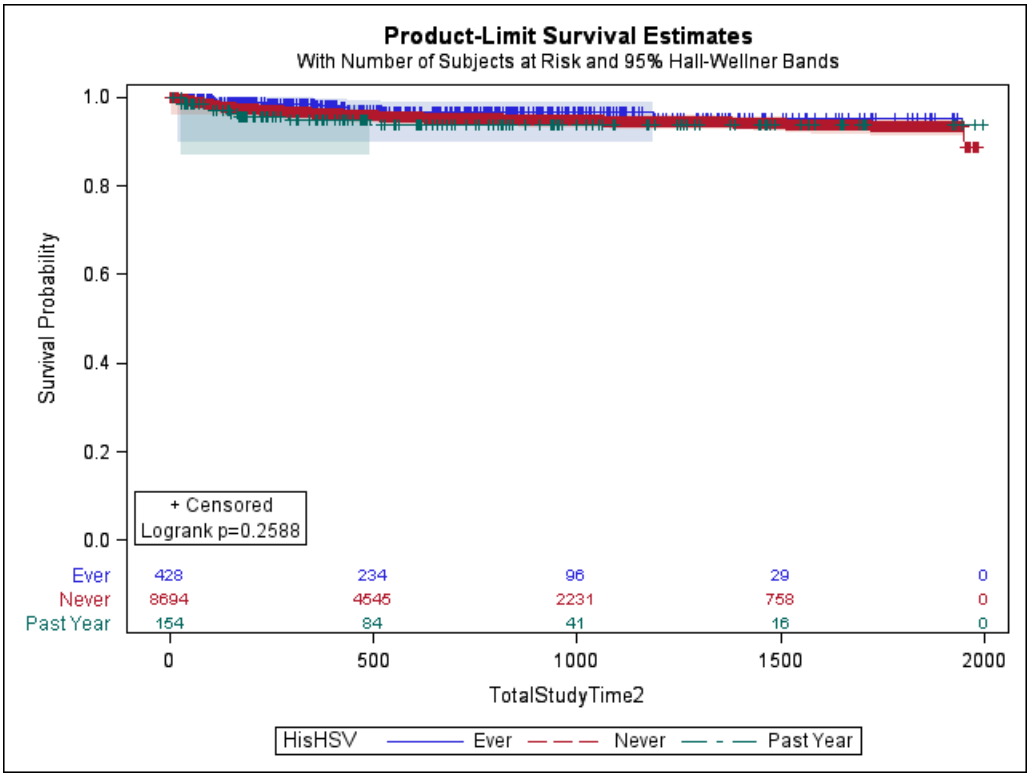


Figure 6.5 - Kaplan-Meier Survival Analysis for History of Any STI

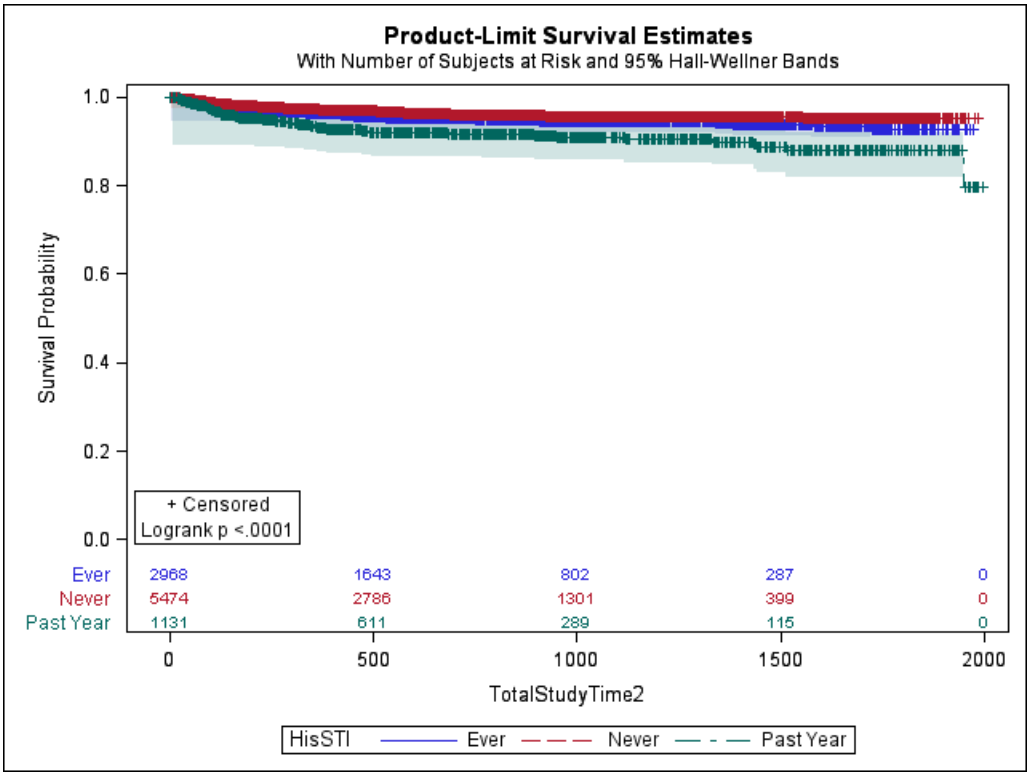


Figure 6.6 - Kaplan-Meier Survival Analysis for Current Chlamydia Infection

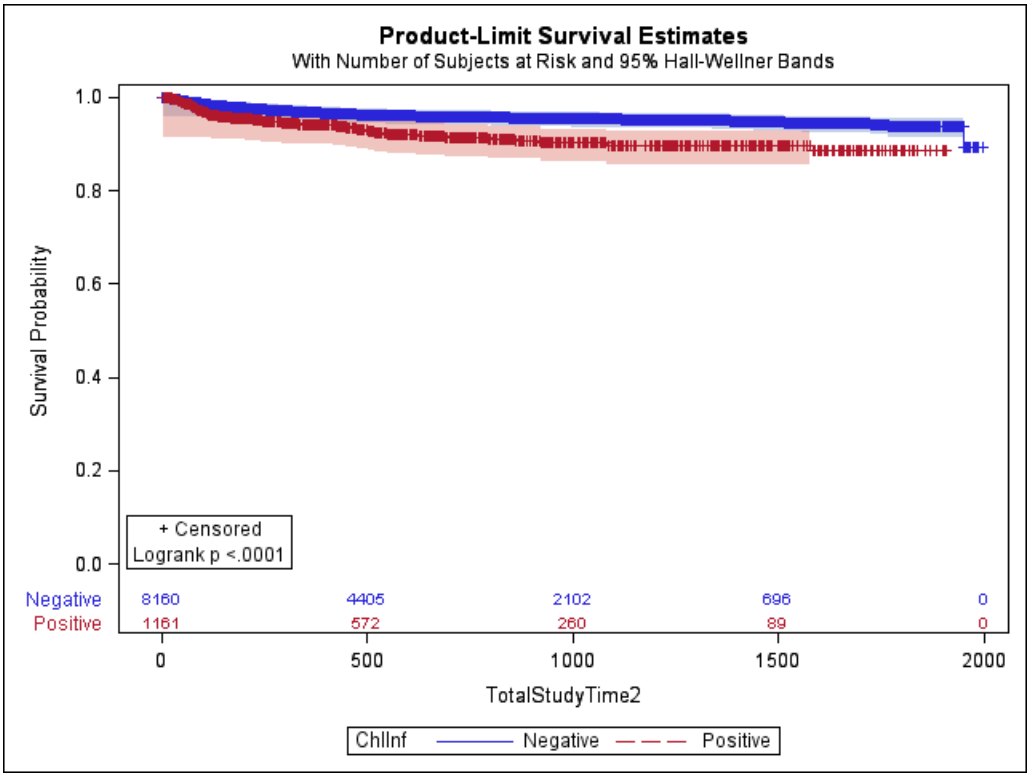


Figure 6.7 - Kaplan-Meier Survival Analysis for Current Gonorrhea Infection

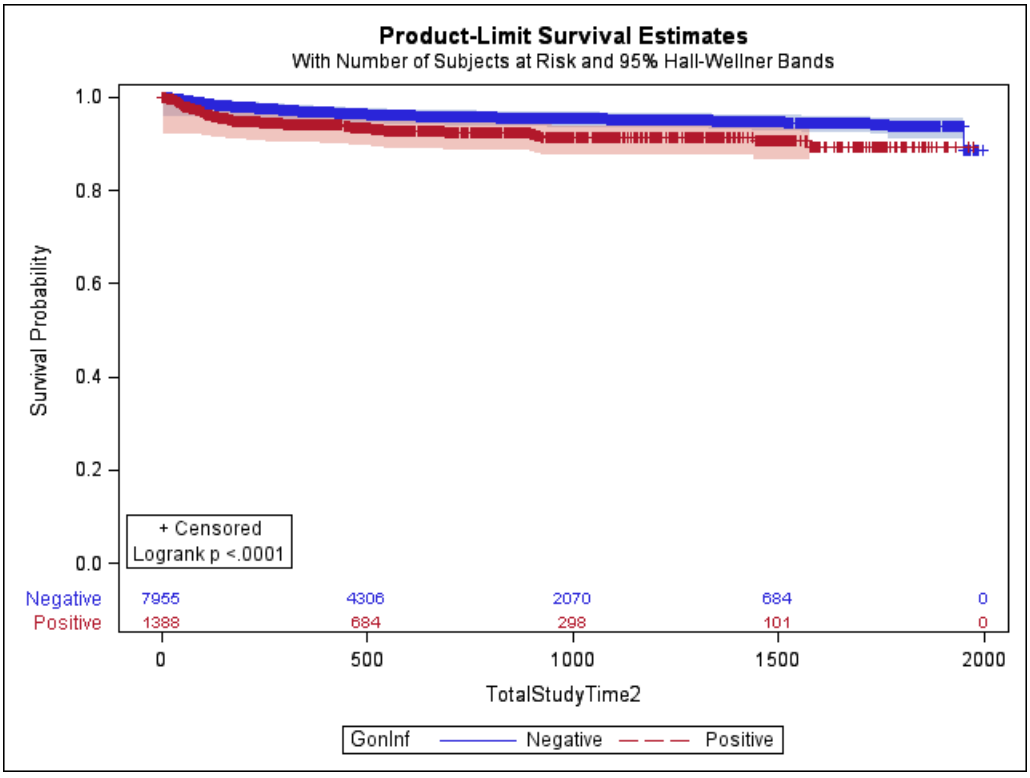


Figure 6.8 - Kaplan-Meier Survival Analysis for Current Syphilis Infection

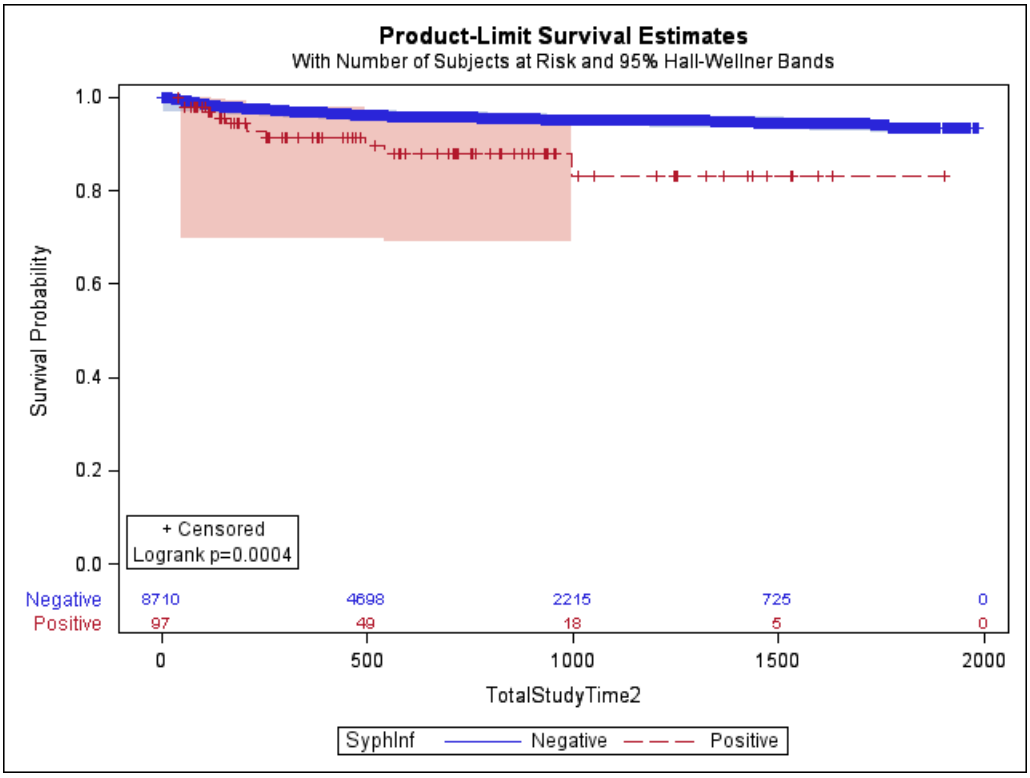
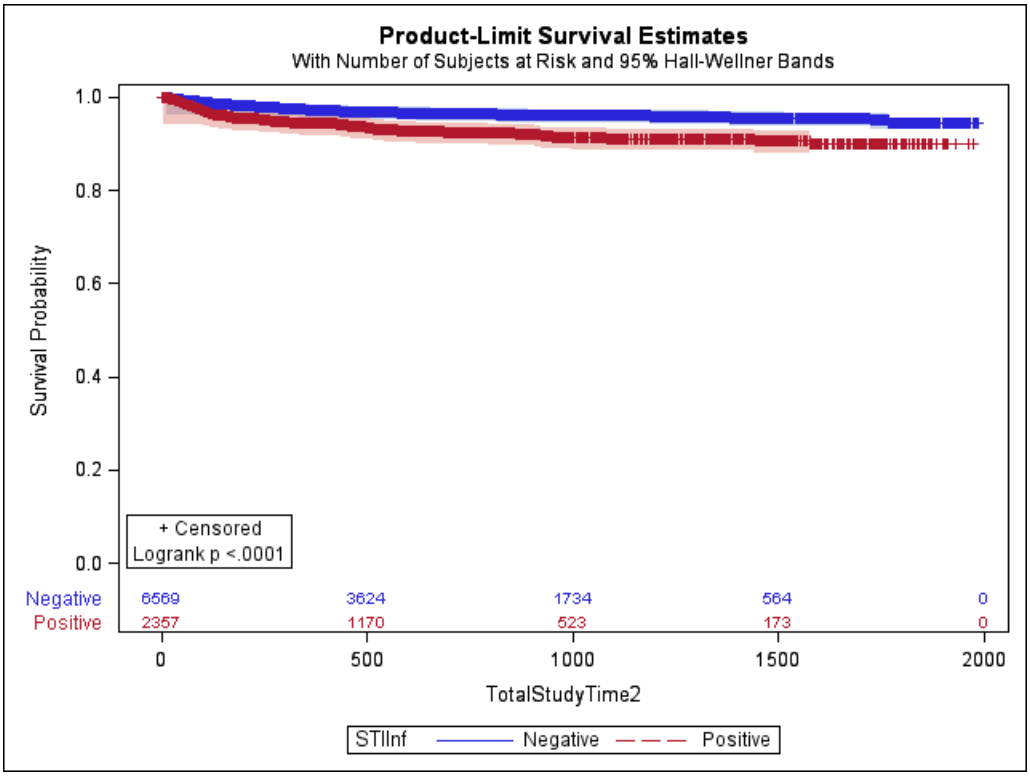


Figure 6.9 - Kaplan-Meier Survival Analysis for Any STI Positive



Bivariate Survival Analyses – Sexual Behavioral Predictors

Eleven biological predictors were analyzed in bivariate analyses: insertive anal sex history (Figure 6.10), receptive anal sex history (Figure 6.11), vaginal sex history (Figure 6.12), venue for finding sexual partners (Figure 6.13), race/ethnicity of the last two sexual partners (Figure 6.14), age of the last two sexual partners (Figure 6.15), number of sexual partners in the last 30 days (Figure 6.16), number of sexual partners in the last 3 months (Figure 6.17), history of intimate partner violence (4 categories: past 3 months, past year, ever, never) (Figure 6.18), and history of intimate partner violence (2 categories: ever vs. never) (Figure 6.19).

Insertive anal sex history was not significantly different between individuals who remained HIV-negative and individuals who became HIV-positive ($p = 0.05$) (Table 6.2). In contrast, individuals who reported receptive anal sex were significantly more likely to test positive for HIV at follow-up compared with individuals who did not report receptive anal sex ($p < 0.0001$). Despite the presence of bisexual men in the sample, vaginal sex history was not statistically significant ($p = 0.11$).

Race/ethnicity of the last two sexual partners ($p = 0.005$) and age of the last two sexual partners ($p = 0.006$) were associated with HIV at follow-up. 5.1% of individuals who reported sex both inside and outside their racial/ethnic group tested HIV-positive compared to only 3.6% of individuals who had sex only outside their group or only within their group. In addition, 4.8% of individuals reporting older partners seroconverted compared to only 3% who reported younger partners for the two sexual encounters directly before the baseline visit.

Intimate partner violence was also associated with HIV at follow-up ($p = 0.0002$): 6.7% of all individuals who reported ever experiencing domestic violence seroconverted at follow-up compared to only 3.7% of individuals who never reported intimate partner violence.

Lastly, both the number of partners in the last 30 days ($p < 0.0001$) as well as the number of partners in the last three months ($p < 0.0001$) were associated with HIV seroconversion at follow-up. Approximately 7.8% of all individuals who reported 10 or more partners in the last 30 days seroconverted compared to only 4.5% who had 2 partners in the last 30 days. Similar results were seen for partners over the last 3 months. Therefore, an increase in the number of sex partners is associated with an increase in the HIV risk based on the bivariate analyses for this population.

Table 6.2 - Bivariate Survival Analyses of Sexual Behavioral Risks at Baseline by Final HIV Serostatus (n = 9,981), January 2009 - June 2014.

	HIV-negatives (n = 9,586)		HIV-positives (n = 395)		Total (n = 9,981)
	n	%	n	%	n
Had Insertive Anal Sex					$p = 0.05$
No	5,435	96.3%	208	3.7%	5,643
Yes with a Condom	1,981	96.1%	80	3.9%	2,061
Yes without a Condom	2,100	95.4%	102	4.6%	2,202
Missing	70	93.3%	5	6.7%	75
Had Recepitve Anal Sex					$p < 0.0001$
No	5,933	96.9%	187	3.1%	6,120
Yes with a Condom	1,710	95.6%	79	4.4%	1,789
Yes without a Condom	1,918	93.7%	128	6.3%	2,046
Missing	25	96.2%	1	3.8%	26
Had Vaginal Sex					$p = 0.11$
No	8,903	96.1%	366	3.9%	9,269
Yes with a Condom	80	100.0%	0	0.0%	80
Yes without a Condom	261	97.8%	6	2.2%	267
Missing	342	93.7%	23	6.3%	365
Venue for Meeting Sexual Partners					$p = 0.35$
In Person	2,450	96.0%	102	4.0%	2,552
Online	1,649	95.0%	87	5.0%	1,736
More than One	2,294	96.4%	85	3.6%	2,379
Missing	3,193	96.3%	121	3.7%	3,314
Race/Ethnicity of the Last Two Sexual Partners					$p = 0.005$
Both Partners Different Race	3,098	96.4%	115	3.6%	3,213
Both Partners Same Race	3,355	96.4%	124	3.6%	3,479
One Partner Same Race, One Different	2,718	94.9%	145	5.1%	2,863
Missing	415	95.8%	18	4.2%	433
Age of the Last Two Sexual Partners*					$p = 0.006$
More than 5 Years Older	2,099	95.2%	105	4.8%	2,204
Within Five Years of Age	4,843	96.0%	202	4.0%	5,045

More than 5 Years Younger	1,979	97.0%	61	3.0%	2,040
Missing	665	96.1%	27	3.9%	692
Number of Partners in the Past 30 Days*					$p < 0.0001$
0	613	96.8%	20	3.2%	633
1	3,786	96.7%	131	3.3%	3,917
2	2,092	95.5%	99	4.5%	2,191
3	1,111	96.5%	40	3.5%	1,151
4	574	94.7%	32	5.3%	606
5	391	96.5%	14	3.5%	405
6	180	94.2%	11	5.8%	191
7	79	97.5%	2	2.5%	81
8	69	95.8%	3	4.2%	72
9	14	93.3%	1	6.7%	15
10 or More	329	92.2%	28	7.8%	357
Missing	348	96.1%	14	3.9%	362
Number of Partners in the Past 3 Months*					$p < 0.0001$
0	221	96.1%	9	3.9%	230
1	2,131	97.0%	67	3.0%	2,198
2	1,889	97.0%	59	3.0%	1,948
3	1,290	95.8%	56	4.2%	1,346
4	926	95.2%	47	4.8%	973
5	703	95.4%	34	4.6%	737
6	436	95.6%	20	4.4%	456
7	222	96.1%	9	3.9%	231
8	213	92.2%	18	7.8%	231
9	74	98.7%	1	1.3%	75
10 or More	1,261	94.9%	68	5.1%	1,329
Missing	220	96.9%	7	3.1%	227
Intimate Partner Violence					$p = 0.003$
Never	8,705	96.3%	339	3.7%	9,044
Ever	559	92.9%	43	7.1%	602
Past Year	119	94.4%	7	5.6%	126
Past Three Months	92	94.8%	5	5.2%	97
Missing	111	99.1%	1	0.9%	112
Intimate Partner Violence (Collapsed)					$p = 0.0002$
Never	8,705	96.3%	339	3.7%	9,044
Ever, Past Year, or Past Three Months	770	93.3%	55	6.7%	825
Missing	111	99.1%	1	0.9%	112
Total	9,586	100.0%	395	100.0%	9,981

**Discrete values for presentation purposes only; continuous values used in all analyses*

Figure 6.10 - Kaplan-Meier Survival Analysis for Insertive Anal Sex

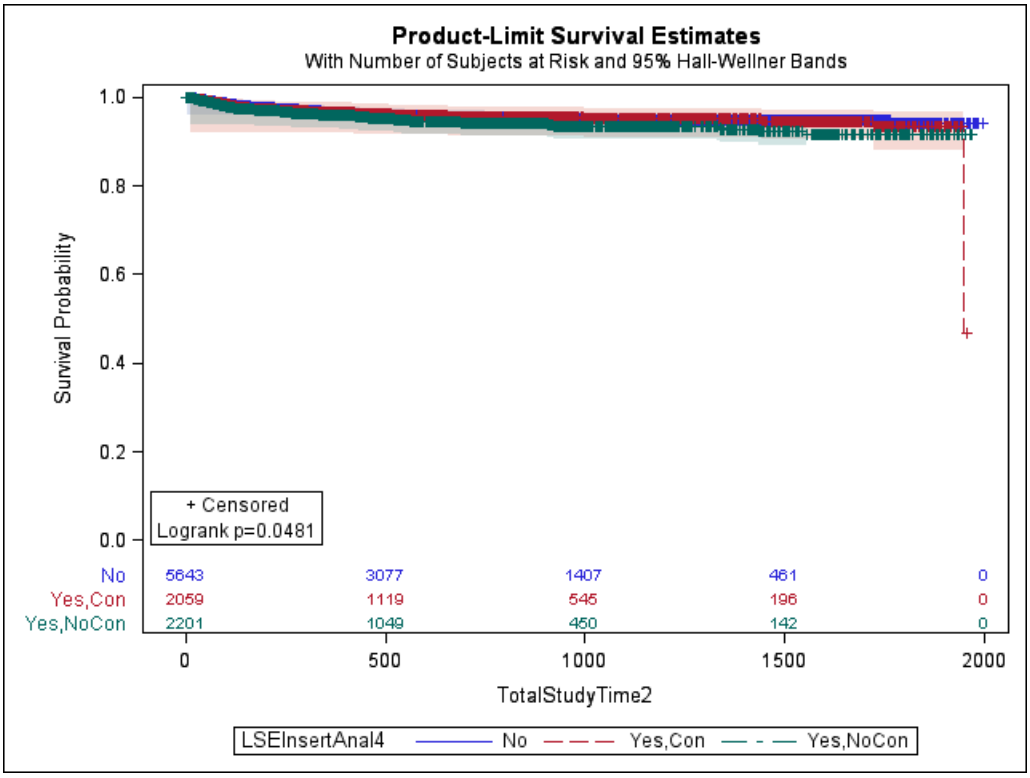


Figure 6.11 - Kaplan-Meier Survival Analysis for Receptive Anal Sex

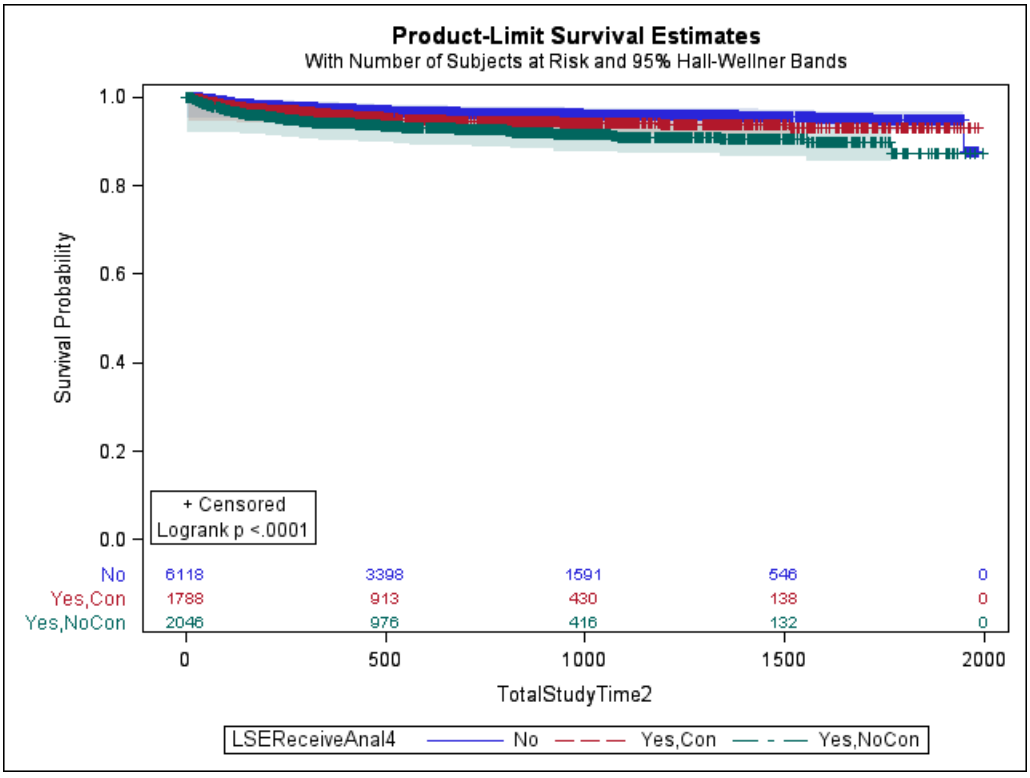


Figure 6.12 - Kaplan-Meier Survival Analysis for Vaginal Sex

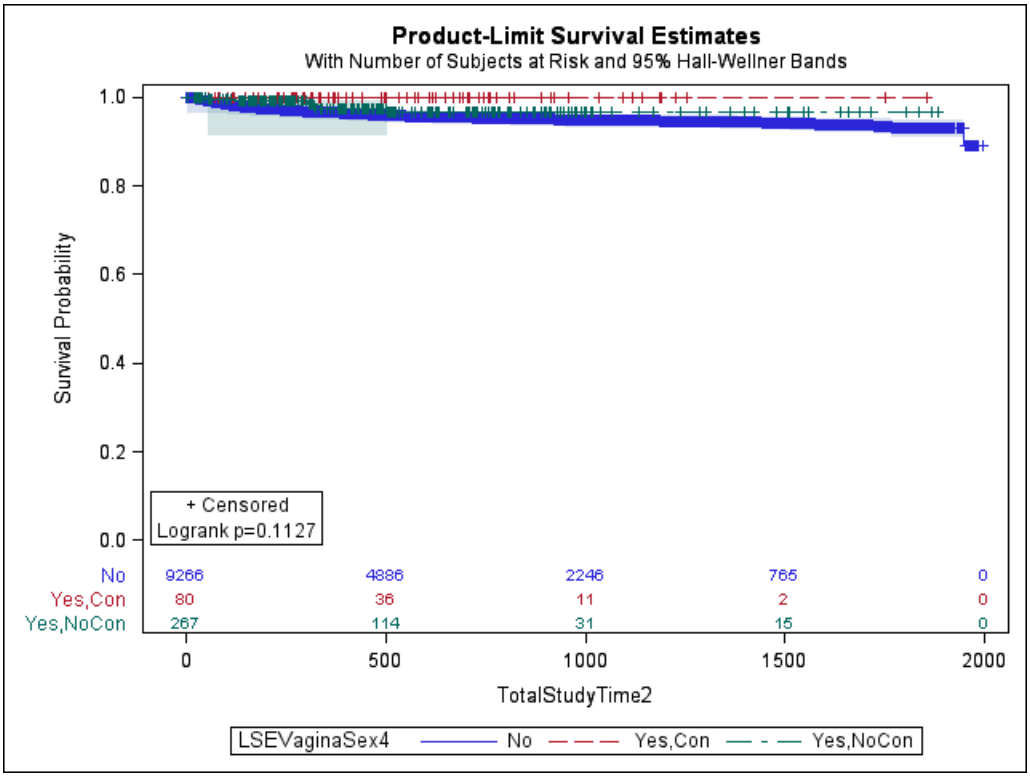


Figure 6.13 - Kaplan-Meier Survival Analysis for Venue for Meeting Partners

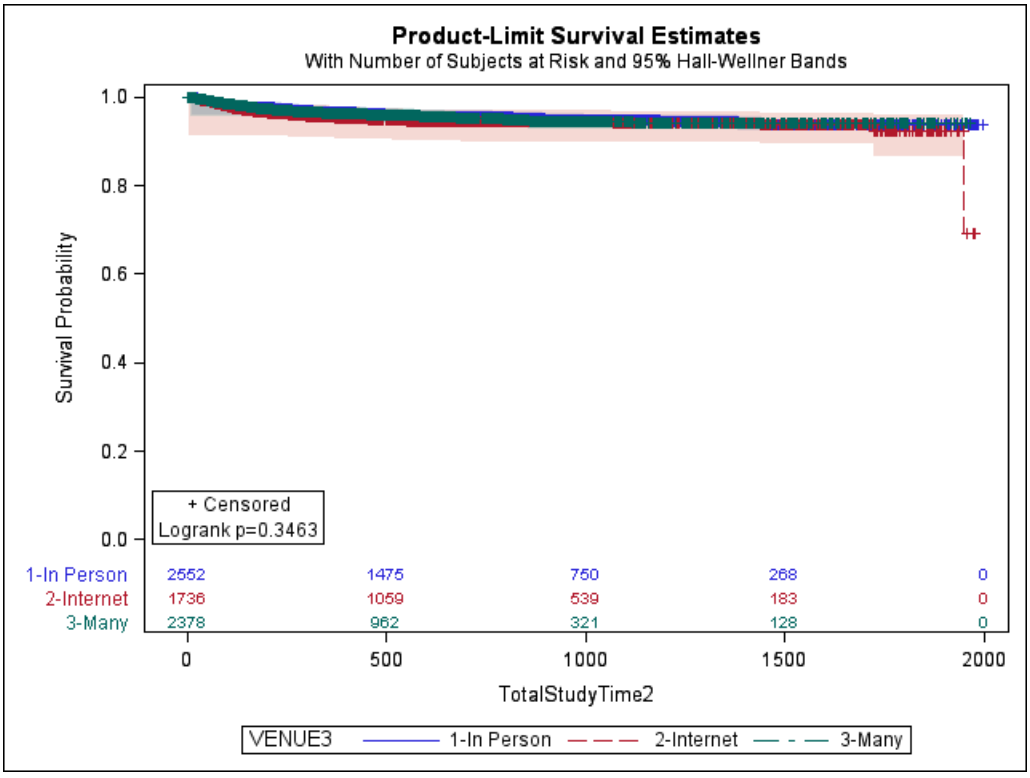


Figure 6.14 - Kaplan-Meier Survival Analysis for Race/Ethnicity of the Last Two Partners

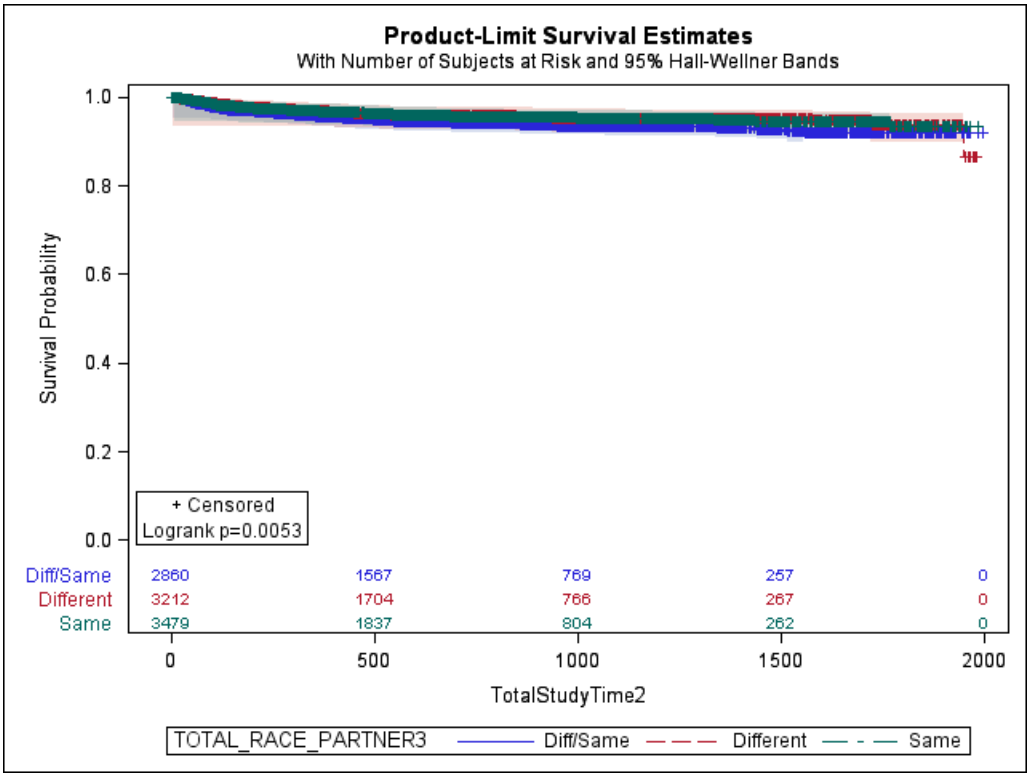
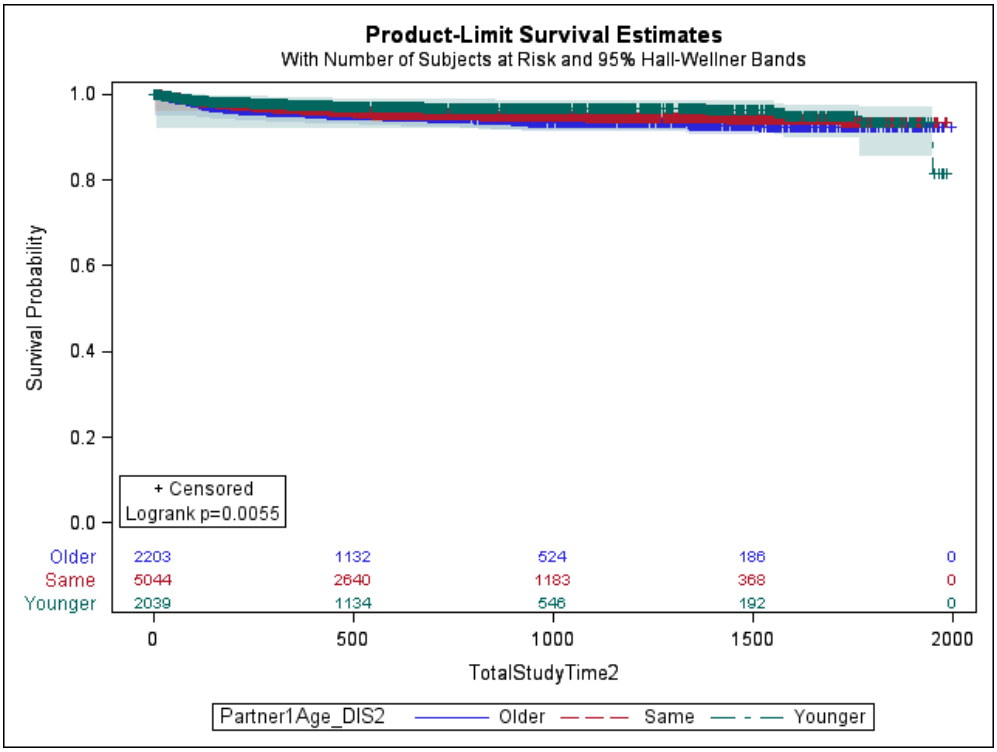
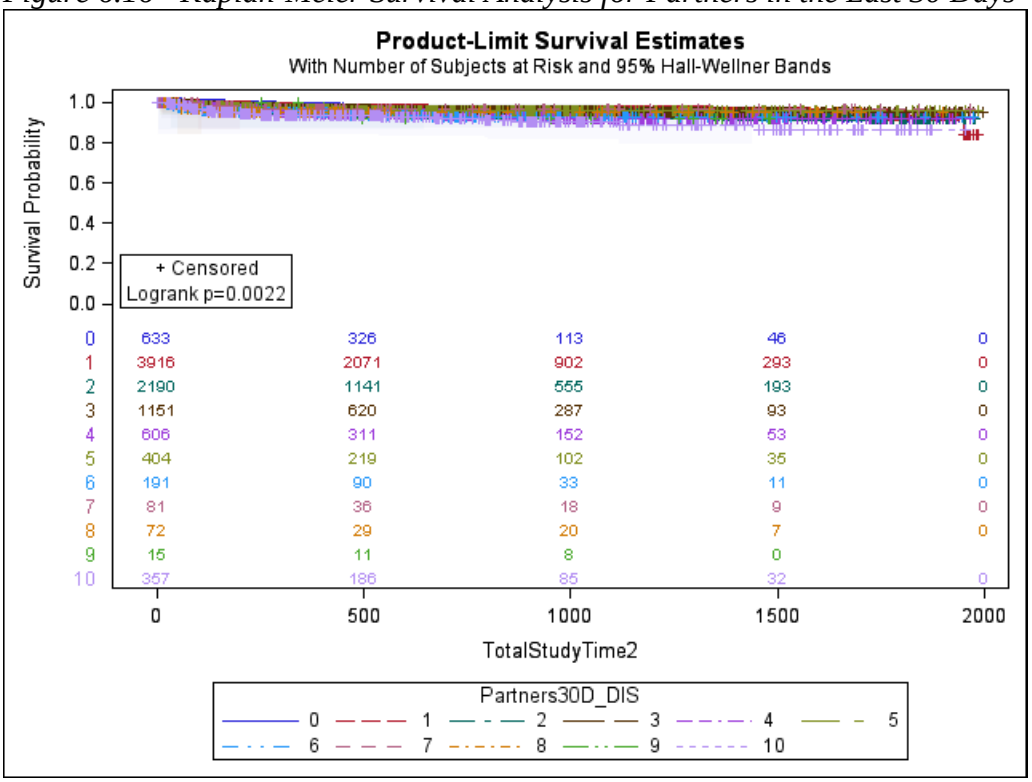


*Figure 6.15 - Kaplan-Meier Survival Analysis for Age of the Last Two Partners**



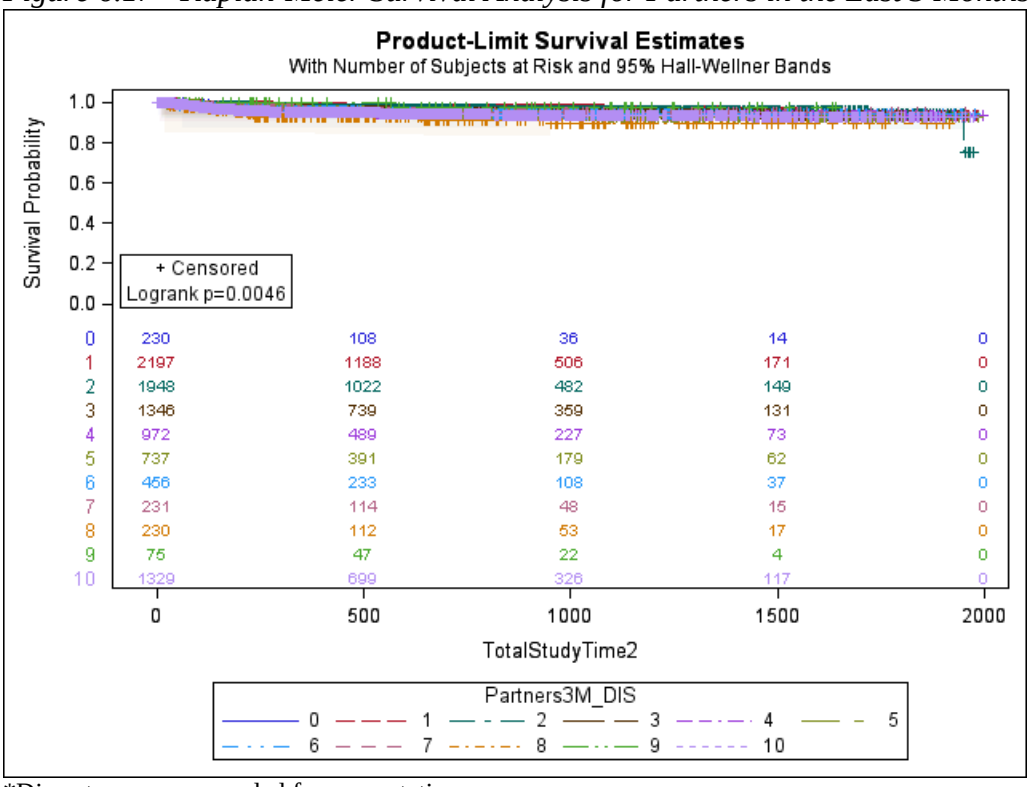
*Discrete responses coded for presentation purposes

*Figure 6.16 - Kaplan-Meier Survival Analysis for Partners in the Last 30 Days**



*Discrete responses coded for presentation purposes

*Figure 6.17 - Kaplan-Meier Survival Analysis for Partners in the Last 3 Months**



*Discrete responses coded for presentation purposes

Figure 6.18 - Kaplan-Meier Survival Analysis for History of Intimate Partner Violence

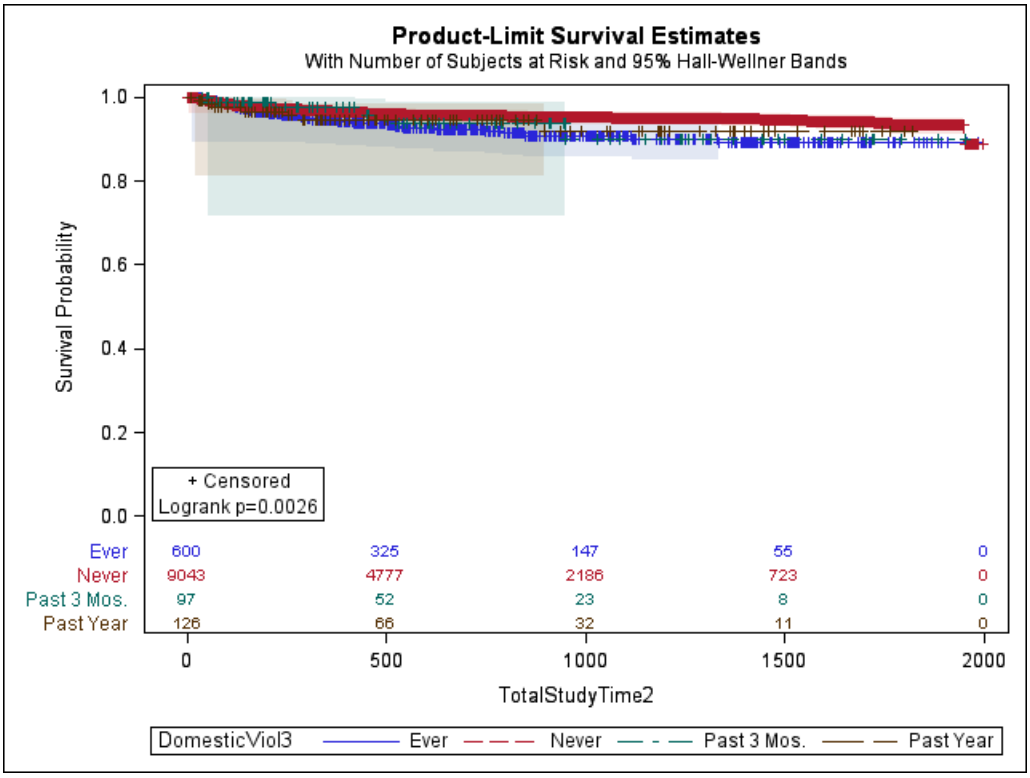
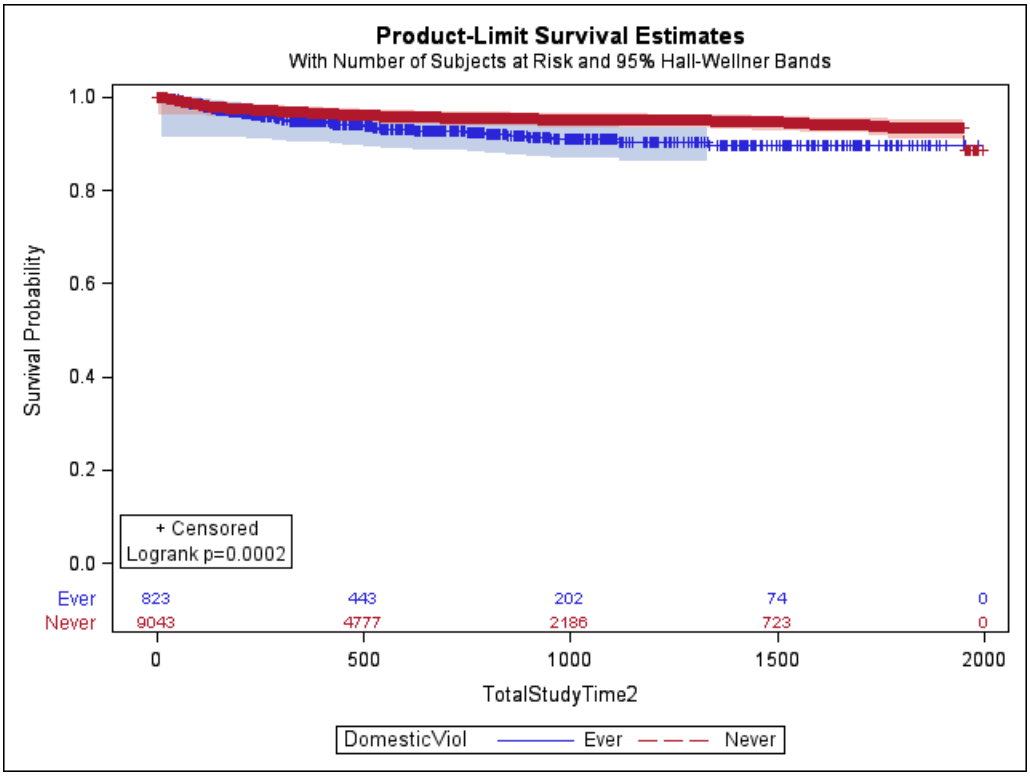


Figure 6.19 - Kaplan-Meier Survival Analysis for History of Intimate Partner Violence (Binary)



Bivariate Survival Analyses – Substance Use Predictors

Seven substance use predictors were analyzed in bivariate analyses: ecstasy use history (Figure 6.20), methamphetamine use history (Figure 6.21), nitrates use history (Figure 6.22), erectile dysfunction drugs (EDD) use history (Figure 6.23), cocaine use history (Figure 6.24), drug count (Figure 6.25), and alcohol use before sex (Figure 6.26).

All substance predictors were significantly associated with HIV seroconversion at follow-up at $p < 0.0001$ except for the use of EDDs ($p = 0.92$), use of cocaine ($p = 0.27$), and alcohol use directly before sex ($p = 0.96$) (Table 6.3). Furthermore, the number of drugs used was significantly related to HIV infection at follow-up ($p < 0.0001$).

Perhaps the most striking differences between HIV-positives and HIV-negatives was in the different proportions of meth use and nitrates use. Approximately 9.7% of meth users tested HIV-positive compared to only 3.6% of individuals who did not report meth use. In addition, 6.7% of nitrate users tested HIV-positive compared to only 3.4% of individuals who did not report nitrate use. Lastly, 12.2% of individuals using five drugs tested HIV-positive versus only 3.2% of individuals reporting no substance use.

Table 6.3 - Bivariate Survival Analyses of Substance Use at Baseline by Final HIV Serostatus (n = 9,981), January 2009 - June 2014.

	HIV-negatives (n = 9,586)		HIV-positives (n = 395)		Total (n = 9,981)
	n	%	n	%	n
Used Ecstasy in the Past 12 Months					$p < 0.0001$
No	8,651	96.3%	330	3.7%	8,981
Yes	860	93.4%	61	6.6%	921
Missing	75	94.9%	4	5.1%	79
Used Meth in the Past 12 Months					$p < 0.0001$
No	9,004	96.4%	338	3.6%	9,342
Yes	502	90.3%	54	9.7%	556
Missing	80	96.4%	3	3.6%	83
Used Nitrates in the Past 12 Months					$p < 0.0001$
No	8,094	96.6%	289	3.4%	8,383
Yes	1,411	93.3%	101	6.7%	1,512
Missing	81	94.2%	5	5.8%	86
Used ED Drugs in the Past 12 Months					$p = 0.92$
No	8,855	96.1%	364	3.9%	9,219
Yes	647	95.9%	28	4.1%	675
Missing	84	96.6%	3	3.4%	87
Used Cocaine in the Past 12 Months					$p = 0.27$
No	8,460	96.1%	343	3.9%	8,803
Yes	1,041	95.5%	49	4.5%	1,090
Missing	85	96.6%	3	3.4%	88
Alcohol Use (Before Sex) in the Past 12 Months					$p = 0.96$
No	5,442	96.2%	214	3.8%	5,656
Yes	4,071	95.8%	179	4.2%	4,250
Missing	73	97.3%	2	2.7%	75
Drug Count (Does Not Include Alcohol)					$p < 0.0001$
0	6,693	96.8%	224	3.2%	6,917
1	1,701	95.2%	86	4.8%	1,787
2	809	93.6%	55	6.4%	864
3	137	91.3%	13	8.7%	150
4	95	94.1%	6	5.9%	101
5	36	87.8%	5	12.2%	41
Missing	115	95.0%	6	5.0%	121
Total	9,586	100.0%	395	100.0%	9,981

Figure 6.20 - Kaplan-Meier Survival Analysis for Ecstasy Use

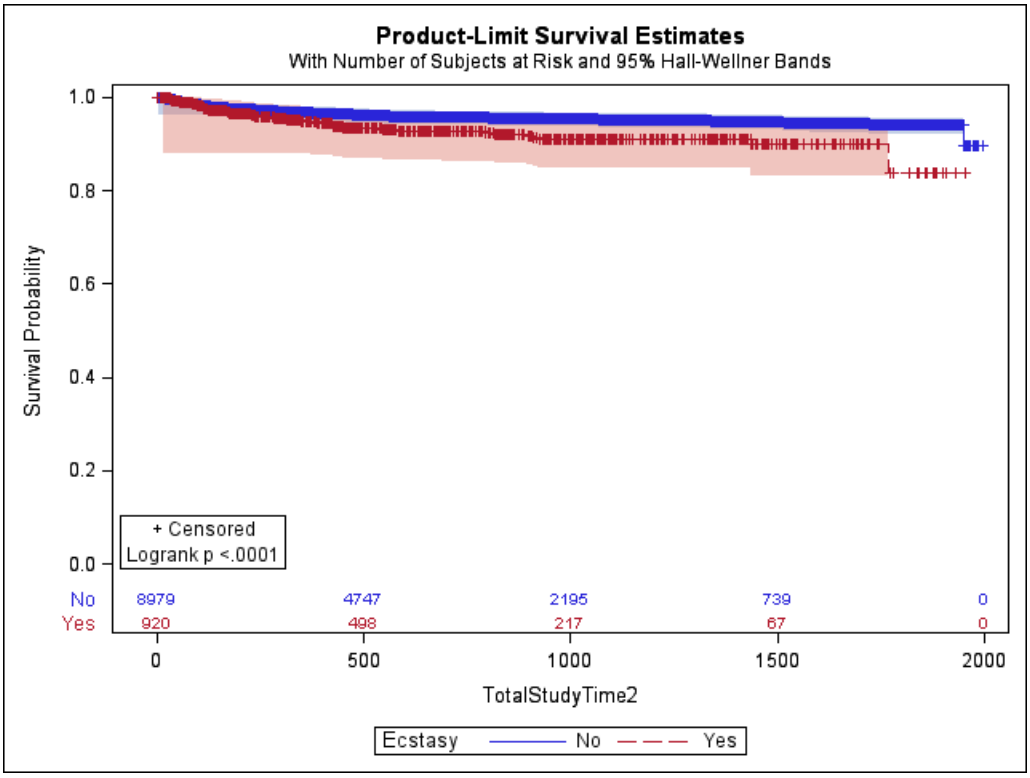


Figure 6.21 - Kaplan-Meier Survival Analysis for Meth Use

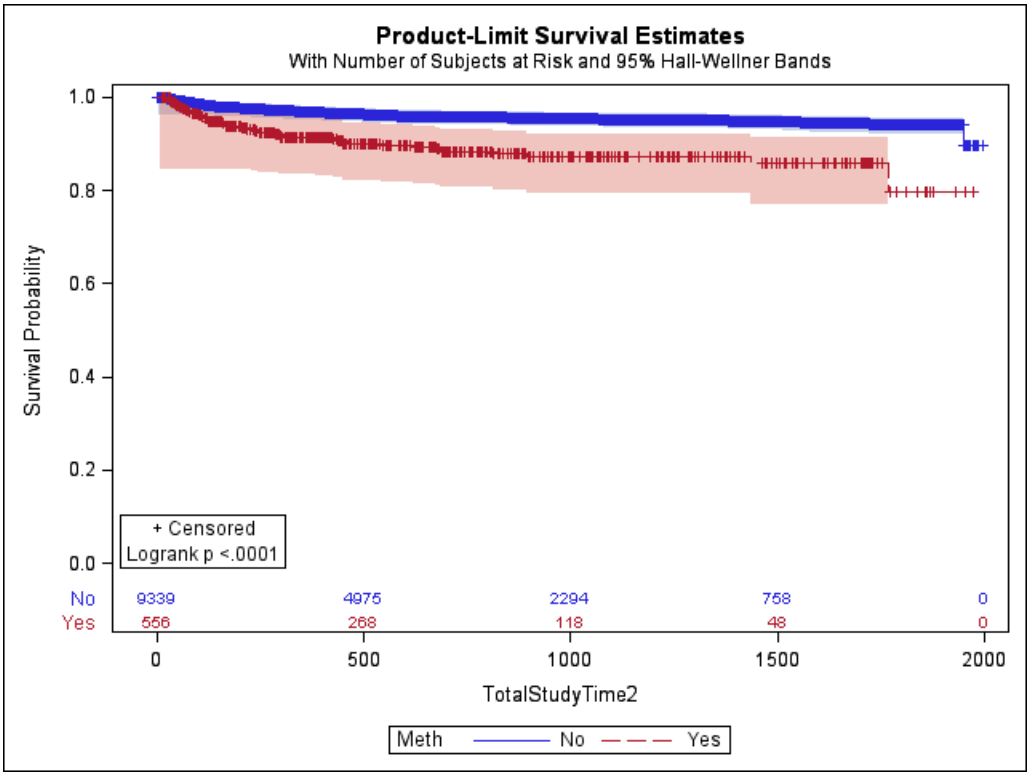


Figure 6.22 - Kaplan-Meier Survival Analysis for Nitrates Use

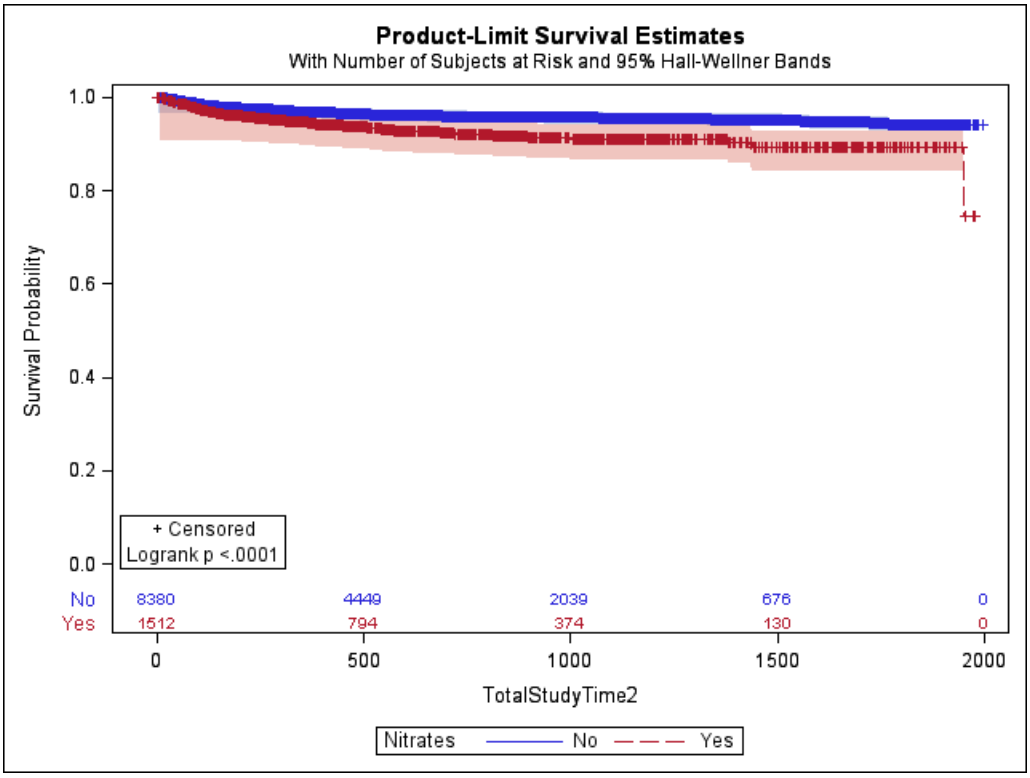


Figure 6.23 - Kaplan-Meier Survival Analysis for ED Drug Use

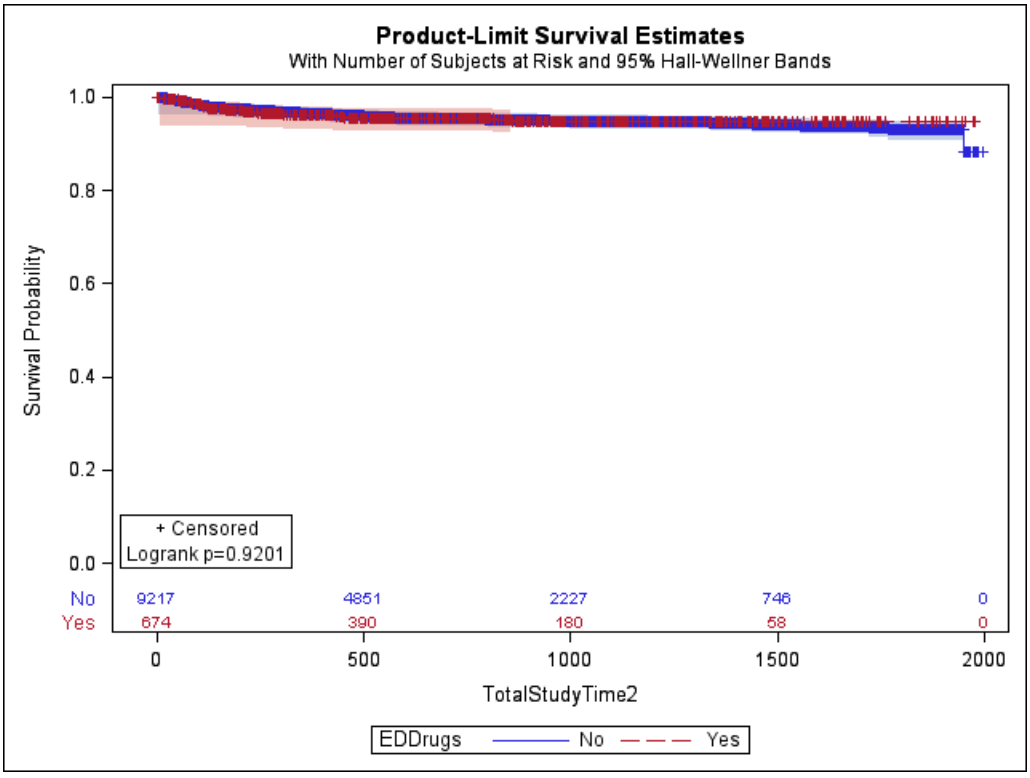


Figure 6.24 - Kaplan-Meier Survival Analysis for Cocaine Use

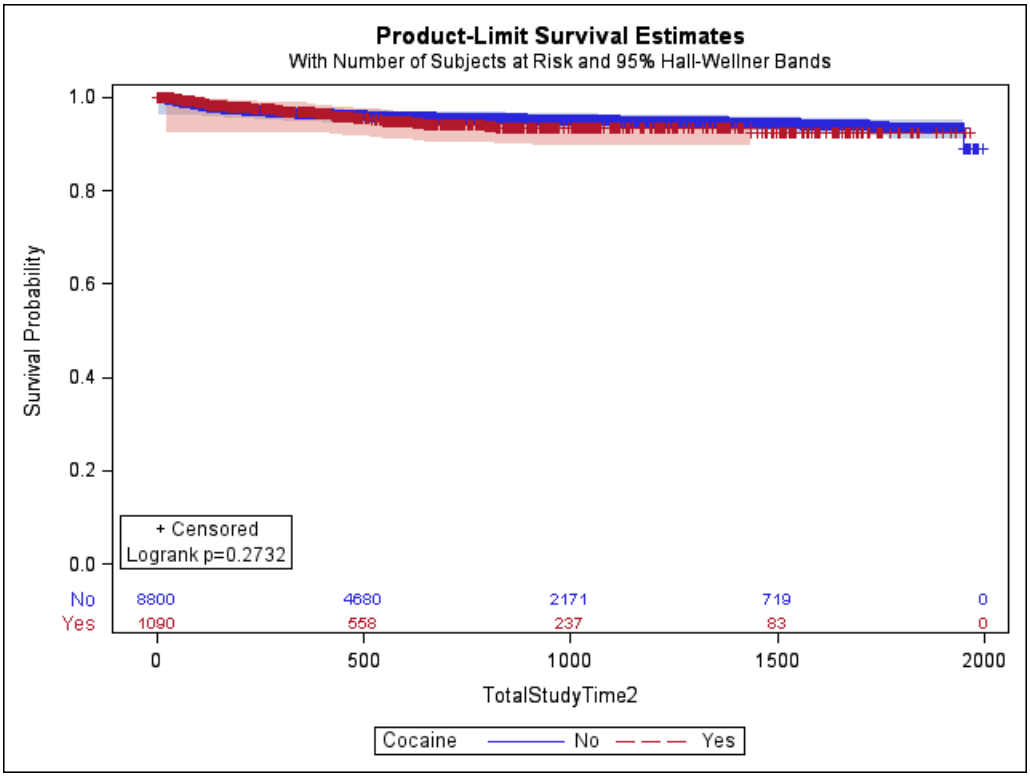


Figure 6.25 - Kaplan-Meier Survival Analysis for Drug Count

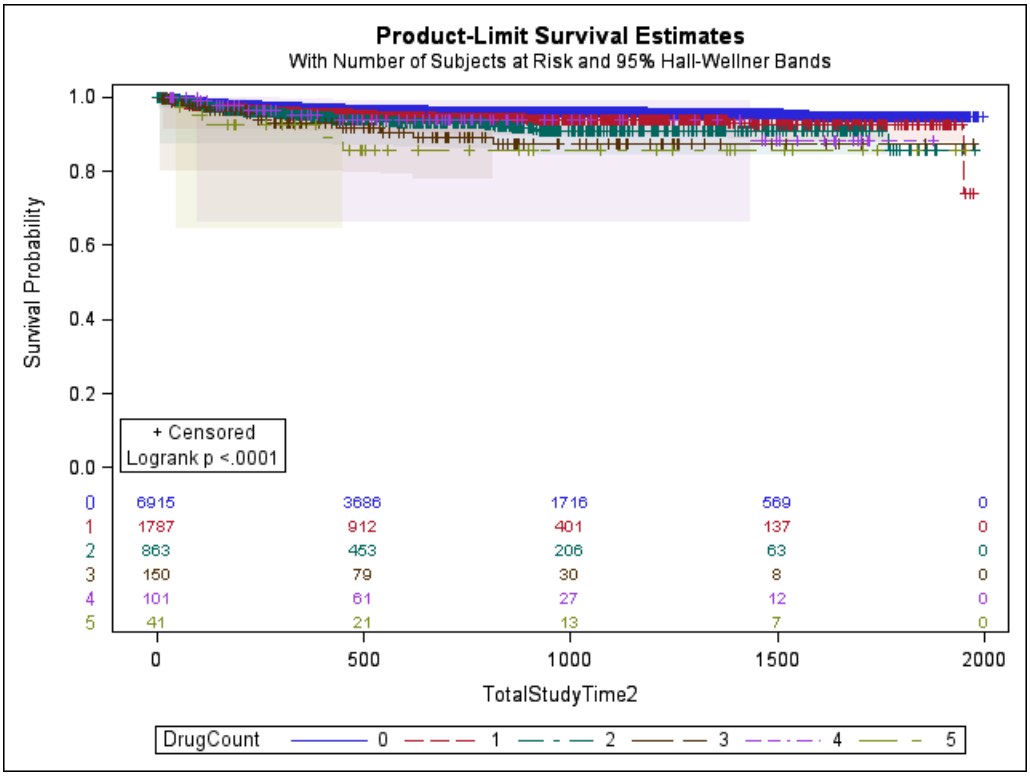
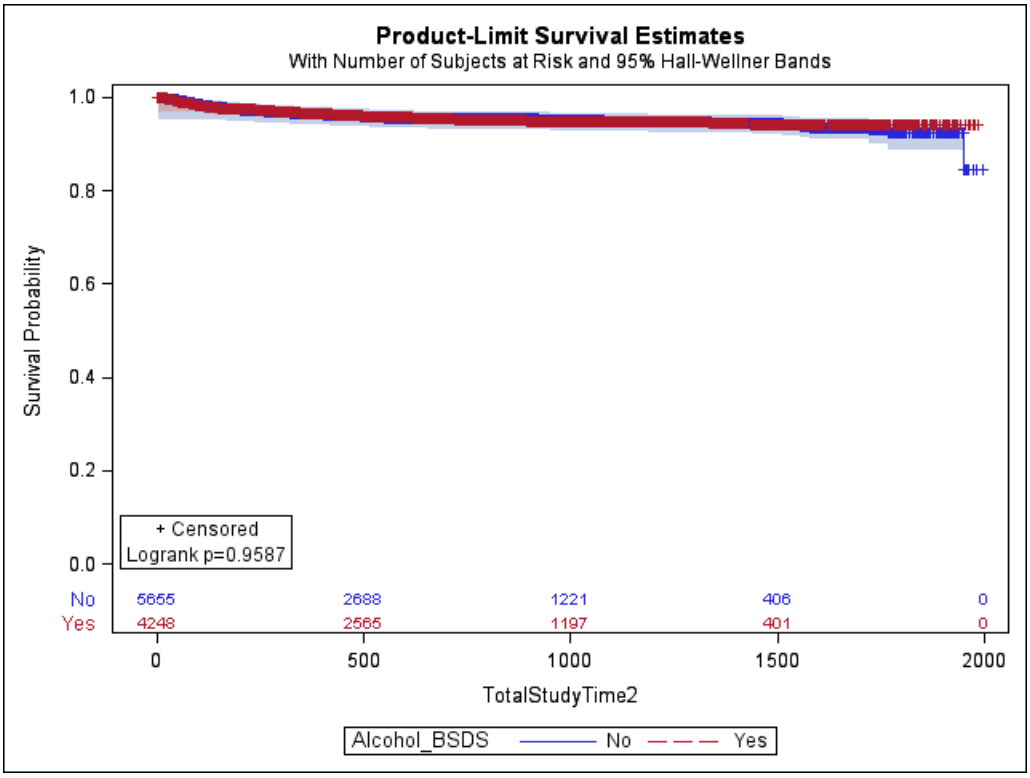


Figure 6.26 - Kaplan-Meier Survival Analysis for Alcohol Use Before Sex



Bivariate Survival Analyses – Demographic Predictors

Lastly, four demographic variables were analyzed in survival analyses: sexual orientation (Figure 6.27), race/ethnicity (six categories) (Figure 6.28), race/ethnicity (four categories) (Figure 6.29), and age group (Figure 6.30). Although orientation was not significantly related to HIV seroconversion ($p = 0.76$), race/ethnicity ($p < 0.0001$) and age group ($p = 0.0001$) were both significantly associated with HIV diagnosis (Table 6.4).

The highest proportion of HIV-positives were among Hispanics (5.4%) and African-Americans (4.9%). The six category version of race/ethnicity showed only a 2.8% seroconversion rate for both Asian/PI testers and individuals who reported a race/ethnicity of "Other." While the Native American seroconversion rate was high at 4.5%, there were only two positive testers out of 42 unique individuals, and thus this estimate is likely unstable. Given the low seroconversion rates among Asian/PI and Other race/ethnicity categories, as well as the low

number of Native Americans, these three categories were collapsed to form the fourth category in a second race/ethnicity variable: White, Hispanic, Black, and Other.

In addition to these findings, individuals in the lowest age categories at baseline were more likely to seroconvert when compared to the higher age categories. Individuals under 25 had the highest seroconversion rates followed by 25-29, 30-39 and 40+. These findings mirror what is found in the literature in that minority MSM as well as young MSM have the highest rates of seroconversion.

Table 6.4 - Bivariate Survival Analyses of Demographics at Baseline by Final HIV Serostatus (n = 9,981), January 2009 - June 2014.

	HIV-negatives (n = 9,586)		HIV-positives (n = 395)		Total (n = 9,981)
	n	%	n	%	n
Orientation					$p = 0.76$
Gay/Homosexual	8,164	96.0%	341	4.0%	8,505
Bisexual	1,174	96.2%	47	3.8%	1,221
Other	248	97.3%	7	2.7%	255
Race/Ethnicity (Six Categories)					$p < 0.0001$
White	4,676	96.8%	155	3.2%	4,831
Hispanic	2,944	94.6%	167	5.4%	3,111
Black	741	95.1%	38	4.9%	779
Asian/PI	828	97.2%	24	2.8%	852
Native American	42	95.5%	2	4.5%	44
Other	280	97.2%	8	2.8%	288
Missing	75	98.7%	1	1.3%	76
Race/Ethnicity (Four Categories)					$p < 0.0001$
White	4,676	96.8%	155	3.2%	4,831
Hispanic	2,944	94.6%	167	5.4%	3,111
Black	741	95.1%	38	4.9%	779
Other	1,150	97.1%	34	2.9%	1,184
Missing	75	98.7%	1	1.3%	76
Age Group					$p = 0.0001$
<25	2,452	95.0%	128	5.0%	2,580
25-29	2,438	95.7%	109	4.3%	2,547
30-39	2,671	96.2%	106	3.8%	2,777
40+	2,025	97.5%	52	2.5%	2,077
Total	9,586	100.0%	395	100.0%	9,981

Figure 6.27 - Kaplan-Meier Survival Analysis for Sexual Orientation

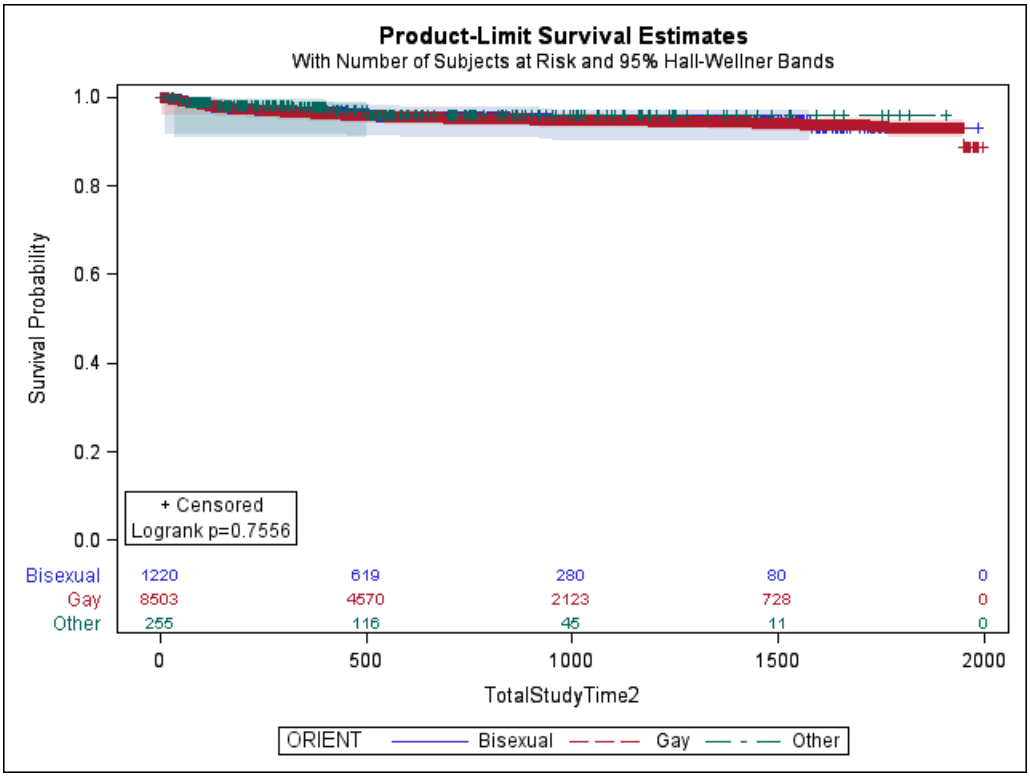


Figure 6.28 - Kaplan-Meier Survival Analysis for Race/Ethnicity (6 Categories)

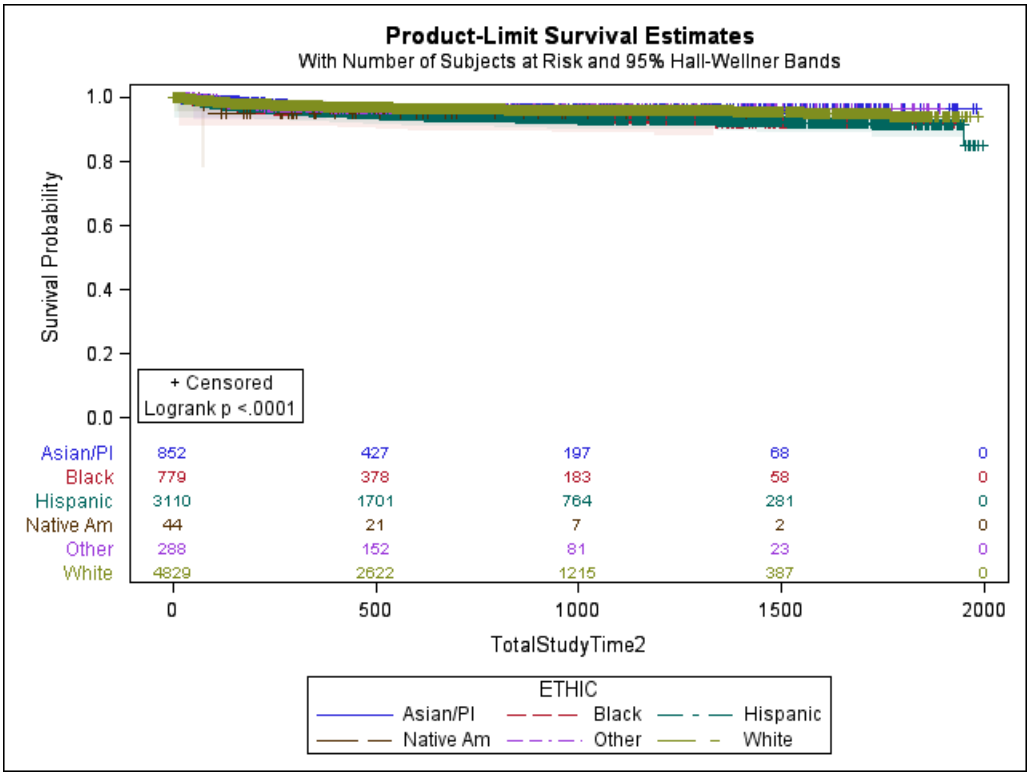


Figure 6.29 - Kaplan-Meier Survival Analysis for Race/Ethnicity (4 Categories)

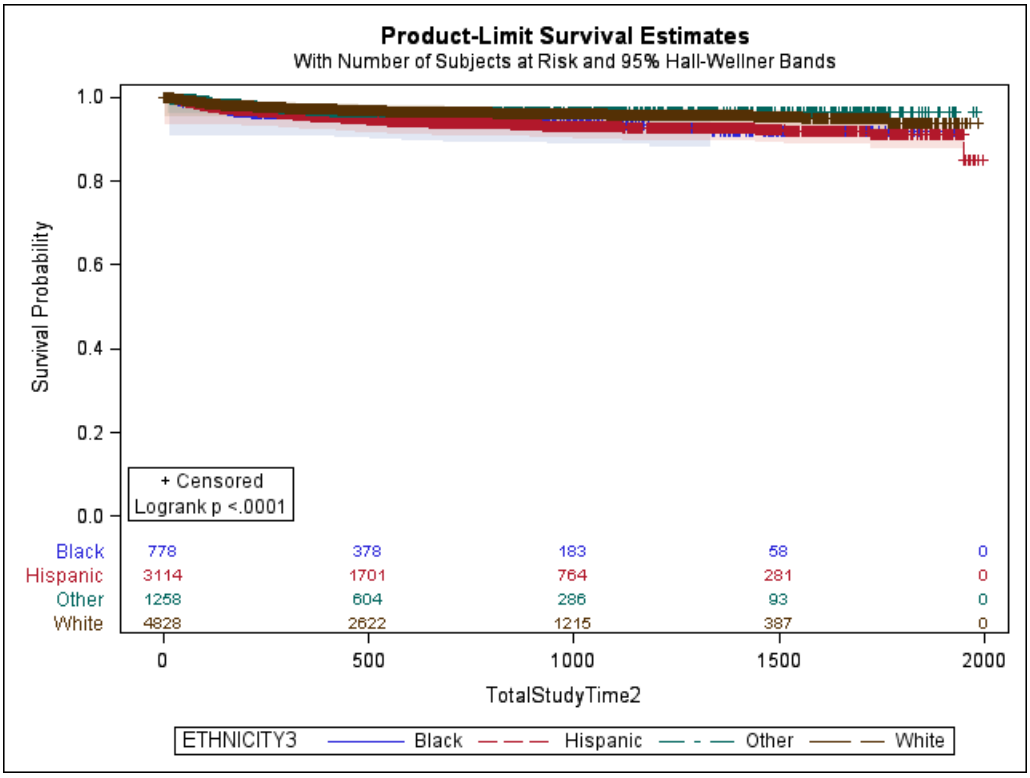
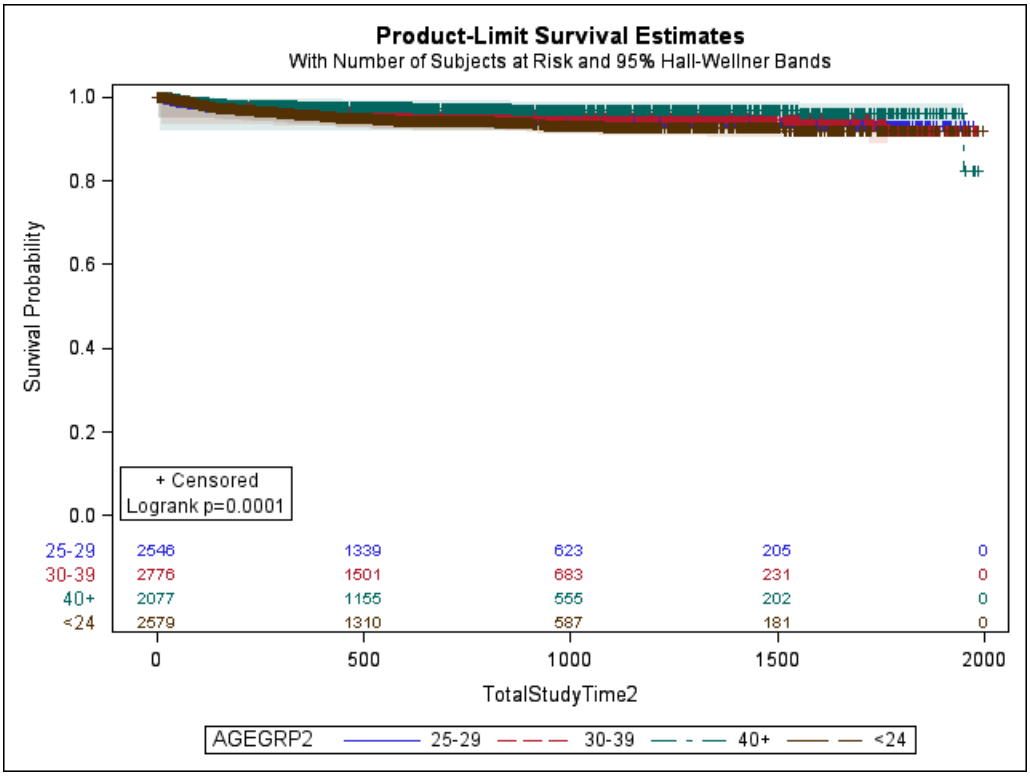


Figure 6.30 - Kaplan-Meier Survival Analysis for Age Group



Investigating Interactions and Different Circumstances for HIV

In addition to the bivariate relationships investigated above, this dissertation also considered moderation and interactions of these variables with race/ethnicity and age group. Moderation indicates that there is a substantively different relationship between the predictor (STI diagnosis) and outcome (HIV infection) by the moderator (age). For example, moderation of the relationship between sexually transmitted infections and HIV infection by race would imply that there is something fundamentally different about the immune responses between races that influences HIV infection when an individual has an STI. More succinctly, this implies that a White person with an STI has a different chance of HIV infection than a African-American person because of a fundamental immune difference between races.

While it may be true that there is an immune system difference by race, this hypothesis is not plausible. Moderation is not likely to exist between the aforementioned bivariate relationships and either age group or race/ethnicity. There is nothing fundamentally different by race/ethnicity or age between these risk factors. Although there are HIV infection disparities affecting young MSM and racial/ethnic minority MSM by race/ethnicity, these disparate rates of infection do *not* necessarily indicate moderation. As stated before, there must be something intrinsically different by the moderating variable for moderation to exist.

In the next investigation, interactions were investigated by plotting survival curves with the variable of interest as the predictor, HIV as the outcome, and either age group or race/ethnicity as the interaction variable (Equation 6.1). Interactions simply state that there is a difference in the relationship between a predictor (meth use) and an outcome (HIV infection) over the level of a third variable (race/ethnicity). For instance, if there was a significant interaction between race and meth use on HIV incidence, it would mean that the relationship

between meth and HIV is impacted by race/ethnicity. Mathematically, the slopes must differ for an interaction to be present. For example, White meth users are more likely to get HIV when compared to African-American meth users.

Equation 6.1 – Interaction Example

$Y = \beta_1 X_1 + \beta_2 X_2 + \beta_1 X_1 * \beta_2 X_2$

$\text{HIV Incidence} = \beta_{Meth} X_{Meth} + \beta_{Race/Ethnicity} X_{Race/Ethnicty} + (\beta_{Meth} X_{Meth} * \beta_{Race/Ethnicity} X_{Race/Ethnicty})$

All potential interactions were tested between each predictor and HIV with both race/ethnicity and age group. This gave a total of 27 potential interactions for race/ethnicity (Table 6.5) and 27 potential interactions for age group (Table 6.6).

In looking at interactions by race/ethnicity, only three interactions were significant: meth use ($p = 0.04$), nitrate use ($p = 0.005$), and number of drugs used ($p = 0.04$). A cross-tabulation revealed that Whites had the highest proportion of meth users at 6% followed closely by Hispanics at 5.8%, African-Americans at 5.2%, and only 4.1% for individuals were classified with an "Other" race/ethnicity (Table 6.5B). Nitrates use patterns were similar with Whites having the greatest proportion (16%) followed by Hispanics (15.1%). However, 15.4% of individuals with an "Other" race/ethnicity reported nitrates use compared with only 11.8% of African-Americans. Although the mean and median were analyzed for the number of drugs used, the mean for each group was below one and the median was zero. Since these measures were not particularly meaningful in interpreting the interaction, they were excluded from the table.

In looking at interactions by age group, only number of partners in the last three months was significant (Table 6.6). As age increased in this sample, a higher average number of sexual partners were reported. Individuals in the Under 25 and 25-29 age groups had a mean of 4.5 partners in the last three months (Table 6.6B). However, individuals in the 30-39 age group had

an average of 5.3 sexual partners and individuals in the 40+ age group reported an average of 5.7 sexual partners in the last three months. However, the median partner count was 3 for all four age categories. The significant interactions for both age group and race/ethnicity will also be tested in the multivariate model for the entire population to determine significance when controlling for other predictors of HIV infection.

Table 6.5 - Testing Interactions by Race/Ethnicity, Controlling for Age (n = 9,981), January 2009 - June 2014.

	DF*	Chi-Square	p-value
Biological Construct			
History of Chlamydia	6	7.3	0.34
History of Gonorrhea	6	6.74	0.35
History of Syphilis	6	2.78	0.82
History of Herpes Simplex Type II	6	1.48	0.97
History of any STI	6	7.54	0.28
Chlamydia Testing Result	3	4.01	0.28
Gonorrhea Testing Result	3	2.98	0.43
Syphilis Testing Result	3	0.23	0.99
Tested Positive for any STI	3	4.71	0.22
Behavioral Construct			
Had Insertive Anal Sex	6	6.08	0.35
Had Recepitve Anal Sex	6	11.79	0.06
Had Vaginal Sex	6	0.29	1.0
Venue for Meeting Partners	6	4.56	0.61
Race/Ethnicity of the Last Two Sexual Partners	6	4.38	0.61
Age of the Last Two Sexual Partners	3	3.91	0.34
Number of Partners in the Past 30 Days	3	0.89	0.9
Number of Partners in the Past 3 Months	3	2.1	0.45
Intimate Partner Violence	3	6.93	0.07
Substance Use Construct			
Used Ecstasy in the Past 12 Months	3	2.72	0.45
Used Meth in the Past 12 Months	3	8.77	**0.04****
Used Nitrates in the Past 12 Months	3	12.6	**0.005****
Used ED Drugs in the Past 12 Months	3	3.47	0.29
Used Cocaine in the Past 12 Months	3	4.31	0.3
Drug Count	3	8.59	**0.04****
Alcohol Use (Before Sex)	3	2.93	0.5
Demographic Construct			
Orientation	6	5.14	0.47
Race/Ethnicity	N/A	N/A	N/A
Age Group	9	1.27	1.0

**Race/ethnicity has four levels (White, Black, Hispanic and Other)*

***Significant at alpha < 0.05*

Table 6.5B - Proportions for Drug Use Variables by Race/Ethnicity, January 2009 - June 2014.

	Meth Use		Nitrates Use	
Race/Ethnicity	n	%	n	%
White	4785	6.0%	4787	16.0%
Hispanic	3088	5.8%	3085	15.1%
Black	773	5.2%	773	11.8%
Other	1177	4.2%	1175	15.4%

Table 6.6 - Testing Interactions by Age Group, Controlling for Race/Ethnicity (n = 9,981), January 2009 - June 2014.

	DF*	Chi-Square	p-value
Biological Construct			
History of Chlamydia	6	4.58	0.60
History of Gonorrhea	6	5.95	0.4
History of Syphilis	6	4.04	0.74
History of Herpes Simplex Type II	6	5.18	0.52
History of any STI	6	4.32	0.7
Chlamydia Testing Result	3	4.62	0.17
Gonorrhea Testing Result	3	5.21	0.18
Syphilis Testing Result	3	1.63	0.6
Tested Positive for any STI	3	2.87	0.44
Behavioral Construct			
Had Insertive Anal Sex	6	3.44	0.72
Had Recepitve Anal Sex	6	2.61	0.87
Had Vaginal Sex	6	2.06	0.92
Venue for Meeting Partners	6	4.88	0.57
Race/Ethnicity of the Last Two Sexual Partners	6	1.22	0.97
Age of the Last Two Sexual Partners	3	2.95	0.44
Number of Partners in the Past 30 Days	3	7.35	0.05
Number of Partners in the Past 3 Months	3	8.92	**0.02****
Intimate Partner Violence	3	3.82	0.32
Substance Use Construct			
Used Ecstasy in the Past 12 Months	3	1.76	0.52
Used Meth in the Past 12 Months	3	4.95	0.16
Used Nitrates in the Past 12 Months	3	2.1	0.54
Used ED Drugs in the Past 12 Months	3	0.48	0.95
Used Cocaine in the Past 12 Months	3	2.17	0.55
Drug Count	3	5.67	0.1
Alcohol Use (Before Sex)	3	0.69	0.92
Demographic Construct			
Orientation	6	6.25	0.29
Race/Ethnicity	9	1.03	1.0
Age Group	N/A	N/A	N/A

**Age group has four levels (<25, 25-29, 30-39 and 40-49)*

***Significant at alpha < 0.05*

Table 6.6B - Measures of Central Tendency for Number of Sexual Partners in the Last Three Months by Age Group, January 2009 - June 2014.

	Number of Sexual Partners in the Last Three Months		
Age Group	Mean	Median	SD
<25	4.5	3	8.5
25-29	4.5	3	6.1
30-39	5.3	3	7.5
40+	5.7	3	7.5

As stated previously, higher rates of infection do not necessarily indicate moderation or interaction. Moderation is not likely present due to the logic previously presented, and there are only a few interactions with these demographic covariates. However, there may just be different circumstances for HIV between demographic subgroups of MSM.

Table 6.7 shows the seropositivity for each combination of race/ethnicity and age group. White MSM 40 years of age or older have a seropositivity rate of 2.3%. In contrast, Hispanics under the age of 25 who have a seropositivty rate of 6.4%. While it is ideal to investigate the circumstances for infection for race/ethnicity and age group simultaneously (e.g., Hispanic MSM under the age of 25), the small number of HIV infections in each group precludes estimation of meaningful results.

However, given the different distributions of age between each racial/ethnic group, and the high rates of seroconversion among some of these subgroups (e.g., African-American MSM between the ages of 25-29 with a seroconversion rate of 6.2%), future analyses looking at these racial/ethnic and age subgroups are important provided said analyses have adequate sample size.

To address the third aim, the race/ethnicity and age subgroups will be analyzed separately to determine if there are different circumstances by subgroup. As shown in Table 6.7, Hispanic MSM have the highest rates of infection among all racial/ethnic subgroups at 5.4%. The first

subgroup analysis will compare Hispanic MSM to White MSM. Furthermore, MSM under the age of 25 have the highest rates of infection among all age groups at 5%. This subgroup will be compared to all individuals 25 years of age or older. These results will be compared to the entire population to determine if there are different circumstances for infection.

Table 6.7 - HIV Seroconversion by Age Group and Race/Ethnicity (n = 9,981)*, January 2009 - June 2014.

	White			Hispanic			Black			Other			Total		
	Total	Positives	%	Total	Positives	%	Total	Positives	%	Total	Positives	%	Total	Positives	%
Age Group															
<25	944	38	4.0%	1,004	64	6.4%	240	13	5.4%	365	13	3.6%	2,553	128	**5.0%**
25-29	1,153	39	3.4%	844	47	5.6%	211	13	6.2%	319	10	3.1%	2,527	109	4.3%
30-39	1,364	46	3.4%	855	43	5.0%	183	8	4.4%	353	8	2.3%	2,755	105	3.8%
40+	1,370	32	2.3%	408	13	3.2%	145	4	2.8%	147	3	2.0%	2,070	52	2.5%
Total	4,831	155	3.2%	3,111	167	**5.4%**	779	38	4.9%	1,184	34	2.9%	9,905	394	4.0%

**76 values are missing for race/ethnicity (respondent either declined or did not provide an answer)*

Bivariate Survival Analyses for African-American and Hispanic MSM Subgroups

In addition to analyzing the results of the entire population, the third aim of the dissertation is to assess if there are different circumstances for HIV infection among African-American and Hispanic subgroups. The sample size for the number of HIV positives was sufficient to warrant analysis for the Hispanic population (n = 3,111 and 167 HIV positives), but the sample size of positives was not large enough to analyze the African-American population (n = 779 and 38 HIV positives). Therefore, Hispanics will be the only racial/ethnic subgroup analyzed in this dissertation. Whites are used as the comparison group since they are the biggest racial/ethnic subgroup and previous studies looking at infection disparities have used Whites as the comparator group (Heckman 1999, Millett 2007, Sullivan 2014).

To determine if there are different circumstances for HIV infection, the bivariate results for the Hispanics will be compared to the bivariate results for Whites. In addition to the thirty variables compared between Whites and Hispanics, four additional variables were analyzed for Hispanics: preferred language, country of origin, length of time in the US (six categories), and length of time in the US (four categories).

For the self-reported history of STI variables, seroconversion in Hispanics was associated with self-reported history of gonorrhea ($p = 0.001$) and self-reported history of syphilis ($p = 0.01$) at baseline (Table 6.8). However, a significant association was not detected between seroconversion and either self-reported history of chlamydia ($p = 0.07$) or self-reported history of Herpes ($p = 0.6$). For the biomedical test results, all STIs tested for at baseline were significantly associated with seroconversion. In contrast, self-reported history of chlamydia was significant in Whites ($p < 0.0001$) (Table 6.9). Furthermore, chlamydia ($p = 0.08$) and syphilis ($p = 0.2$) test results were not significant for Whites, but they were significant for Hispanics.

Table 6.8 - Bivariate Survival Analyses of Biological Risk Behaviors at Baseline by Final HIV Serostatus of Hispanics (n = 3,111), January 2009 - June 2014.

	HIV-negatives (n = 2,944)		HIV-positives (n = 167)		Total (n = 3,111)
	n	%	n	%	n
History of Chlamydia					$p = 0.07$
Never Diagnosed	2,425	94.9%	130	5.1%	2,555
Diagnosed More than One Year Ago	368	94.1%	23	5.9%	391
Diagnosed Less than One Year Ago	132	90.4%	14	9.6%	146
Missing	19	100.0%	0	0.0%	19
History of Gonorrhea					$p = 0.001$
Never Diagnosed	2,306	95.1%	120	4.9%	2,426
Diagnosed More than One Year Ago	478	94.5%	28	5.5%	506
Diagnosed Less than One Year Ago	141	88.1%	19	11.9%	160
Missing	19	100.0%	0	0.0%	19
History of Syphilis					$p = 0.01$
Never Diagnosed	2,698	94.9%	146	5.1%	2,844
Diagnosed More than One Year Ago	133	94.3%	8	5.7%	141
Diagnosed Less than One Year Ago	78	86.7%	12	13.3%	90
Missing	35	97.2%	1	2.8%	36
History of Herpes Simplex Type II					$p = 0.60$
Never Diagnosed	2,576	94.5%	150	5.5%	2,726
Diagnosed More than One Year Ago	158	93.5%	11	6.5%	169
Missing	210	97.2%	6	2.8%	216
History of any STI					$p = 0.0008$
Never Diagnosed	1,700	95.4%	82	4.6%	1,782
Diagnosed More than One Year Ago	752	94.4%	45	5.6%	797
Diagnosed Less than One Year Ago	367	90.4%	39	9.6%	406
Missing	125	99.2%	1	0.8%	126
Chlamydia Testing Result					$p = 0.02$
Negative	2,419	94.8%	132	5.2%	2,551
Positive	396	92.1%	34	7.9%	430
Missing	129	99.2%	1	0.8%	130
Gonorrhea Testing Result					$p = 0.002$
Negative	2,366	95.0%	125	5.0%	2,491
Positive	455	91.7%	41	8.3%	496
Missing	123	99.2%	1	0.8%	124
Syphilis Testing Result					$p = 0.0002$
Negative	2,554	95.0%	134	5.0%	2,688
Positive	39	83.0%	8	17.0%	47
Missing	351	93.4%	25	6.6%	376
Tested Positive for any STI					$p < 0.0001$
Negative	1,870	95.9%	80	4.1%	1,950
Positive	784	91.9%	69	8.1%	853
Missing	290	94.2%	18	5.8%	308
Total	2,944	94.6%	167	5.4%	3,111

Table 6.9 - Bivariate Survival Analyses of Biological Risk Behaviors at Baseline by Final HIV Serostatus of Whites (n = 4,831), January 2009 - June 2014.

	HIV-negatives (n = 4,676)		HIV-positives (n = 155)		Total (n = 4,831)
	n	%	n	%	n
History of Chlamydia					$p < 0.0001$
Never Diagnosed	3,771	97.4%	99	2.6%	3,870
Diagnosed More than One Year Ago	723	94.9%	39	5.1%	762
Diagnosed Less than One Year Ago	153	91.1%	15	8.9%	168
Missing	29	93.5%	2	6.5%	31
History of Gonorrhea					$p < 0.0001$
Never Diagnosed	3,393	97.5%	88	2.5%	3,481
Diagnosed More than One Year Ago	1,048	96.0%	44	4.0%	1,092
Diagnosed Less than One Year Ago	197	90.4%	21	9.6%	218
Missing	38	95.0%	2	5.0%	40
History of Syphilis					$p = 0.0005$
Never Diagnosed	4,360	97.1%	132	2.9%	4,492
Diagnosed More than One Year Ago	183	93.8%	12	6.2%	195
Diagnosed Less than One Year Ago	81	91.0%	8	9.0%	89
Missing	52	94.5%	3	5.5%	55
History of Herpes Simplex Type II					$p = 0.51$
Never Diagnosed	4,007	96.7%	137	3.3%	4,144
Diagnosed More than One Year Ago	249	98.0%	5	2.0%	254
Diagnosed Less than One Year Ago	77	97.5%	2	2.5%	79
Missing	343	96.9%	11	3.1%	354
History of any STI					$p < 0.0001$
Never Diagnosed	2,479	98.0%	51	2.0%	2,530
Diagnosed More than One Year Ago	1,528	96.0%	63	4.0%	1,591
Diagnosed Less than One Year Ago	471	93.3%	34	6.7%	505
Missing	198	96.6%	7	3.4%	205
Chlamydia Testing Result					$p = 0.08$
Negative	3,851	97.1%	115	2.9%	3,966
Positive	440	93.0%	33	7.0%	473
Missing	385	98.2%	7	1.8%	392
Gonorrhea Testing Result					$p = 0.0002$
Negative	3,740	97.0%	114	3.0%	3,854
Positive	564	94.3%	34	5.7%	598
Missing	372	98.2%	7	1.8%	379
Syphilis Testing Result					$p = 0.2$
Negative	4,103	97.0%	126	3.0%	4,229
Positive	28	93.3%	2	6.7%	30
Missing	545	95.3%	27	4.7%	572
Tested Positive for any STI					$p < 0.0001$
Negative	3,219	97.5%	83	2.5%	3,302
Positive	933	94.3%	56	5.7%	989
Missing	524	97.0%	16	3.0%	540
Total	4,676	96.8%	155	3.2%	4,831

Similar to the White population, the relationship was significant between seroconversion and receptive anal sex ($p = 0.007$) (Table 6.10 for Hispanics and 6.11 for Whites). Also similar to the White population, there were no statistically significant differences between seroconversion and insertive anal sex ($p = 0.72$), vaginal sex ($p = 0.38$), venue for meeting partners ($p = 0.26$), and age of the last two sexual partners ($p = 0.47$). In contrast to the White population, there was a significant relationship between seroconversion and race/ethnicity of the last two sexual partners ($p = 0.0008$) and intimate partner violence ($p = 0.003$). Also in contrast to the White population, there was no significant relationship for Hispanics between seroconversion and number of partners in the last 30 days ($p = 0.28$) and number of partners in the last three months ($p = 0.07$).

Table 6.10 - Bivariate Survival Analyses of Sexual Behavioral Risks at Baseline by Final HIV Serostatus of Hispanics (n = 3,111), January 2009 - June 2014.

	HIV-negatives (n = 2,944)		HIV-positives (n = 167)		Total (n = 3,111)
	n	%	n	%	n
Had Insertive Anal Sex					$p = 0.72$
No	1,558	94.9%	84	5.1%	1,642
Yes, with Condom	657	94.5%	38	5.5%	695
Yes, without Condom	712	94.2%	44	5.8%	756
Missing	17	94.4%	1	5.6%	18
Had Receptive Anal Sex					$p = 0.007$
No	1,680	95.6%	78	4.4%	1,758
Yes, with Condom	556	93.8%	37	6.2%	593
Yes, without Condom	700	93.1%	52	6.9%	752
Missing	8	100.0%	0	0.0%	8
Had Vaginal Sex					$p = 0.38$
No	2,752	94.5%	159	5.5%	2,911
Yes with a Condom	21	100.0%	0	0.0%	21
Yes without a Condom	73	97.3%	2	2.7%	75
Missing	98	94.2%	6	5.8%	104
Venue for Meeting Partners					$p = 0.26$
In Person	818	94.2%	50	5.8%	868
Online	408	92.7%	32	7.3%	440
More than One	609	96.2%	24	3.8%	633
Missing	1,109	94.8%	61	5.2%	1,170

Race/Ethnicity of the Last Two Sexual Partners					$p = 0.0008$
Both Partners Different Race	1,252	96.0%	52	4.0%	1,304
Both Partners Same Race	574	95.7%	26	4.3%	600
One Partner Same Race, One Different	1,100	92.5%	89	7.5%	1,189
Missing	18	100.0%	0	0.0%	18
Age of the Last Two Sexual Partners*					$p = 0.47$
More than 5 Years Older	738	94.6%	42	5.4%	780
Within Five Years of Age	1,587	94.5%	93	5.5%	1,680
More than 5 Years Younger	416	95.6%	19	4.4%	435
Missing	203	94.0%	13	6.0%	216
Number of Partners in the Past 30 Days*					$p = 0.28$
0	185	93.9%	12	6.1%	197
1	1,271	95.3%	63	4.7%	1,334
2	636	93.9%	41	6.1%	677
3	316	96.0%	13	4.0%	329
4	142	91.6%	13	8.4%	155
5	95	95.0%	5	5.0%	100
6	53	91.4%	5	8.6%	58
7	18	100.0%	0	0.0%	18
8	14	93.3%	1	6.7%	15
9	6	85.7%	1	14.3%	7
10 or More	87	91.6%	8	8.4%	95
Missing	121	96.0%	5	4.0%	126
Number of Partners in the Past 3 Months*					$p = 0.07$
0	74	91.4%	7	8.6%	81
1	755	96.3%	29	3.7%	784
2	640	95.4%	31	4.6%	671
3	393	94.2%	24	5.8%	417
4	254	92.4%	21	7.6%	275
5	187	94.0%	12	6.0%	199
6	126	92.6%	10	7.4%	136
7	61	93.8%	4	6.2%	65
8	47	88.7%	6	11.3%	53
9	18	100.0%	0	0.0%	18
10 or More	302	93.5%	21	6.5%	323
Missing	87	97.8%	2	2.2%	89
Intimate Partner Violence					$p = 0.003$
Never	2,604	95.0%	136	5.0%	2,740
Ever	213	89.5%	25	10.5%	238
Past Year	50	90.9%	5	9.1%	55
Past Three Months	37	97.4%	1	2.6%	38
Missing	40	100.0%	0	0.0%	40
Intimate Partner Violence					$p = 0.001$
Never	2,604	95.0%	136	5.0%	2,740
Ever, Past Year, or Past Three Months	300	90.6%	31	9.4%	331
Missing	40	100.0%	0	0.0%	40
Total	2,944	94.6%	167	100.0%	3,111

**Discrete values for presentation purposes only; continuous values used in all analyses*

Table 6.11 - Bivariate Survival Analyses of Sexual Behavioral Risks at Baseline by Final HIV Serostatus of Whites (n = 4,831), January 2009 - June 2014.

	HIV-negatives (n = 4,676)		HIV-positives (n = 155)		Total (n = 4,831)
	n	%	n	%	n
Had Insertive Anal Sex					$p = 0.31$
No	2,745	96.8%	91	3.2%	2,836
Yes, with Condom	944	97.2%	27	2.8%	971
Yes, without Condom	953	96.5%	35	3.5%	988
Missing	34	94.4%	2	5.6%	36
Had Receptive Anal Sex					$p < 0.0001$
No	3,098	97.8%	70	2.2%	3,168
Yes, with Condom	781	96.7%	27	3.3%	808
Yes, without Condom	788	93.3%	57	6.7%	845
Missing	9	90.0%	1	10.0%	10
Had Vaginal Sex					$p = 0.56$
No	4,347	96.9%	140	3.1%	4,487
Yes with a Condom	36	100.0%	0	0.0%	36
Yes without a Condom	128	97.7%	3	2.3%	131
Missing	165	93.2%	12	6.8%	177
Venue for Meeting Partners					$p = 0.2$
In Person	1,167	97.4%	31	2.6%	1,198
Online	884	96.1%	36	3.9%	920
More than One	1,170	96.6%	41	3.4%	1,211
Missing	1,455	96.9%	47	3.1%	1,502
Race/Ethnicity of the Last Two Sexual Partners					p = 0.3
Both Partners Different Race	736	97.6%	18	2.4%	754
Both Partners Same Race	2,544	96.8%	84	3.2%	2,628
One Partner Same Race, One Different	1,366	96.4%	51	3.6%	1,417
Missing	30	93.8%	2	6.3%	32
Age of the Last Two Sexual Partners*					p = 0.06
More than 5 Years Older	836	95.7%	38	4.3%	874
Within Five Years of Age	2,260	97.0%	71	3.0%	2,331
More than 5 Years Younger	1,250	97.2%	36	2.8%	1,286
Missing	330	97.1%	10	2.9%	340
Number of Partners in the Past 30 Days*					p = 0.04
0	292	99.0%	3	1.0%	295
1	1,718	97.2%	50	2.8%	1,768
2	1,034	96.7%	35	3.3%	1,069
3	571	97.6%	14	2.4%	585
4	309	96.0%	13	4.0%	322
5	218	96.0%	9	4.0%	227
6	95	95.0%	5	5.0%	100
7	46	95.8%	2	4.2%	48
8	39	95.1%	2	4.9%	41
9	4	100.0%	0	0.0%	4
10 or More	187	93.0%	14	7.0%	201

Missing	163	95.3%	8	4.7%	171
Number of Partners in the Past 3 Months*					p = 0.008
0	103	100.0%	0	0.0%	103
1	928	97.3%	26	2.7%	954
2	856	98.1%	17	1.9%	873
3	618	96.9%	20	3.1%	638
4	492	96.1%	20	3.9%	512
5	354	97.3%	10	2.7%	364
6	231	97.1%	7	2.9%	238
7	131	97.0%	4	3.0%	135
8	117	92.1%	10	7.9%	127
9	44	100.0%	0	0.0%	44
10 or More	718	95.2%	36	4.8%	754
Missing	84	94.4%	5	5.6%	89
Intimate Partner Violence					$p = 0.42$
Never	4,280	96.8%	141	3.2%	4,421
Ever	253	96.6%	9	3.4%	262
Past Year	56	98.2%	1	1.8%	57
Past Three Months	38	92.7%	3	7.3%	41
Missing	49	98.0%	1	2.0%	50
Intimate Partner Violence					$p = 0.88$
Never	4,280	96.8%	141	3.2%	4,421
Ever, Past Year, or Past Three Months	347	96.4%	13	3.6%	360
Missing	49	98.0%	1	2.0%	50
Total	4,675	96.8%	155	3.2%	4,830

**Discrete values for presentation purposes only; continuous values used in all analyses*

The bivariate values for the substance use construct for Hispanics (Table 6.12) were much different than the values for the White population (Table 6.13). The only significant relationship for the substance use construct for Hispanics was between seroconversion and meth use ($p = 0.0005$). In contrast to the White population, there was no relationship between seroconversion and ecstasy use ($p = 0.22$), nitrate use ($p = 0.41$), ED drug use ($p = 0.27$), cocaine use ($p = 0.76$), or number of drugs reported ($p = 0.38$).

Table 6.12 - Bivariate Survival Analyses of Substance Use at Baseline by Final HIV Serostatus of Hispanics (n = 3,111), January 2009 - June 2014.

	HIV-negatives (n = 2,944)		HIV-positives (n = 167)		Total (n = 3,111)
	n	%	n	%	n
Used Ecstasy in the Past 12 Months					$p = 0.22$
No	2,684	94.8%	147	5.2%	2,831
Yes	238	93.0%	18	7.0%	256
Missing	22	91.7%	2	8.3%	24
Used Meth in the Past 12 Months					$p = 0.0005$
No	2,761	94.9%	147	5.1%	2,908
Yes	161	89.4%	19	10.6%	180
Missing	22	95.7%	1	4.3%	23
Used Nitrates in the Past 12 Months					$p = 0.41$
No	2,484	94.8%	136	5.2%	2,620
Yes	436	93.8%	29	6.2%	465
Missing	24	92.3%	2	7.7%	26
Used ED Drugs in the Past 12 Months					$p = 0.27$
No	2,807	94.5%	162	5.5%	2,969
Yes	113	96.6%	4	3.4%	117
Missing	24	96.0%	1	4.0%	25
Used Cocaine in the Past 12 Months					$p = 0.76$
No	2,629	94.6%	149	5.4%	2,778
Yes	290	94.5%	17	5.5%	307
Missing	25	96.2%	1	3.8%	26
Alcohol Use (Before Sex) in the Past 12 Months					$p = 0.29$
No	1,687	94.5%	99	5.5%	1,786
Yes	1,239	94.8%	68	5.2%	1,307
Missing	18	100.0%	0	0.0%	18
Drug Count					$p = 0.38$
0	2,108	95.0%	111	5.0%	2,219
1	518	94.4%	31	5.6%	549
2	217	92.7%	17	7.3%	234
3	31	93.9%	2	6.1%	33
4	27	96.4%	1	3.6%	28
5	9	81.8%	2	18.2%	11
Missing	34	91.9%	3	8.1%	37
Total	2,944	94.6%	167	100.0%	3,111

Table 6.13 - Bivariate Survival Analyses of Substance Use at Baseline by Final HIV Serostatus of Whites (n = 4,831), January 2009 - June 2014.

	HIV-negatives (n = 4,676)		HIV-positives (n = 155)		Total (n = 4,831)
	n	%	n	%	n
Used Ecstasy in the Past 12 Months					$p < 0.0001$
No	4,180	97.2%	121	2.8%	4,301
Yes	456	93.4%	32	6.6%	488
Missing	40	95.2%	2	4.8%	42
Used Meth in the Past 12 Months					$p < 0.0001$
No	4,378	97.3%	122	2.7%	4,500
Yes	254	89.1%	31	10.9%	285
Missing	44	95.7%	2	4.3%	46
Used Nitrates in the Past 12 Months					$p < 0.0001$
No	3,923	97.5%	100	2.5%	4,023
Yes	712	93.2%	52	6.8%	764
Missing	41	93.2%	3	6.8%	44
Used ED Drugs in the Past 12 Months					$p = 0.03$
No	4,178	97.1%	124	2.9%	4,302
Yes	453	95.0%	24	5.0%	477
Missing	45	95.7%	2	4.3%	47
Used Cocaine in the Past 12 Months					$p = 0.02$
No	4,032	97.0%	124	3.0%	4,156
Yes	602	95.4%	29	4.6%	631
Missing	42	95.5%	2	4.5%	44
Alcohol Use (Before Sex) in the Past 12 Months					$p = 0.25$
No	2,507	97.2%	72	2.8%	2,579
Yes	2,127	96.3%	81	3.7%	2,208
Missing	42	95.5%	2	4.5%	44
Drug Count					$p < 0.0001$
0	3,135	97.8%	69	2.2%	3,204
1	855	96.3%	33	3.7%	888
2	467	93.4%	33	6.6%	500
3	87	90.6%	9	9.4%	96
4	56	91.8%	5	8.2%	61
5	21	87.5%	3	12.5%	24
Missing	55	94.8%	3	5.2%	58
Total	4,676	96.8%	155	100.0%	4,831

Similar to the White population, there was no difference in seroconversion by reported sexual orientation ($p = 0.44$) or age group ($p = 0.11$) (Table 6.14 for Hispanics and 6.15 for Whites). While there was no discernable trend by sexual orientation, there was a trend by age group with individuals in the less than 25 category for both Whites and Hispanics presenting

with the highest seropositivity rates. Therefore, while the p-value was not significant for either subgroup, this may represent a Type II error, or a false non-significant result, given the trend for lower seropositivity as age increases in both these groups.

In addition, four more demographic variables were analyzed for the Hispanic population including preferred language, country of origin, and length of time in the United States (2 variables: one with four categories and one dichotomous variable). There were no differences detected between seroconverters and non-seroconverters by either language ($p = 0.73$) or length of time in the US ($p = 0.23$). However, there were differences detected by country of origin ($p = 0.008$). Approximately 10.6% of all individuals from Central America seroconverted during the study period compared to only 4.8% of individuals who were born in the United States. This result, along with the results discussed previously, show that there may be different circumstances for HIV infection between the White MSM and Hispanic MSM subgroups.

Table 6.14 - Bivariate Survival Analyses of Demographics at Baseline by Final HIV Serostatus of Hispanics (n = 3,111), January 2009 - June 2014.

	HIV-negatives (n = 2,944)		HIV-positives (n = 167)		Total (n = 3,111)
	n	%	n	%	n
Orientation					$p = 0.44$
Gay/Homosexual	2,527	94.6%	144	5.4%	2,671
Bisexual	356	94.2%	22	5.8%	378
Other	61	98.4%	1	1.6%	62
Age Group					$p = 0.11$
<25	940	93.6%	64	6.4%	1,004
25-29	797	94.4%	47	5.6%	844
30-39	812	95.0%	43	5.0%	855
40+	395	96.8%	13	3.2%	408
Preferred Language					$p = 0.73$
English	2,326	94.7%	131	5.3%	2,457
Spanish	434	93.3%	31	6.7%	465
Other	2	100.0%	0	0.0%	2
Unknown	182	97.3%	5	2.7%	187
Country of Origin					$p = 0.008$
United States / US Territory	1,893	95.2%	95	4.8%	1,988
Mexico	534	93.4%	38	6.6%	572
Central America	168	89.4%	20	10.6%	188
South America	114	96.6%	4	3.4%	118
Other	25	100.0%	0	0.0%	25
Unknown	210	95.5%	10	4.5%	220
Length of Time in US*					$p = 0.6$
Less than 5 Years	32	97.0%	1	3.0%	33
Between 5 and 9 Years	43	95.6%	2	4.4%	45
Between 10 and 20 Years	116	91.3%	11	8.7%	127
20 Years or More	95	94.1%	6	5.9%	101
Not Applicable	1,893	95.2%	95	4.8%	1,988
Unknown	765	93.6%	52	6.4%	817
Length of Time in US (Collapsed)*					p = 0.23
Less than 10 Years	75	96.2%	3	3.8%	78
10 Years or More	211	92.5%	17	7.5%	228
Not Applicable	1,893	95.2%	95	4.8%	1,988
Unknown	765	93.6%	52	6.4%	817
Total	2,944	94.6%	167	100.0%	3,111

**p-value calculation does NOT include the not applicable or unknown categories*

Table 6.15 - Bivariate Survival Analyses of Demographics at Baseline by Final HIV Serostatus of Whites (n = 4,831), January 2009 - June 2014.

	HIV-negatives (n = 4,676)		HIV-positives (n = 155)		Total (n = 4,831)
	n	%	n	%	n
Orientation					$p = 0.98$
Gay/Homosexual	4,046	96.8%	134	3.2%	4,180
Bisexual	519	99.4%	3	0.6%	522
Other	111	86.0%	18	14.0%	129
Age Group					$p = 0.11$
<25	906	96.0%	38	4.0%	944
25-29	1,114	96.6%	39	3.4%	1,153
30-39	1,318	96.6%	46	3.4%	1,364
40+	1,338	97.7%	32	2.3%	1,370
Total	4,676	96.8%	155	3.2%	4,831

Bivariate Survival Analyses for Young MSM Subgroup

In the following subgroup analysis, the circumstances for HIV infection were compared between young MSM (MSM under the age of 25 at baseline) to older MSM (MSM aged 25 years or older at baseline). The age cut-point of 25 was chosen to be consistent with the young MSM (ages 13-24) definition provided by the Centers for Disease Control and Prevention (CDC 2014a). Similar to the Hispanic/White comparison, the results for YMSM will be presented and discuss how they differ from older MSM.

For the biological construct among YMSM (Table 6.16), seroconversion was associated with all self-reported STI history variables except for Herpes ($p = 0.5$) and all biomedical test result variables except for chlamydia ($p = 0.08$) and syphilis ($p = 0.55$). In contrast, seroconversion was associated with all biomedical test result variables among older MSM (Table 6.17).

Table 6.16 - Bivariate Survival Analyses of Biological Risk Behaviors at Baseline by Final HIV Serostatus of Young MSM (n = 2,580), January 2009 - June 2014.

	HIV-negatives (n = 2,452)		HIV-positives (n = 128)		Total (n = 2,580)
	n	%	n	%	n
History of Chlamydia					$p < 0.0001$
Never Diagnosed	2,140	95.4%	103	4.6%	2,243
Diagnosed More than One Year Ago	188	95.4%	9	4.6%	197
Diagnosed Less than One Year Ago	107	87.0%	16	13.0%	123
Missing	17	100.0%	0	0.0%	17
History of Gonorrhea					$p < 0.0001$
Never Diagnosed	2,049	95.8%	90	4.2%	2,139
Diagnosed More than One Year Ago	245	94.2%	15	5.8%	260
Diagnosed Less than One Year Ago	141	86.0%	23	14.0%	164
Missing	17	100.0%	0	0.0%	17
History of Syphilis					$p = 0.001$
Never Diagnosed	2,346	95.2%	117	4.8%	2,463
Diagnosed More than One Year Ago	40	95.2%	2	4.8%	42
Diagnosed Less than One Year Ago	43	82.7%	9	17.3%	52
Missing	23	100.0%	0	0.0%	23
History of Herpes Simplex Type II					$p = 0.5$
Never Diagnosed	2,223	95.0%	117	5.0%	2,340
Diagnosed More than One Year Ago	53	93.0%	4	7.0%	57
Diagnosed Less than One Year Ago	17	100.0%	0	0.0%	17
Missing	159	95.8%	7	4.2%	166
History of any STI					$p < 0.0001$
Never Diagnosed	1,658	95.8%	72	4.2%	1,730
Diagnosed More than One Year Ago	401	95.0%	21	5.0%	422
Diagnosed Less than One Year Ago	297	90.0%	33	10.0%	330
Missing	96	98.0%	2	2.0%	98
Chlamydia Testing Result					$p = 0.08$
Negative	2,005	95.2%	100	4.8%	2,105
Positive	335	93.1%	25	6.9%	360
Missing	112	97.4%	3	2.6%	115
Gonorrhea Testing Result					$p < 0.0001$
Negative	1,892	95.8%	82	4.2%	1,974
Positive	451	91.1%	44	8.9%	495
Missing	109	98.2%	2	1.8%	111
Syphilis Testing Result					$p = 0.55$
Negative	2,194	95.2%	110	4.8%	2,304
Positive	28	93.3%	2	6.7%	30
Missing	230	93.5%	16	6.5%	246
Tested Positive for any STI					$p < 0.0001$
Negative	1,553	96.3%	59	3.7%	1,612
Positive	710	92.1%	61	7.9%	771
Missing	189	95.9%	8	4.1%	197
Total	2,452	95.0%	128	5.0%	2,580

Table 6.17 - Bivariate Survival Analyses of Biological Risk Behaviors at Baseline by Final HIV Serostatus of MSM Aged 25 and Older (n = 7,401), January 2009 - June 2014.

	HIV-negatives (n = 7,134)		HIV-positives (n = 267)		Total (n = 7,401)
	n	%	n	%	n
History of Chlamydia					$p < 0.0001$
Never Diagnosed	5,653	96.9%	182	3.1%	5,835
Diagnosed More than One Year Ago	1,182	94.8%	65	5.2%	1,247
Diagnosed Less than One Year Ago	257	93.5%	18	6.5%	275
Missing	42	95.5%	2	4.5%	44
History of Gonorrhea					$p < 0.0001$
Never Diagnosed	5,148	96.9%	167	3.1%	5,315
Diagnosed More than One Year Ago	1,638	95.9%	70	4.1%	1,708
Diagnosed Less than One Year Ago	295	91.3%	28	8.7%	323
Missing	53	96.4%	2	3.6%	55
History of Syphilis					$p = 0.0002$
Never Diagnosed	6,570	96.7%	227	3.3%	6,797
Diagnosed More than One Year Ago	353	93.9%	23	6.1%	376
Diagnosed Less than One Year Ago	134	91.2%	13	8.8%	147
Missing	77	95.1%	4	4.9%	81
History of Herpes Simplex Type II					$p = 0.09$
Never Diagnosed	6,118	96.3%	238	3.7%	6,356
Diagnosed More than One Year Ago	364	98.1%	7	1.9%	371
Diagnosed Less than One Year Ago	129	94.2%	8	5.8%	137
Missing	523	97.4%	14	2.6%	537
History of any STI					$p < 0.0001$
Never Diagnosed	3,647	97.4%	98	2.6%	3,745
Diagnosed More than One Year Ago	2,438	95.8%	108	4.2%	2,546
Diagnosed Less than One Year Ago	748	93.4%	53	6.6%	801
Missing	301	97.4%	8	2.6%	309
Chlamydia Testing Result					$p < 0.0001$
Negative	5,860	96.7%	197	3.3%	6,057
Positive	744	92.9%	57	7.1%	801
Missing	530	97.6%	13	2.4%	543
Gonorrhea Testing Result					$p = 0.004$
Negative	5,776	96.5%	207	3.5%	5,983
Positive	846	94.7%	47	5.3%	893
Missing	512	97.5%	13	2.5%	525
Syphilis Testing Result					$p < 0.0001$
Negative	6,195	96.7%	212	3.3%	6,407
Positive	59	88.1%	8	11.9%	67
Missing	880	94.9%	47	5.1%	927
Tested Positive for any STI					$p < 0.0001$
Negative	4,816	97.1%	142	2.9%	4,958
Positive	1,497	94.4%	89	5.6%	1,586
Missing	821	95.8%	36	4.2%	857
Total	7,134	96.4%	267	3.6%	7,401

For the behavioral construct among YMSM, seroconversion was associated with insertive anal sex ($p = 0.03$) and number of partners in the last 3 months ($p = 0.002$) (Table 6.18). In contrast to YMSM, seroconversion was associated in older MSM with vaginal sex ($p = 0.03$), race/ethnicity of the last two sexual partners ($p = 0.01$), number of partners in the past 30 days ($p = 0.004$), and intimate partner violence ($p = 0.005$) (Table 6.19). However, seroconversion was associated with receptive anal sex among both YMSM ($p = 0.001$) and older MSM ($p < 0.0001$).

Table 6.18 - Bivariate Survival Analyses of Sexual Behavioral Risks at Baseline by Final HIV Serostatus of Young MSM (n = 2,580), January 2009 - June 2014.

	HIV-negatives (n = 2,452)		HIV-positives (n = 128)		Total (n = 2,580)
	n	%	n	%	n
Had Insertive Anal Sex					$p = 0.03$
No	1,497	95.7%	68	4.3%	1,565
Yes, with Condom	464	95.3%	23	4.7%	487
Yes, without Condom	478	93.0%	36	7.0%	514
Missing	13	92.9%	1	7.1%	14
Had Receptive Anal Sex					$p = 0.001$
No	1,298	96.2%	51	3.8%	1,349
Yes, with Condom	533	94.8%	29	5.2%	562
Yes, without Condom	616	92.8%	48	7.2%	664
Missing	5	100.0%	0	0.0%	5
Had Vaginal Sex					$p = 0.28$
No	2,294	95.2%	115	4.8%	2,409
Yes with a Condom	20	100.0%	0	0.0%	20
Yes without a Condom	58	92.1%	5	7.9%	63
Missing	80	90.9%	8	9.1%	88
Venue for Meeting Partners					$p = 0.42$
In Person	547	94.0%	35	6.0%	582
Online	366	94.1%	23	5.9%	389
More than One	573	96.5%	21	3.5%	594
Missing	966	95.2%	49	4.8%	1,015
Race/Ethnicity of the Last Two Sexual Partners					$p = 0.32$
Both Partners Different Race	801	95.6%	37	4.4%	838
Both Partners Same Race	807	95.1%	42	4.9%	849
One Partner Same Race, One Different	676	93.8%	45	6.2%	721
Missing	168	97.7%	4	2.3%	172
Age of the Last Two Sexual Partners*					$p = 0.30$
More than 5 Years Older	1,001	94.6%	57	5.4%	1,058
Within Five Years of Age	1,410	95.4%	68	4.6%	1,478
Missing	41	93.2%	3	6.8%	44

Number of Partners in the Past 30 Days*					$p = 0.05$
0	168	95.5%	8	4.5%	176
1	1,078	95.8%	47	4.2%	1,125
2	523	94.4%	31	5.6%	554
3	255	96.2%	10	3.8%	265
4	122	87.8%	17	12.2%	139
5	79	95.2%	4	4.8%	83
6	28	96.6%	1	3.4%	29
7	16	100.0%	0	0.0%	16
8	12	92.3%	1	7.7%	13
9	3	100.0%	0	0.0%	3
10 or More	69	93.2%	5	6.8%	74
Missing	99	96.1%	4	3.9%	103
Number of Partners in the Past 3 Months*					$p = 0.002$
0	66	95.7%	3	4.3%	69
1	632	96.0%	26	4.0%	658
2	501	96.5%	18	3.5%	519
3	351	95.9%	15	4.1%	366
4	220	92.1%	19	7.9%	239
5	171	93.4%	12	6.6%	183
6	90	90.0%	10	10.0%	100
7	58	100.0%	0	0.0%	58
8	49	87.5%	7	12.5%	56
9	16	100.0%	0	0.0%	16
10 or More	237	94.0%	15	6.0%	252
Missing	61	95.3%	3	4.7%	64
Intimate Partner Violence					$p = 0.27$
Never	2,221	95.2%	111	4.8%	2,332
Ever	128	91.4%	12	8.6%	140
Past Year	44	91.7%	4	8.3%	48
Past Three Months	35	97.2%	1	2.8%	36
Missing	24	100.0%	0	0.0%	24
Intimate Partner Violence					$p = 0.13$
Never	2,221	95.2%	111	4.8%	2,332
Ever, Past Year, or Past Three Months	207	92.4%	17	7.6%	224
Missing	24	100.0%	0	0.0%	24
Total	2,452	95.0%	128	5.0%	2,580

**Discrete values for presentation purposes only; continuous values used in all analyses*

Table 6.19 - Bivariate Survival Analyses of Sexual Behavioral Risks at Baseline by Final HIV Serostatus of MSM Aged 25 and Older (n = 7,401), January 2009 - June 2014.

	HIV-negatives (n = 7,134)		HIV-positives (n = 267)		Total (n = 7,401)
	n	%	n	%	n
Had Insertive Anal Sex					$p = 0.38$
No	3,938	96.6%	140	3.4%	4,078
Yes, with Condom	1,517	96.4%	57	3.6%	1,574
Yes, without Condom	1,622	96.1%	66	3.9%	1,688
Missing	57	93.4%	4	6.6%	61
Had Receptive Anal Sex					$p < 0.0001$
No	4,635	97.1%	136	2.9%	4,771
Yes, with Condom	1,177	95.9%	50	4.1%	1,227
Yes, without Condom	1,302	94.2%	80	5.8%	1,382
Missing	20	95.2%	1	4.8%	21
Had Vaginal Sex					$p = 0.03$
No	6,609	96.3%	251	3.7%	6,860
Yes with a Condom	60	100.0%	0	0.0%	60
Yes without a Condom	203	99.5%	1	0.5%	204
Missing	262	94.6%	15	5.4%	277
Venue for Meeting Partners					$p = 0.19$
In Person	1,903	96.6%	67	3.4%	1,970
Online	1,283	95.2%	64	4.8%	1,347
More than One	1,721	96.4%	64	3.6%	1,785
Missing	2,227	96.9%	72	3.1%	2,299
Race/Ethnicity of the Last Two Sexual Partners					$p = 0.01$
Both Partners Different Race	2,260	96.7%	76	3.3%	2,336
Both Partners Same Race	2,530	96.9%	81	3.1%	2,611
One Partner Same Race, One Different	2,039	95.3%	100	4.7%	2,139
Missing	305	96.8%	10	3.2%	315
Age of the Last Two Sexual Partners*					$p = 0.11$
More than 5 Years Older	1,098	95.8%	48	4.2%	1,146
Within Five Years of Age	3,433	96.2%	134	3.8%	3,567
More than 5 Years Younger	1,979	97.0%	61	3.0%	2,040
Missing	624	96.3%	24	3.7%	648
Number of Partners in the Past 30 Days*					$p = 0.004$
0	445	97.4%	12	2.6%	457
1	2,708	97.0%	84	3.0%	2,792
2	1,569	95.8%	68	4.2%	1,637
3	856	96.6%	30	3.4%	886
4	452	96.8%	15	3.2%	467
5	312	96.9%	10	3.1%	322
6	152	93.8%	10	6.2%	162
7	63	96.9%	2	3.1%	65
8	57	96.6%	2	3.4%	59
9	11	91.7%	1	8.3%	12
10 or More	260	91.9%	23	8.1%	283

Missing	249	96.1%	10	3.9%	259
Number of Partners in the Past 3 Months*					$p = 0.07$
0	155	96.3%	6	3.7%	161
1	1,499	97.3%	41	2.7%	1,540
2	1,388	97.1%	41	2.9%	1,429
3	939	95.8%	41	4.2%	980
4	706	96.2%	28	3.8%	734
5	532	96.0%	22	4.0%	554
6	346	97.2%	10	2.8%	356
7	164	94.8%	9	5.2%	173
8	164	93.7%	11	6.3%	175
9	58	98.3%	1	1.7%	59
10 or More	1,024	95.1%	53	4.9%	1,077
Missing	159	97.5%	4	2.5%	163
Intimate Partner Violence					$p = 0.005$
Never	6,484	96.6%	228	3.4%	6,712
Ever	431	93.3%	31	6.7%	462
Past Year	75	96.2%	3	3.8%	78
Past Three Months	57	93.4%	4	6.6%	61
Missing	87	98.9%	1	1.1%	88
Intimate Partner Violence					$p = 0.0007$
Never	6,484	96.6%	228	3.4%	6,712
Ever, Past Year, or Past Three Months	563	93.7%	38	6.3%	601
Missing	87	98.9%	1	1.1%	88
Total	7,134	96.4%	267	3.6%	7,401

**Discrete values for presentation purposes only; continuous values used in all analyses*

For the substance use construct among YMSM, seroconversion was only associated with meth use ($p = 0.005$) and nitrate use ($p = 0.04$) (Table 6.20). Among older MSM, ecstasy use ($p = 0.0001$) and the number of drugs ($p < 0.0001$) used were also associated with seroconversion in addition to meth and nitrate use (Table 6.21).

Table 6.20 - Bivariate Survival Analyses of Substance Use at Baseline by Final HIV Serostatus of Young MSM (n = 2,580), January 2009 - June 2014.

	HIV-negatives (n = 2,452)		HIV-positives (n = 128)		Total (n = 2,580)
	n	%	n	%	n
Used Ecstasy in the Past 12 Months					$p = 0.12$
No	2,149	95.3%	107	4.7%	2,256
Yes	287	93.2%	21	6.8%	308
Missing	16	100.0%	0	0.0%	16
Used Meth in the Past 12 Months					$p = 0.005$
No	2,336	95.2%	117	4.8%	2,453
Yes	95	89.6%	11	10.4%	106
Missing	21	100.0%	0	0.0%	21
Used Nitrates in the Past 12 Months					$p = 0.04$
No	2,172	95.3%	106	4.7%	2,278
Yes	260	92.5%	21	7.5%	281
Missing	20	95.2%	1	4.8%	21
Used ED Drugs in the Past 12 Months					$p = 0.74$
No	2,380	95.0%	126	5.0%	2,506
Yes	50	96.2%	2	3.8%	52
Missing	22	100.0%	0	0.0%	22
Used Cocaine in the Past 12 Months					$p = 0.56$
No	2,165	94.9%	116	5.1%	2,281
Yes	269	95.7%	12	4.3%	281
Missing	18	100.0%	0	0.0%	18
Alcohol Use (Before Sex) in the Past 12 Months					$p = 0.78$
No	1,417	95.2%	71	4.8%	1,488
Yes	1,020	94.7%	57	5.3%	1,077
Missing	15	100.0%	0	0.0%	15
Drug Count					$p = 0.06$
0	1,849	95.7%	84	4.3%	1,933
1	322	93.1%	24	6.9%	346
2	203	92.3%	17	7.7%	220
3	28	96.6%	1	3.4%	29
4	18	100.0%	0	0.0%	18
5	7	87.5%	1	12.5%	8
Missing	25	96.2%	1	3.8%	26
Total	2,452	95.0%	128	5.0%	2,580

Table 6.21 - Bivariate Survival Analyses of Substance Use at Baseline by Final HIV Serostatus of MSM Aged 25 and Older (n = 7,401), January 2009 - June 2014.

	HIV-negatives (n = 7,134)		HIV-positives (n = 267)		Total (n = 7,401)
	n	%	n	%	n
Used Ecstasy in the Past 12 Months					$p = 0.0001$
No	6,502	96.7%	223	3.3%	6,725
Yes	573	93.5%	40	6.5%	613
Missing	59	93.7%	4	6.3%	63
Used Meth in the Past 12 Months					$p < 0.0001$
No	6,668	96.8%	221	3.2%	6,889
Yes	407	90.4%	43	9.6%	450
Missing	59	95.2%	3	4.8%	62
Used Nitrates in the Past 12 Months					$p < 0.0001$
No	5,922	97.0%	183	3.0%	6,105
Yes	1,151	93.5%	80	6.5%	1,231
Missing	61	93.8%	4	6.2%	65
Used ED Drugs in the Past 12 Months					$p = 0.67$
No	6,475	96.5%	238	3.5%	6,713
Yes	597	95.8%	26	4.2%	623
Missing	62	95.4%	3	4.6%	65
Used Cocaine in the Past 12 Months					$p = 0.08$
No	6,295	96.5%	227	3.5%	6,522
Yes	772	95.4%	37	4.6%	809
Missing	67	95.7%	3	4.3%	70
Alcohol Use (Before Sex) in the Past 12 Months					$p = 0.88$
No	4,025	96.6%	143	3.4%	4,168
Yes	3,051	96.2%	122	3.8%	3,173
Missing	58	96.7%	2	3.3%	60
Drug Count					$p < 0.0001$
0	4,844	97.2%	140	2.8%	4,984
1	1,379	95.7%	62	4.3%	1,441
2	606	94.1%	38	5.9%	644
3	109	90.1%	12	9.9%	121
4	77	92.8%	6	7.2%	83
5	29	87.9%	4	12.1%	33
Missing	90	94.7%	5	5.3%	95
Total	7,134	96.4%	267	3.6%	7,401

Lastly, neither orientation ($p = 0.72$) nor race/ethnicity ($p = 0.06$) was associated with HIV infection among YMSM (Table 6.22). Among older MSM, orientation was not associated with seroconversion ($p = 0.70$), but race/ethnicity was associated with seroconversion ($p = 0.001$) (Table 6.23).

Table 6.22 - Bivariate Survival Analyses of Demographics at Baseline by Final HIV Serostatus of Young MSM (n = 2,580), January 2009 - June 2014.

	HIV-negatives (n = 2,452)		HIV-positives (n = 128)		Total (n = 2,580)
	n	%	n	%	n
Orientation					$p = 0.72$
Gay/Homosexual	2,047	95.0%	107	5.0%	2,154
Bisexual	341	94.7%	19	5.3%	360
Other	64	97.0%	2	3.0%	66
Race/Ethnicity					$p = 0.06$
White	953	96.1%	39	3.9%	992
Hispanic	896	93.2%	65	6.8%	961
Black	200	94.8%	11	5.2%	211
Other	403	96.9%	13	3.1%	416
Age Group					$p = 0.84$
<18	39	90.7%	4	9.3%	43
18	107	94.7%	6	5.3%	113
19	202	96.2%	8	3.8%	210
20	267	95.0%	14	5.0%	281
21	355	94.9%	19	5.1%	374
22	463	94.7%	26	5.3%	489
23	481	94.7%	27	5.3%	508
24	538	95.7%	24	4.3%	562
Total	2,452	95.0%	128	5.0%	2,580

Table 6.23 - Bivariate Survival Analyses of Demographics at Baseline by Final HIV Serostatus of MSM Aged 25 and Older (n = 7,401), January 2009 - June 2014.

	HIV-negatives (n = 7,134)		HIV-positives (n = 267)		Total (n = 7,401)
	n	%	n	%	n
Orientation					$p = 0.70$
Gay/Homosexual	6,117	96.3%	234	3.7%	6,351
Bisexual	833	96.7%	28	3.3%	861
Other	184	97.4%	5	2.6%	189
Race/Ethnicity					$p = 0.001$
White	3,850	97.0%	118	3.0%	3,968
Hispanic	1,931	95.0%	101	5.0%	2,032
Black	486	95.3%	24	4.7%	510
Other	867	97.3%	24	2.7%	891
Total	7,134	96.4%	267	3.6%	7,401

Chapter 7 – Multivariate Results

Variable Selection for the Multivariate Models

To conduct an empirical test of the Syndemics Theory model, variables that were significant in bivariate tests were selected from each construct to ensure adequate construct representation while minimizing multicollinearity. To determine what variables may present a multicollinearity problem, correlation matrices were analyzed for variables within the same construct.

There were two classes of variables available for the biological construct: self-reported history of STIs and biomedical test results. Since an individual's entire STI history of testing is likely more representative of their STI morbidity than the results from their baseline testing visit, the self-reported history of STI variables were chosen instead of the biomedical STI results. Since these variables are all ordinal, a Spearman correlation matrix was used to determine if there was significant overlap between any of these variables (Table 7.1). Since correlations between self-reported history variables were all below 0.8 (Range: 0.09-0.25), all three variables (history of chlamydia, history of gonorrhea, and history of syphilis) were inserted into the multivariate algorithm

Table 7.1 - Spearman Correlation Matrix of the Statistically Significant History of STI Predictors, January 2009 - June 2014.

	History of Chlamydia	History of Gonorrhea	History of Syphilis	History of any STI	Chlamydia Testing Result	Gonorrhea Testing Result	Syphilis Testing Result	Tested Positive for any STI
History of Chlamydia	1							
History of Gonorrhea	0.25*	1						
History of Syphilis	0.09*	0.13*	1					
History of any STI	0.56*	0.66*	0.33*	1				
Chlamydia Testing Result	0.02	-0.004	-0.003	0.007	1			
Gonorrhea Testing Result	0.008	0.028	0.009	0.05*	0.07*	1		
Syphilis Testing Result	0.004	0.03	0.08*	0.05*	0.04	0.002	1	
Tested Positive for any STI	0.02	0.02	0.05*	0.06*	0.65*	0.72*	0.18*	1

**p < 0.0001*

For the behavioral construct, receptive anal sex, race/ethnicity of the last two sexual partners, age of the last two sexual partners, and number of sexual partners in the last three months were chosen as covariates. These variables collectively represent the type of sexual behavior (receptive anal sex), the network of sexual partners (race/ethnicity and age of the last two sexual partners), and the frequency of sexual encounters (number of sexual partners in the last three months).

For the mental health component of the behavioral construct, the binary variable version of the intimate partner violence variable was selected over the four category variable due to stratum-level sample size. Intimate partner violence was the only mental health variable available for analysis.

For the substance use construct, ecstasy, methamphetamine and nitrates were each significantly associated with seroconversion in bivariate analyses. Since these variables are all binary, tetrachoric correlations were set up do determine if multicollinearity was present (Table 7.2). All correlations were between 0.43 and 0.49 and therefore could all justifiably be added to the multivariate model. Number of drugs used was not inserted into the multivariate model since it is directly dependent on ecstasy use, meth use, and nitrates use.

Table 7.2 - Tetrachoric Correlation Matrix of the Statistically Significant Substance Use Predictors, January 2009 - June 2014.

	Ecstasy	Meth	Nitrates
Ecstasy	1		
Meth	0.43*	1	
Nitrates	0.44*	0.49*	1

**p < 0.0001*

In summary, the following variables were inserted into a multivariate model, controlling for age group and race/ethnicity: history of chlamydia, history of gonorrhea, history of syphilis,

receptive anal sex, race/ethnicity of last two sexual partners, age of the last two sexual partners, number of sexual partners in the last 3 months, intimate partner violence, ecstasy use, meth use, and nitrate use. This model was first analyzed for the whole population to fulfill Aim 1. Following this analysis, the risk score was constructed to fulfill Aim 2. Lastly, separate algorithms were run for Hispanic MSM, White MSM, young MSM, and older MSM. These five models were subsequently compared to determine if circumstances for HIV infection differed between Hispanic and White MSM or young MSM and older MSM. These results are discussed in more detail below.

Multivariate Results among the Entire Population

Among the entire population, all variables were significantly associated with seroconversion except for age of the last two sexual partners ($p = 0.52$), intimate partner violence ($p = 0.09$), and ecstasy use ($p = 0.26$) (Table 7.3). More specifically, MSM who were African-American (Hazard Ratio (HR): 1.89; CI: 1.23-2.91) or Hispanic (HR: 1.6; CI: 1.25-2.06) had a significantly higher risk of seroconversion when compared to MSM who identified with an "Other" race/ethnicity (e.g., Asian, Pacific Islander, Native American) ($p = 0.0004$). MSM less than 25 years of age at baseline (YMSM) had a hazard rate of seroconversion 1.89-fold higher when compared to MSM 40 years of age of older ($p = 0.03$).

MSM who were diagnosed with gonorrhea ($p < 0.0001$) or syphilis ($p = 0.007$) less than a year ago had a higher hazard of seroconversion when compared to MSM who were never diagnosed with these STIs. Furthermore, receptive anal sex, regardless of reported condom use, was associated with a higher rate of seroconversion ($p < 0.0001$). MSM who either had sex with both partners of the same race ($p = 0.03$), or one individual of the same race and one of a

different race ($p = 0.001$), had a higher hazard of seroconversion when compared to MSM who exclusively had sex outside their racial/ethnic group.

MSM who reported meth use had a 1.76 greater hazard of seroconversion when compared to MSM who did not report meth use ($p = 0.0008$). Lastly, MSM who reported nitrates use had a 1.5 greater hazard of seroconversion when compared to MSM who did not report nitrates use ($p = 0.002$).

Table 7.3 - Final Multivariate Survival Analysis of Demographic, Biological, Sexual Behavioral, and Substance Use Operationalized Constructs at Baseline on Final HIV Serostatus (n = 9,158 / 9,981), January 2009 - June 2014.

	Est	SE	p-value	HR (95% CI)
Race/Ethnicity (REF = White)				$p = 0.0004$
Black	0.63	0.20	0.001	1.89 (1.29-2.77)
Hispanic	0.47	0.13	0.0002	1.60 (1.25-2.06)
Other	0.18	0.23	0.43	1.20 (0.76-1.88)
Age Group (REF = 40+)				$p = 0.03$
<25	0.64	0.22	0.004	1.89 (1.23-2.91)
25-29	0.45	0.21	0.03	1.57 (1.05-2.36)
30-39	0.33	0.19	0.08	1.39 (0.96-2.01)
History of Chlamydia (REF = Never Diagnosed)				$p = 0.03$
Diagnosed More than One Year Ago	0.33	0.14	0.02	1.40 (1.06-1.84)
Diagnosed Less than One Year Ago	0.31	0.21	0.14	1.36 (0.91-2.05)
History of Gonorrhea (REF = Never Diagnosed)				$p < 0.0001$
Diagnosed More than One Year Ago	0.14	0.14	0.30	1.15 (0.88-1.51)
Diagnosed Less than One Year Ago	0.77	0.18	<.0001	2.17 (1.53-3.07)
History of Syphilis (REF = Never Diagnosed)				$p = 0.01$
Diagnosed More than One Year Ago	0.30	0.22	0.17	1.34 (0.88-2.06)
Diagnosed Less than One Year Ago	0.61	0.23	0.007	1.84 (1.18-2.87)
Receptive Anal Sex (REF = No)				$p < 0.0001$
Yes With Condom	0.38	0.14	0.007	1.46 (1.11-1.93)
Yes Without Condom	0.72	0.12	<.0001	2.05 (1.62-2.61)
Race of Last Two Sexual Partners (REF = Both Partners Different Race)				$p = 0.005$
Both Partners Same Race	0.32	0.15	0.03	1.38 (1.03-1.86)
One Partner Same Race, One Different	0.44	0.14	0.001	1.55 (1.19-2.03)
Age Difference of Last Two Sexual Partners	0.01	0.01	0.52	1.01 (0.99-1.02)
Number of Sexual Partners in the Last 3 Months	0.01	0.00	0.0003	1.01 (1.01-1.02)
Intimate Partner Violence (REF = Never)	0.27	0.16	0.09	1.31 (0.96-1.78)
Ecstasy Use (REF = No)	0.18	0.16	0.26	1.19 (0.88-1.62)
Methamphetamine Use (REF = No)	0.56	0.17	0.0008	1.76 (1.27-2.44)
Nitrates Use (REF = No)	0.41	0.13	0.002	1.50 (1.16-1.95)

Construction of the HIV Risk Algorithm

To appropriately construct the algorithm, the continuous variables (number of sexual partners in the last 3 months and age difference of last two sexual partners) were transformed into categorical variables using measures of central tendency (Tables 7.4 and 7.5). Due to a skewed distribution for the number of sexual partners in the last three months, the medians were used to dichotomize this variable with the value of 3 chosen as the cut-off.

The measures of central tendency for the average age of the last two partners were not readily intuitive to inform categorization. To review, the age difference of the last two sexual partners was calculated as follows (Equation 7.1):

Equation 7.1 – Age Difference of Last Two Sexual Partners Calculation

Age Difference of Last Two Sexual Partners = Age of the Client - ((First Sexual Partner's Age + Second Sexual Partner's Age)/2)

Values less than -5 made up the first level of the three-category ordinal variable and were classified as "older." For example, a client who is 40 at baseline and has an average sex partner age of 50 will have an Age Difference of Last Two Sexual Partners value of -10, and be classified as having older partners on average. Values greater than 5 made up the second level of the three-category ordinal variable and were classified as "younger." For example, a client who is 40 at baseline and has an average sex partner age of 32 will have an Age Difference of Last Two Sexual Partners value of 8, and be classified as having younger partners on average. Lastly, individuals who had values between -5 and 5 were classified as having partners of the same age. For example, a client who is 40 at baseline and has an average sex partner age between of 35 will have an Age Difference of Last Two Sexual Partners value of 5, and be classified as having partners of the same age.

Table 7.4 - Measures of Central Tendency for the Number of Sexual Partners in the Last Three Months, January 2009 - June 2014.

Number of Partners	HIV Negatives	HIV Positives	Seropositivity Rate
Mean	5.17	7.11	N/A
Median	3	4	N/A
3 or Less	5531	191	3.3%
4 or More	3835	197	4.9%

Table 7.5 - Measures of Central Tendency for the Average Age of the Last Two Partners, January 2009 - June 2014.

Number of Partners	HIV Negatives	HIV Positives	Seropositivity Rate
Mean	1.17	-0.43	N/A
Median	0	-1	N/A
More than 5 Years Older	2,099	105	4.8%
Within Five Years of Age	4,843	202	4.0%
More than 5 Years Younger	1,979	61	3.0%

Following categorization of the continuous predictors, all predictors were arranged so the reference group had the lowest risk for each coefficient (Beta). This assigned a risk number to each category of each predictor with zero assigned to the reference group. These coefficients were then added for each individual in the dataset who had values for all predictors (n = 9,158, see "Assessing Selection Bias" at the end of this chapter for a discussion of individuals who did not have values for all coefficients). The sum was then exponentiated to create a risk score that compares that person to a hypothetical person in the lowest risk group (Wilson et al. 1998, Wang et al. 2003, O'Seaghdha 2012 et al.) (Table 7.6). After rounding the risk score, the final range of values were between 1 and 174. This method was utilized over rounding prior to addition to preserve the precision of the Beta estimates and maximize the accuracy of the measure.

It should be emphasize that Table 7.6 is different from Table 7.3 in two important ways: 1) all continuous predictors have been transformed into categorical predictors, and 2) only the coefficient (Beta) is presented to demonstrate the item that was added to create the risk score.

In the next step, the number of values greater than or equal to each risk score were calculated (Table 7.7). The risk score of 5 will be used as an example to explain this table. 75.9% of all HIV positive individuals, or three-fourths, had a risk score greater than or equal to 5 at their intake visit. However, 47.8% of all HIV negative individuals had a risk score greater than or equal to 5 at their intake visit. For all individuals with a score greater than or equal to 5, approximately 6.3% (281 positives / (281 positives + 4,204 negatives)), or approximately 1 in 15, would seroconvert.

Table 7.6 - Composite Risk Score Calculation*

Variable	Coefficient (Beta)
Race/Ethnicity (REF = White)	
Black	0.62238
Hispanic	0.47318
Other	0.15259
Age Group (REF = 40+)	
<25	0.68264
25-29	0.47654
30-39	0.35133
History of Chlamydia (REF = Never Diagnosed)	
Diagnosed More than One Year Ago	0.34409
Diagnosed Less than One Year Ago	0.35432
History of Gonorrhea (REF = Never Diagnosed)	
Diagnosed More than One Year Ago	0.12165
Diagnosed Less than One Year Ago	0.80525
History of Syphilis (REF = Never Diagnosed)	
Diagnosed More than One Year Ago	0.33921
Diagnosed Less than One Year Ago	0.63258
Receptive Anal Sex (REF = No)	
Yes With Condom	0.36627
Yes Without Condom	0.6957
Race of Last Two Sexual Partners (REF = Both Partners Different Race)	
Both Partners Same Race	0.33713
One Partner Same Race, One Different	0.42801
Age Difference of Last Two Sexual Partners (REF = More than 5 Years Older)	
Within Five Years of Age	0.04587
More than 5 Years Younger	0.14813
Number of Sexual Partners in the Last Three Months (REF = Three or Less Sexual Partners)	0.30585
Intimate Partner Violence (REF = Never)	0.27174
Ecstasy Use (REF = No)	0.13470
Methamphetamine Use (REF = No)	0.56824
Nitrates Use (REF = No)	0.39132

**The betas were added for each individual and then exponentiated to obtain the risk score. This final score was then rounded. The risk score range was 1-174.*

Table 7.7 - Sensitivity and Specificity for HIV Risk Algorithm Cut-Points

	HIV Positives			HIV Negatives		
Cut Point	n	Number greater than or equal to Cut-Point*	% greater than or equal to Cut-Point	n	Number greater than or equal to Cut-Point*	% greater than or equal to Cut-Point
1	2	370	100.0%	155	8788	100.0%
2	13	368	99.5%	1337	8633	98.2%
3	30	355	95.9%	1713	7296	83.0%
4	44	325	87.8%	1379	5583	63.5%
5	41	281	75.9%	1208	4204	47.8%
6	37	240	64.9%	717	2996	34.1%
7	30	203	54.9%	522	2279	25.9%
8	25	173	46.8%	391	1757	20.0%
9	15	148	40.0%	270	1366	15.5%
10	17	133	35.9%	253	1096	12.5%
11	9	116	31.4%	167	843	9.6%
12	12	107	28.9%	92	676	7.7%
13	17	95	25.7%	110	584	6.6%
14	8	78	21.1%	74	474	5.4%
15	6	70	18.9%	70	400	4.6%
16	8	64	17.3%	43	330	3.8%
17	7	56	15.1%	35	287	3.3%
18	3	49	13.2%	25	252	2.9%
19	7	46	12.4%	28	227	2.6%
20	9	39	10.5%	27	199	2.3%
21	2	30	8.1%	20	172	2.0%
22	3	28	7.6%	13	152	1.7%
23	1	25	6.8%	12	139	1.6%
24	1	24	6.5%	15	127	1.4%
25	1	23	6.2%	9	112	1.3%
26	2	22	5.9%	10	103	1.2%
27	0	20	5.4%	14	93	1.1%
28	3	20	5.4%	6	79	0.9%
29	5	17	4.6%	5	73	0.8%
30	1	12	3.2%	7	68	0.8%
31	1	11	3.0%	5	61	0.7%
32	1	10	2.7%	3	56	0.6%
33	0	9	2.4%	4	53	0.6%
34	1	9	2.4%	1	49	0.6%
35	2	8	2.2%	5	48	0.5%
36	0	6	1.6%	4	43	0.5%
37	0	6	1.6%	1	39	0.4%
38	0	6	1.6%	2	38	0.4%
39	0	6	1.6%	2	36	0.4%
40 or above	6	6	1.6%	34	34	0.4%
Total	370			8788		

**Calculated by subtracting the cumulative sum before that row from the total for each category*

Multivariate Results among At-Risk Subgroups

Based on these tables, it appeared that Hispanic MSM (Table 7.8) had different circumstances for HIV infection when compared to White MSM (Table 7.9). Country of origin ($p = 0.009$), race/ethnicity of last two sexual partners ($p = 0.005$), and intimate partner violence ($p = 0.01$) were significantly different between seroconverters and non-seroconverters among Hispanics but not among Whites. In addition, nitrates use was not significant among Hispanics ($p = 0.4$) but was significant among Whites ($p = 0.0009$). However, there were also many similarities in that receptive anal sex and number of sexual partners were significantly different between seroconverters and non-seroconverters among both Hispanics and Whites.

Statistical significance alone should not be the sole criterion for comparison, the magnitude of coefficients should also be compared. For example, methamphetamine use is significant for both Hispanics ($p = 0.01$; $\beta = 0.71$) and Whites ($p = 0.002$; $\beta = 0.74$). The Betas are relatively similar suggesting a similar magnitude of effect on HIV seroconversion. However, receptive anal sex without a condom has a much different magnitude for Hispanics ($p = 0.007$; $\beta = 0.52$) and Whites ($p < 0.0001$; $\beta = 1.02$), showing a nearly two-fold different impact of this variable between groups on HIV seroconversion. Therefore, a variable may be significant in both groups, but the difference in effect should really be assessed by comparing coefficients.

In order to truly assess differences between these groups, it's necessary to include an interaction into a model that includes both Hispanics and Whites. Models were created that had the all of the original variables in the equation plus all of the potential interactions between race/ethnicity (Table 7.10). Only two circumstances truly differed for HIV infection between White and Hispanics: nitratres use ($p = 0.007$) and IPV ($p = 0.03$). Whites were more likely to seroconvert provided they used nitrates, and Hispanics were more likely to seroconvert if they

reported IPV. While these differences are important, the similarity between groups is a lot higher than initially presented with separate analyses.

Table 7.8 - Multivariate Survival Analyses of Demographic, Biological, Sexual Behavioral, and Substance Use Operationalized Constructs at Baseline by Final HIV Serostatus of Hispanics (n = 2,698 / 3,111), January 2009 - June 2014.

Construct	Estimate	SE	p-value	HR (95% CI)
Country of Birth (REF = South America)				$p = 0.009$
Central America	0.89	0.55	0.11	2.43 (0.82-7.21)
Mexico	0.33	0.54	0.54	1.39 (0.49-3.97)
USA	0.05	0.52	0.92	1.05 (0.38-2.90)
Age Group (REF = 40+)				$p = 0.09$
<25	0.95	0.40	0.02	2.59 (1.18-5.67)
25-29	0.81	0.38	0.03	2.25 (1.06-4.76)
30-39	0.51	0.36	0.15	1.67 (0.83-3.37)
History of Chlamydia (REF = Never Diagnosed)				$p = 0.66$
Diagnosed More than One Year Ago	-0.12	0.28	0.67	0.89 (0.51-1.53)
Diagnosed Less than One Year Ago	0.24	0.32	0.46	1.27 (0.67-2.39)
History of Gonorrhea (REF = Never Diagnosed)				$p = 0.04$
Diagnosed More than One Year Ago	0.01	0.24	0.96	1.01 (0.63-1.63)
Diagnosed Less than One Year Ago	0.72	0.29	0.01	2.05 (1.16-3.60)
History of Syphilis (REF = Never Diagnosed)				$p = 0.04$
Diagnosed More than One Year Ago	-0.01	0.38	0.98	0.99 (0.48-2.07)
Diagnosed Less than One Year Ago	0.79	0.31	0.01	2.21 (1.19-4.08)
Receptive Anal Sex (REF = No)				$p = 0.02$
Yes With Condom	0.34	0.22	0.12	1.40 (0.92-2.13)
Yes Without Condom	0.52	0.19	0.007	1.69 (1.15-2.47)
Race of Last Two Sexual Partners (REF = Both Partners Different Race)				$p = 0.005$
Both Partners Same Race	0.10	0.27	0.73	1.10 (0.65-1.87)
One Partner Same Race, One Different	0.58	0.19	0.003	1.78 (1.22-2.59)
Age Difference of Last Two Sexual Partners	0.03	0.01	0.08	1.03 (1.00-1.06)
Number of Sexual Partners in the Last 3 Months	0.01	0.01	0.02	1.01 (1.00-1.03)
Intimate Partner Violence (REF = Never)	0.56	0.22	0.01	1.76 (1.14-2.70)
Ecstasy Use (REF = No)	0.23	0.28	0.42	1.26 (0.72-2.20)
Methamphetamine Use (REF = No)	0.71	0.28	0.01	2.04 (1.18-3.55)
Nitrates Use (REF = No)	-0.21	0.24	0.40	0.81 (0.50-1.31)

Table 7.9 - Multivariate Survival Analyses of Demographic, Biological, Sexual Behavioral, and Substance Use Operationalized Constructs at Baseline by Final HIV Serostatus of Whites (n = 4,626 / 4,831), January 2009 - June 2014.

Construct	Estimate	SE	p-value	HR (95% CI)
Age Group (REF = 40+)				$p = 0.5$
<25	0.51	0.33	0.13	1.66 (0.87-3.19)
25-29	0.35	0.30	0.24	1.42 (0.79-2.56)
30-39	0.25	0.26	0.34	1.28 (0.77-2.15)
History of Chlamydia (REF = Never Diagnosed)				$p = 0.004$
Diagnosed More than One Year Ago	0.61	0.20	0.003	1.84 (1.23-2.74)
Diagnosed Less than One Year Ago	0.64	0.32	0.05	1.90 (1.01-3.57)
History of Gonorrhea (REF = Never Diagnosed)				$p = 0.16$
Diagnosed More than One Year Ago	0.19	0.20	0.36	1.20 (0.81-1.79)
Diagnosed Less than One Year Ago	0.54	0.30	0.07	1.72 (0.97-3.07)
History of Syphilis (REF = Never Diagnosed)				$p = 0.06$
Diagnosed More than One Year Ago	0.53	0.33	0.11	1.69 (0.90-3.20)
Diagnosed Less than One Year Ago	0.73	0.38	0.05	2.08 (0.99-4.38)
Receptive Anal Sex (REF = No)				$p < 0.0001$
Yes With Condom	0.38	0.24	0.11	1.46 (0.91-2.32)
Yes Without Condom	1.02	0.19	<.0001	2.78 (1.92-4.03)
Race of Last Two Sexual Partners (REF = Both Partners Different Race)				$p = 0.7$
Both Partners Same Race	0.12	0.28	0.65	1.13 (0.66-1.95)
One Partner Same Race, One Different	0.23	0.29	0.43	1.26 (0.71-2.23)
Age Difference of Last Two Sexual Partners	0.00	0.01	0.77	1.00 (0.97-1.02)
Number of Sexual Partners in the Last 3 Months	0.02	0.01	0.008	1.02 (1.00-1.03)
Intimate Partner Violence (REF = Never)	-0.33	0.31	0.29	0.72 (0.39-1.32)
Ecstasy Use (REF = No)	0.28	0.23	0.21	1.33 (0.85-2.06)
Methamphetamine Use (REF = No)	0.74	0.24	0.002	2.10 (1.30-3.38)
Nitrates Use (REF = No)	0.64	0.19	0.0009	1.91 (1.30-2.79)

Table 7.10 - Multivariate Survival Analyses Interactions on Final HIV Serostatus between Whites and Hispanics (n = 7,561 / 7,942), January 2009 - June 2014.

Interaction	df	Chi-Square	p-value
Race/Ethnicity and Age Group	3	0.76	0.86
Race/Ethnicity and History of Chlamydia	2	2.87	0.24
Race/Ethnicity and History of Gonorrhea	2	0.70	0.70
Race/Ethnicity and History of Syphilis	2	1.49	0.47
Race/Ethnicity and History of Receptive Anal Sex	2	4.42	0.11
Race/Ethnicity and Race of Last Two Sexual Partners	2	1.74	0.42
Race/Ethnicity and Age of Last Two Sexual Partners	1	2.36	0.12
Race/Ethnicity and Number of Sexual Partners (Last 3 Months)	1	0.11	0.74
Race/Ethnicity and Intimate Partner Violence	1	4.81	**0.0283**
Race/Ethnicity and Ecstasy Use	1	0.08	0.78
Race/Ethnicity and Meth Use	1	0.04	0.84
Race/Ethnicity and Nitrates Use	1	7.39	**0.0066**

In addition to the Hispanic and White comparison, multivariate models were compared between YMSM (Table 7.11) and older MSM (Table 7.12). Like Hispanic and White MSM, receptive anal sex were significant for both YMSM and older MSM. There were no detectable differences between YMSM seroconverters and non-seroconverters by race/ethnicity of last two sexual partners ($p = 0.19$), number of sexual partners in the past three months ($p = 0.23$), meth use ($p = 0.19$), or nitrate use ($p = 0.34$). In contrast, there were significant differences in older MSM by race/ethnicity of last two sexual partners ($p = 0.009$), number of sexual partners in the past three months ($p = 0.0005$), meth use ($p = 0.0006$), and nitrate use ($p = 0.002$). Intimate partner violence was not significant for either YMSM ($p = 0.2$) or older MSM ($p = 0.19$).

As with the Hispanic and White MSM comparisons, interactions were added to a composite model and assessed to determine if there were significant differences (Table 7.13). No p-values were below the chosen alpha of 0.05, and thus no differences were detected between YMSM and older MSM.

Table 7.11 - Multivariate Survival Analyses of Demographic, Biological, Sexual Behavioral, and Substance Use Operationalized Constructs at Baseline by Final HIV Serostatus of Young MSM (n = 2,336 / 2,580), January 2009 - June 2014.

Construct	Estimate	SE	p-value	HR (95% CI)
Race/Ethnicity (REF = White)				$p = 0.09$
Black	0.60	0.35	0.08	1.83 (0.92-3.62)
Hispanic	0.56	0.23	0.02	1.74 (1.11-2.74)
Other	0.45	0.38	0.23	1.57 (0.75-3.31)
History of Chlamydia (REF = Never Diagnosed)				$p = 0.41$
Diagnosed More than One Year Ago	-0.06	0.38	0.87	0.94 (0.44-1.98)
Diagnosed Less than One Year Ago	0.42	0.32	0.19	1.53 (0.81-2.89)
History of Gonorrhea (REF = Never Diagnosed)				$p = 0.0004$
Diagnosed More than One Year Ago	0.34	0.30	0.26	1.40 (0.78-2.53)
Diagnosed Less than One Year Ago	1.09	0.28	<.0001	2.98 (1.74-5.13)
History of Syphilis (REF = Never Diagnosed)				$p = 0.03$
Diagnosed More than One Year Ago	-0.57	0.74	0.44	0.57 (0.13-2.39)
Diagnosed Less than One Year Ago	0.86	0.35	0.02	2.37 (1.18-4.75)
Receptive Anal Sex (REF = No)				$p = 0.02$
Yes With Condom	0.28	0.24	0.25	1.32 (0.82-2.14)
Yes Without Condom	0.59	0.21	0.006	1.81 (1.19-2.75)
Race of Last Two Sexual Partners (REF = Both Partners Different Race)				$p = 0.22$
Both Partners Same Race	0.41	0.26	0.11	1.51 (0.92-2.49)
One Partner Same Race, One Different	0.34	0.24	0.15	1.41 (0.88-2.24)
Age Difference of Last Two Sexual Partners	0.02	0.02	0.28	1.02 (0.98-1.06)
Number of Sexual Partners in the Last 3 Months	0.01	0.01	0.23	1.01 (1.00-1.02)
Intimate Partner Violence (REF = Never)	0.37	0.27	0.17	1.46 (0.85-2.49)
Ecstasy Use (REF = No)	0.09	0.27	0.75	1.09 (0.64-1.87)
Methamphetamine Use (REF = No)	0.53	0.36	0.14	1.70 (0.84-3.43)
Nitrates Use (REF = No)	0.23	0.27	0.40	1.26 (0.74-2.15)

Table 7.12 - Multivariate Survival Analyses of Demographic, Biological, Sexual Behavioral, and Substance Use Operationalized Constructs at Baseline by Final HIV Serostatus of MSM Aged 25 Years and Older (n = 6,820 / 7,401), January 2009 - June 2014.

Construct	Estimate	SE	p-value	HR (95% CI)
Race/Ethnicity (REF = White)				$p = 0.002$
Black	0.69	0.24	0.004	1.99 (1.25-3.17)
Hispanic	0.50	0.16	0.002	1.64 (1.21-2.23)
Other	0.11	0.29	0.71	1.12 (0.63-1.97)
History of Chlamydia (REF = Never Diagnosed)				$p = 0.02$
Diagnosed More than One Year Ago	0.41	0.16	0.008	1.51 (1.12-2.06)
Diagnosed Less than One Year Ago	0.29	0.27	0.28	1.34 (0.79-2.28)
History of Gonorrhea (REF = Never Diagnosed)				$p = 0.02$
Diagnosed More than One Year Ago	0.07	0.15	0.67	1.07 (0.79-1.45)
Diagnosed Less than One Year Ago	0.64	0.23	0.006	1.89 (1.20-2.98)
History of Syphilis (REF = Never Diagnosed)				$p = 0.09$
Diagnosed More than One Year Ago	0.42	0.23	0.07	1.52 (0.97-2.38)
Diagnosed Less than One Year Ago	0.42	0.30	0.16	1.52 (0.85-2.72)
Receptive Anal Sex (REF = No)				$p < 0.0001$
Yes With Condom	0.42	0.17	0.01	1.53 (1.09-2.14)
Yes Without Condom	0.79	0.15	<.0001	2.20 (1.64-2.95)
Race of Last Two Sexual Partners (REF = Both Partners Different Race)				$p = 0.005$
Both Partners Same Race	0.35	0.19	0.07	1.41 (0.98-2.04)
One Partner Same Race, One Different	0.54	0.17	0.001	1.72 (1.24-2.38)
Age Difference of Last Two Sexual Partners	-0.01	0.01	0.20	0.99 (0.98-1.01)
Number of Sexual Partners in the Last 3 Months	0.02	0.01	0.0005	1.02 (1.01-1.03)
Intimate Partner Violence (REF = Never)	0.23	0.19	0.23	1.26 (0.86-1.83)
Ecstasy Use (REF = No)	0.23	0.19	0.24	1.26 (0.86-1.84)
Methamphetamine Use (REF = No)	0.56	0.20	0.004	1.76 (1.20-2.57)
Nitrates Use (REF = No)	0.44	0.15	0.004	1.55 (1.15-2.08)

Table 7.13 - Multivariate Survival Analyses Interactions on Final HIV Serostatus between MSM Under 25 and MSM 25 Years of Age or Older (n = 9,156 / 9,981), January 2009 - June 2014.

Interaction	df	Chi-Square	p-value
Age Group and Race/Ethnicity	3	0.65	0.88
Age Group and History of Chlamydia	2	1.48	0.48
Age Group and History of Gonorrhea	2	1.84	0.40
Age Group and History of Syphilis	2	2.78	0.25
Age Group and History of Receptive Anal Sex	2	0.66	0.72
Age Group and Race of Last Two Sexual Partners	2	0.89	0.64
Age Group and Age of Last Two Sexual Partners	1	2.23	0.14
Age Group and Number of Sexual Partners (Last 3 Months)	1	2.11	0.15
Age Group and Intimate Partner Violence	1	0.18	0.67
Age Group and Ecstasy Use	1	0.16	0.69
Age Group and Meth Use	1	0.02	0.90
Age Group and Nitrates Use	1	0.42	0.52

Lastly, the p-values from these four subgroups were compared to the entire population at both the stratum level (Table 7.14) and the Type III level (Table 7.15). These results show that history of STIs, receptive anal sex, and number of sex partners in the last three months are consistently related to HIV seroconversion across all at-risk groups. However, race of the last two sexual partners is important for Hispanic and older MSM but not significantly different between White and YMSM seroconverters and non-seroconverters. In addition, methamphetamine use is important for all groups except young MSM. In contrast, intimate partner violence is associated with seroconversion only for Hispanic MSM. Given the large sample size of each of these strata, these findings show that not all homosexual men are homogeneous and that different circumstances for infection do indeed exist between subgroups.

Table 7.14 - Multivariate Survival Analyses p-value Comparisons (Maximum Likelihood Estimates p-values), January 2009 - June 2014.

Construct	All (n = 9,981)	Hispanics (n = 3,111)	Whites (n = 4,831)	Young MSM (n = 2,580)	Older MSM (n = 7,401)
Demographic					
Country of Origin	N/A	●	N/A	N/A	N/A
Race/Ethnicity (REF = Other)					
Black	●	N/A	N/A	○	●
Hispanic	●	N/A	N/A	●	●
White	○	N/A	N/A	○	○
Age Group (REF = 40+)					
<25	●	●	○	N/A	N/A
25-29	●	●	○	N/A	N/A
30-39	○	○	○	N/A	N/A
Biological					
History of Chlamydia (REF = Never Diagnosed)					
Diagnosed More than One Year Ago	●	○	●	○	●
Diagnosed Less than One Year Ago	○	○	○	○	○
History of Gonorrhea (REF = Never Diagnosed)					
Diagnosed More than One Year Ago	○	○	○	○	○
Diagnosed Less than One Year Ago	●	●	○	●	●
History of Syphilis (REF = Never Diagnosed)					
Diagnosed More than One Year Ago	○	○	○	○	○
Diagnosed Less than One Year Ago	●	●	○	●	○
Behavioral					
Receptive Anal Sex (REF = No)					
Yes With Condom	●	○	○	○	●
Yes Without Condom	●	●	●	●	●
Race of Last Two Sexual Partners (REF = Both Partners Different Race)					
Both Partners Same Race	●	○	○	○	○
One Partner Same Race, One Different	●	●	○	○	●
Age Difference of Last Two Sexual Partners	○	○	○	○	○
Number of Sex Partners in the Last 3 Months	●	●	●	○	●
Mental Health					
Intimate Partner Violence (REF = Never)	○	●	○	○	○
Substance Use					
Ecstasy Use (REF = No)	○	○	○	○	○
Methamphetamine Use (REF = No)	●	●	●	○	●
Nitrates Use (REF = No)	●	○	●	○	●

● = *Significant at $p < 0.05$*

○ = *NOT statistically significant*

Table 7.15 - Multivariate Survival Analyses Variable Level-Comparison (Type III p-values), January 2009 - June 2014.

Construct	All (n = 9,981)	Hispanics (n = 3,111)	Whites (n = 4,831)	Young MSM (n = 2,580)	Older MSM (n = 7,401)
Demographic					
Country of Origin	N/A	●	N/A	N/A	N/A
Race/Ethnicity (REF = Other)	●	N/A	N/A	○	●
Age Group (REF = 40+)	●	○	○	N/A	N/A
Biological					
History of Chlamydia (REF = Never Diagnosed)	●	○	●	○	●
History of Gonorrhea (REF = Never Diagnosed)	●	●	○	●	●
History of Syphilis (REF = Never Diagnosed)	●	●	○	●	○
Behavioral					
Receptive Anal Sex (REF = No)	●	●	●	●	●
Race of Last Two Sexual Partners (REF = Both Partners Different Race)	●	●	○	○	●
Age Difference of Last Two Sexual Partners	○	○	○	○	○
Number of Sex Partners in the Last 3 Months	●	●	●	○	●
Mental Health					
Intimate Partner Violence (REF = Never)	○	●	○	○	○
Substance Use					
Ecstasy Use (REF = No)	○	○	○	○	○
Methamphetamine Use (REF = No)	●	●	●	○	●
Nitrates Use (REF = No)	●	○	●	○	●

● = *Significant at $p < 0.05$*

○ = *NOT statistically significant*

Assessing Selection Bias

The PROC PHREG command conducts listwise deletion for all individuals who are missing values for at least one of the variables specified in the model. Of the 9,981 individuals available for analysis in the composite model, 823 (8%) had a value missing for at least one specified variable (Table 7.16).

Table 7.16 - Chi-Square Comparisons of Categorical Predictors Between Individuals Excluded from the Multivariate Survival Analysis by Listwise Deletion (n = 823) and Individuals Included in the Analysis (n = 9,158), January 2009 - June 2014.*

	Not Included (n = 823)		Included (n = 9,158)		Total (n = 9,981)
	n	%	n	%	n
Race/Ethnicity (REF = Other)					$p < 0.0001$
White	204	24.8%	4,627	50.5%	4,831
Hispanic	175	21.3%	2,936	32.1%	3,111
Black	35	4.3%	744	8.1%	779
Other	333	40.5%	851	9.3%	1,184
Missing	75	9.1%	1	0.0%	76
Age Group (REF = 40+)					$p = 0.0055$
<25	243	29.5%	2,337	25.5%	2,580
25-29	202	24.5%	2,345	25.6%	2,547
30-39	240	29.2%	2,537	27.7%	2,777
40+	138	16.8%	1,939	21.2%	2,077
History of Chlamydia					$p = 0.06$
Never Diagnosed	644	78.3%	7,434	81.2%	8,078
Diagnosed More than One Year Ago	96	11.7%	1,348	14.7%	1,444
Diagnosed Less than One Year Ago	22	2.7%	376	4.1%	398
Missing	61	7.4%	0	0.0%	61
History of Gonorrhea					$p = 0.05$
Never Diagnosed	579	70.4%	6,875	75.1%	7,454
Diagnosed More than One Year Ago	127	15.4%	1,841	20.1%	1,968
Diagnosed Less than One Year Ago	45	5.5%	442	4.8%	487
Missing	72	8.7%	0	0.0%	72
History of Syphilis					$p = 0.33$
Never Diagnosed	674	81.9%	8,586	93.8%	9,260
Diagnosed More than One Year Ago	35	4.3%	383	4.2%	418
Diagnosed Less than One Year Ago	10	1.2%	189	2.1%	199
Missing	104	12.6%	0	0.0%	104
Receptive Anal Sex					$p = 0.54$
No	476	57.8%	5,644	61.6%	6,120
Yes with Condom	147	17.9%	1,642	17.9%	1,789
Yes without Condom	174	21.1%	1,872	20.4%	2,046
Missing	26	3.2%	0	0.0%	26
Race/Ethnicity of the Last Two Sexual Partners					$p = 0.89$
Both Partners Different Race	134	16.3%	3,080	33.6%	3,214
Both Partners Same Race	140	17.0%	3,339	36.5%	3,479
One Partner Same Race, One Different	122	14.8%	2,739	29.9%	2,861
Missing	427	51.9%	0	0.0%	427
Intimate Partner Violence					$p = 0.52$
Never	647	78.6%	8,397	91.7%	9,044
Ever, Past Year, or Past Three Months	64	7.8%	761	8.3%	825
Missing	112	13.6%	0	0.0%	112
Used Ecstasy in the Past 12 Months					$p = 0.58$
No	679	82.5%	8,302	90.7%	8,981

Yes	65	7.9%	856	9.3%	921
Missing	79	9.6%	0	0.0%	79
Used Meth in the Past 12 Months					$p = 0.57$
No	695	84.4%	8,647	94.4%	9,342
Yes	45	5.5%	511	5.6%	556
Missing	83	10.1%	0	0.0%	83
Used Nitrates in the Past 12 Months					$p = 0.42$
No	632	76.8%	7,751	84.6%	8,383
Yes	105	12.8%	1,407	15.4%	1,512
Missing	86	10.4%	0	0.0%	86
Total	823	8.2%	9,158	91.8%	9981

**Percents represent column percents*

Chi-squared tests were run for categorical variables and an independent samples t-test for the continuous variable to determine if the proportion of individuals in each category was significantly different between the analyzed group and the listwise-deleted group.

The only significant differences between those analyzed and those deleted were by race/ethnicity ($p < 0.0001$), age group ($p = 0.0055$), and age of last two sexual partners ($p = 0.03$). A greater proportion of individuals who were deleted were classified as "Other" for race/ethnicity when compared to those who were analyzed (41% vs. 9%). Individuals who were analyzed were slightly older than individuals who were not analyzed (30% vs. 26% in the <25 age group). Lastly, individuals who were analyzed had a slightly older average age of partners when compared to those who were deleted.

However, the analyzed and deleted groups did not differ by history of chlamydia ($p = 0.06$), history of gonorrhea ($p = 0.05$), history of syphilis ($p = 0.33$), receptive anal sex ($p = 0.54$), race/ethnicity of the last two sexual partners ($p = 0.89$), intimate partner violence ($p = 0.52$), ecstasy use ($p = 0.58$), meth use ($p = 0.57$), or nitrates use ($p = 0.42$).

Given these findings, it appears that selection bias may be present by the demographic variables. This limitation, as well as other limitations, strengths, and policy implications of this algorithm, will be discussed extensively in Chapter 8.

Chapter 8 – Discussion of Findings, Limitations and Policy Implications

Summary of Findings

This dissertation utilized data from a sample of 9,981 MSM to determine what variables were significantly different between MSM who became HIV-positive over the follow-up period and MSM who remained HIV-negative. Previous literature findings and bivariate results from this analysis were used to select variables to operationalize the constructs outlined in Syndemics Theory. The biological construct was operationalized through history of chlamydia, history of gonorrhea, and history of syphilis; the behavioral construct was operationalized through receptive anal sex, race/ethnicity of the last two sexual partners, age of the last two sexual partners, and number of sexual partners in the last three months; the mental health construct was operationalized through intimate partner violence; lastly, the substance use construct was operationalized through ecstasy use, methamphetamine use, and nitrates use in the past year. These variables were inserted into a multivariate survival analysis to perform an empirical test of Sydemics Theory for the MSM population served by the Los Angeles LGBT Center.

When controlling for age group and race/ethnicity, all variables except age of the last two sexual partners, intimate partner violence, and ecstasy use were significantly related to HIV seroconversion in this population. While this information is useful, the goal of this dissertation was to use these results to inform future HIV prevention efforts. To accomplish this aim, the coefficients for each stratum were summed and exponentiated to create a hazard ratio that would serve as the HIV risk score for each unique individual.

If PrEP was given in a non-discriminant way to everyone, and assumed to be 100% effective, it would take 9,981 individuals on PrEP to avert all 395 infections (Seroconversion rate of 3.96%). If using an HIV risk score of 5 as the cut-point, there would be 4,485 individuals on

PrEP to advert 281 HIV infections (Seroconversion rate of 6.3%). By using this cut-point, only 48% of the total population are treated with PrEP, yet 76% of all HIV infections are averted. Using an informed cut-point has the potential to save the healthcare system a significant amount of money while ensuring PrEP is only prescribed to the patients who are most at-risk.

Following the construction of the HIV risk score and the determination of cut-points for PrEP, the final aim of this dissertation was to investigate if there were any differences between at-risk MSM subgroups when compared to the general population. Hispanic MSM were first compared to White MSM and then young MSM (MSM under 25 years of age) were compared to older MSM (MSM 25 years of age or older).

The only variables significant in the Syndemics framework for Whites were history of chlamydia, receptive anal sex, number of sex partners in the last three months, meth use, and nitrate use. The Hispanic subgroup also had a significant relationship between receptive anal sex, number of sex partners in the last three months, and meth use. However, history of gonorrhea, history of syphilis, race/ethnicity of the last two sexual partners, intimate partner violence, and country of origin were also significant for Hispanics and thus presented unique circumstances for HIV when compared to Whites. When testing for differences, only nitrates use and IPV were significantly different between Hispanics and Whites.

When comparing young MSM and older MSM, the only variables significant for YMSM were history of gonorrhea, history of syphilis, and receptive anal sex. While history of gonorrhea and receptive anal sex were also significant for older MSM, race/ethnicity of the last two sexual partners, number of sexual partners, methamphetamine use, and nitrates use were significant in older MSM but not YMSM. Therefore, racial/ethnic networks and substance use may be more

impactful for older MSM in contracting HIV but not as impactful for young MSM. When interactions were tested, there were no significant differences detected.

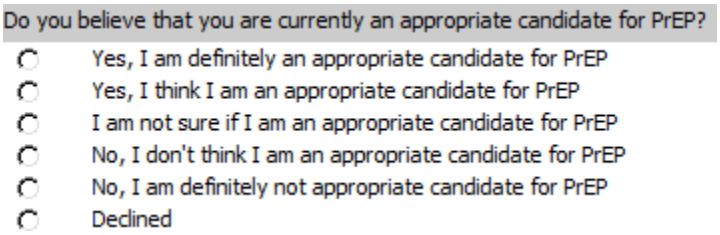
These results indicate that the circumstances for HIV infection may be different between Hispanic MSM and White MSM, but may not be different between young MSM and older MSM. While these groups have been treated as one homogeneous group in previous studies (Menza et al. 2009, Smith et al. 2012), these results show that circumstances for HIV infection need to be explored separately for these most at-risk subgroups.

This dissertation showed that Syndemics Theory was valid for the entire population. We learned that the biological, behavioral, and mental health (in the case of Hispanics) were all significant in predicting HIV and thus validated the use of Syndemics as a framework. Furthermore, the dissertation also showed that Syndermics Theory could effectively inform the creation of a risk score that prospectively triages an individual to the appropriate HIV prevention strategy. Lastly, this dissertation revealed that there are different circumstances for HIV infection depending on both race/ethnicity and age group. While these findings are informative, the following sections will discuss how these results will be implemented in the application of the HIV risk algorithm.

HIV Risk Algorithm Implementation – Client Experience

From January 2009 to July 2015, the risk assessment at the Los Angeles LGBT Center was administered by counselors in face-to-face interviews and did not contain questions on either nPEP or PrEP. In the newest risk assessment version launched in August 2015, counselors provide educational statements about nPEP and PrEP in face-to-face interviews, and then ask clients a Likert-type question to assess the individual's self-perceived candidacy for PrEP (Figure 8.1).

Figure 8.1 – PrEP Candidacy Question



Preliminary data from this question collected in August and September (n = 2,353) shows that most individuals are not sure if they are candidates for PrEP (Table 8.1). More specifically, 20% stated that they are definitely appropriate candidates, 15% said they think they are appropriate candidates, 26% stated that they are not sure, 18% said they do not think they are appropriate candidates, 14% stated that they are definitely not appropriate candidates, and 7% declined. This means that 59% are either not certain (33%) or not sure (26%) of their PrEP candidacy, showing the potential utility of this HIV risk algorithm as a triage mechanism for PrEP.

Table 8.1 - PrEP Candidacy Self-Assessment, August 3rd, 2015 - September 11th, 2015.

	n	%
Yes, I am definitely an appropriate candidate for PrEP	471	20.0%
Yes, I think I am an appropriate candidate for PrEP	346	14.7%
I am not sure if I am an appropriate candidate for PrEP	622	26.4%
No, I don't think I am an appropriate candidate for PrEP	420	17.8%
No, I am definitely not appropriate candidate for PrEP	323	13.7%
Declined	171	7.3%
Total	2,353	100.0%

Starting in October 2015, the risk assessment will be self-administered in a computer-assisted interview via the Healthvana platform. When asked the PrEP candidacy question, individuals who definitely think they are appropriate candidates will automatically be referred to a PrEP provider. However, individuals who are either not sure or think they may be candidates will be asked an additional question: “Would you like your PrEP candidacy assessed today?”

The risk score and accompanying recommendation will be sent directly to the provider which will prompt a conversation when face-to-face with the client. The medical provider and client can then collaboratively decide whether or not the client should begin on PrEP. The experience from the provider side will be discussed in more detail below.

HIV Risk Algorithm Implementation – Provider Experience

Provided a client elects to have their PrEP candidacy assessed, the answers from their risk assessment, their HIV risk score, and PrEP recommendation will be sent to the provider. If the client was exposed to HIV in the last 72 hours (the time point for PrEP candidacy), the chart will have an alert that states "Administer nPEP." The client will be provided a 28-day supply of nPEP and instructed to return for follow-up HIV testing at which point PrEP candidacy can be reassessed.

If a client has not been exposed to HIV in the last 72 hours but has a risk score greater than or equal to five, the medical provider will be alerted with the following statement, "Given this individual's risk behavior, they are a good candidate for PrEP. Assess potential for medication adherence and begin on PrEP if appropriate." The medical provider will have a conversation with the client about beginning PrEP given their risk behaviors, and answer any concerns about medication or side effects. The medical provider and the client will jointly consider the PrEP recommendation, potential for medication adherence, and side effects. This information will allow the medical provider and the client to collaboratively determine if PrEP should be initiated.

If a client has not been exposed to HIV in the last 72 hours but has a risk score less than five, the medical provider will be alerted with the following statement, "Given this individual's risk behavior, they are not a good candidate for PrEP." As stated before, this is only one item to

consider in beginning PrEP. Therefore, the HIV risk score is just one piece of the conversation between the medical provider and client in ultimately determining if PrEP should be initiated.

Limitations of the Dataset

The first limitation is there may have been a selection bias between the population analyzed (n = 9,158) and the group that was removed in the multivariate model via listwise deletion (n= 823). While the population that was deleted only represented 8% of the overall population, they were more likely to identify with an "Other" race/ethnicity, be under the age of 30, and report younger sexual partners during their last two sexual experiences. These trends likely indicate that there is a slight selection bias by age group and race/ethnicity, and interpretations for the "Other" race/ethnicity category should be kept in mind when making any assessments of generalizability.

The second limitation also concerns generalizability, specifically among the African-American and Asian/Pacific Islander (PI) populations. African-American MSM have the highest rates of HIV infection in the United States (CDC 2014b), but there were only 38 HIV infections within this group (4.9% of African-American testers and 9.6% of all positives). In comparison, 20% of all HIV infections nationally are among African-American MSM (CDC 2014b). In absolute numbers, African-American MSM accounted for 10,600 new HIV infections in the United States in 2010, a figure comparable to the number of new HIV infections in White MSM, despite the much lower population size (CDC 2014). A possible reason for such low representation of African-American HIV positives in this sample is that an inclusion criterion was two or more HIV testing encounters in the study period, and many of African-American HIV positives were eliminated (n = 138) because they only tested once within the study period.

Individuals of Asian/PI descent have the lowest overall HIV risk among racial/ethnic MSM (CDC 2015), but they were underrepresented in the testing population. For example, Asian/PI individuals made up only 8.5% of the testing population at the Los Angeles LGBT Center but, in 2013, made up 15% of the population in Los Angeles County (US Census 2015).

In contrast, the sample size was robust and allowed for comparisons between Hispanic (n = 167 HIV infections) and White MSM (n = 155 HIV infections) as well as young MSM (n = 128 HIV infections) and older MSM (n = 267 HIV infections). Although over 50% of the total sample was a racial/ethnic minority, the lack of African-Americans and Asian/PIs present a significant limitation to this analysis.

A third limitation is that the dataset may not be representative when applying these results to the United States. Los Angeles County, and by extension the Los Angeles LGBT Center, has a significantly higher proportion of Hispanics than many other parts of the Country. Furthermore, the concentration of African-Americans in Los Angeles County is only 9% versus 44% in Fulton County, Georgia (the County that contains the city of Atlanta) (US Census 2013; US Census 2014). Therefore, generalizability issues at the local, County, and national level must all be taken into consideration when reviewing these results.

A fourth limitations is that we have incomplete data on HIV positives. It is estimated that 16% of all individuals who have HIV in the US are not aware of their infection (Hall et al. 2013). If we are to assume a similar proportion in Los Angeles County, this dataset is not able to account for the individuals who may become HIV-positive but have no baseline data. Furthermore, for individuals who do test HIV positive, we are only able to determine when they were *diagnosed* and not when they were *infected*. Therefore, sexual behavior directly prior to the diagnosis may not truly tell the story of how they were infected given they were infected years

before and only recently diagnosed. Therefore, the unknown HIV infections as well as the unknown timing of actual infection may bias the predictors in the dataset in either direction depending on the risk profile of this undiagnosed population.

A fifth limitation is the likelihood of recall bias. While all studies relying on self-report are susceptible to recall bias, the length of recall is often associated with the degree of accuracy in HIV prevention research (Catania et al. 1990). Therefore, data may be less susceptible to recall bias for individuals reporting recent sexual experiences when compared to individuals whose last two sexual experiences were less recent.

Lastly, there were a number of omitted variables that have been shown to be related to HIV infection but were not available for analysis. Sexual compulsivity (Grov et al. 2010, Parsons et al. 2012, Woolf-King et al. 2013) and childhood sexual abuse (Mimiaga et al. 2009, Sweet et al. 2012, Phillips et al. 2014) are Syndemic conditions that have been verified by other researchers as being linked to HIV contraction. However, the risk assessment was created in a time where researchers were not cognizant of these cofactors and thus they were not included in the risk assessment.

Strengths of the Dataset

This dataset also has a number of strengths. The Los Angeles LGBT Center is the largest single testing site for HIV in Los Angeles County and is one of the largest LGBT service organizations in the world (LGBT 2015). Therefore, the sample size (n = 9,981 unique MSM) allows for adequate power in making comparisons of risk behaviors that may be relatively rare within the overall MSM population.

The second strength is the representation racial/ethnic minority MSM within the Los Angeles LGBT Center's population, specifically Hispanic MSM. Previous studies utilizing survival analyses have had much fewer racial or ethnic minorities at 23% (Menza et al. 2009) and

19% (Smith et al. 2012). In contrast, 51% of unique MSM in this study population identify with a racial/ethnic minority group. Therefore, these analyses were able to determine much more clearly the risk profiles that may be unique to different racial/ethnic minority MSM communities.

The third strength is that model construction and subsequent analysis is based in theory. Syndemics Theory states that the HIV epidemic is driven by the "mutually reinforcing" issues of substance use and psychosocial problems within the MSM population (Halkitis et al. 2010). While Menza et al. (2009) and Smith et al. (2012) identified numerous variables that are predictive of HIV infection, this dissertation allows for a more theoretically-informed analysis.

The fourth strength is that the data are much newer than previous analyses. Menza et al. used HIV testing data from 2001 to 2008, and Smith used testing data from 1998 to 1999. The contemporary nature of these data allow this analysis to more accurately assess the current risk environment including variables that have only recently been associated with HIV incidence (e.g., intimate partner violence). These four dataset strengths give the analysis an advantage over previous studies and allow for a novel contribution to the HIV prevention literature.

Limitations of the Algorithm

The first limitation is that it may be unethical to prescribe PrEP based on a cut-point, even if it is informed by statistical analyses. However, as stated in the HIV Risk Algorithm Implementation sub-section, the position of the Los Angeles LGBT Center is to provide PrEP to whomever wants to take PrEP. Therefore, this tool will mainly be used to assess candidacy for individuals who are not sure if this intervention is best for them.

The second limitation is that the survival analyses may not capture the complexity that is accounted for by analyses that utilize repeated measures. An individual may change their risk profile from baseline to follow-up, and the chosen method of analysis does not account for shifts

over time in the risk profile. Therefore, this analysis method makes the assumption that an individual's risk behavior does not change over time. While this may be a significant limitation for other types of analyses, the goal of this dissertation is to form a predictive score utilizing baseline measures. Therefore, survival analysis was deemed the best way to accomplish this goal given the population and study objectives. While these two limitations are important, there are a number of important strengths.

Strengths of the Algorithm

The first strength is that this is the first algorithm, to our knowledge, which automatically triages individuals to biomedical interventions like nPEP and PrEP. While knowledge of these tools has typically been low, the automatic triage to these tools removes the need for individuals to be aware of these tools a priori.

The second strength is that this is the first PrEP algorithm to actually use retrospective data to determine candidacy. While previous analyses have used population-level data and limited individual-level data (Chen et al. 2014), this is the first algorithm to use actual testing data from HIV-negatives and HIV-positives to project future HIV risk.

The third strength is that the algorithm is based entirely on the operationalization of the constructs found in Syndemics Theory. This theory has been shown to be valid across numerous subgroups of MSM and was therefore the ideal theory to use in the formulation of this algorithm. The final sub-section will discuss the policy implications of these findings at the Los Angeles LGBT Center.

Policy Implications for the Los Angeles LGBT Center

To address the poor representation of African-Americans in the testing population, the Center has applied for various grants to enhance its outreach to this MSM subgroup. In 2014, the

Center was awarded funds from Gilead (the pharmaceutical company that makes the most popular HIV nPEP, PrEP, and treatment medication, Truvada) to conduct nPEP and PrEP education among members of this population. Although it may be too early to determine the effect of this program, these funds will hopefully boost representation of this subgroup in the HIV testing population and thus allow for generalizations to African-American MSM in future analyses. As of this writing, there have been no official grants submitted to increase testing among the Asian/PI population.

For individuals who have not been diagnosed and have not tested at this site, the Los Angeles LGBT Center is currently participating in an HIV vending machine program that dispenses vending machine kits to individuals who do not want to receive regular testing services due to feelings of stigma from walking into an LGBT-identified organization. As with the program designed to reach more African-Americans, preliminary data are not yet available for the efficacy of the vending machine program. However, both programs will hopefully boost testing numbers among African-American MSM and individuals who are at greater risk for not knowing their status due to stigma.

The literature search also revealed that there were a number of variables which were not available and thus precluded more detailed analyses. As mentioned previously, sexual compulsivity and childhood sexual abuse have been shown recently in the literature to be linked to HIV infection but were not asked about in this risk assessment. In the four years since this dissertation was initiated, the Los Angeles LGBT Center's risk assessment has undergone a substantial revision to account for these additional risk factors. The revised risk assessment was implemented in August 2015 and now includes questions on depression, self-perceived feelings of microaggressions (e.g., racism and homophobia), and sexual compulsivity. Future analyses

should be able to assess a more comprehensive picture of HIV risk in this population given these additional Syndemic variables.

Further evaluation should also be conducted to determine if such algorithms make individuals more mindful about their risk practices. While the algorithm's intent is to prescribe a biomedical tool based on an individual's HIV risk profile, informing an individual of their candidacy for PrEP may both biomedically reduce their risk through the intervention as well as behaviorally reduce their risk through reflection and subsequent sexual risk reduction.

In contrast, the act of taking PrEP may embolden PrEP users and make them even more sexually risky because of their perceived biomedical safety net. Furthermore, MSM who are informed that they are not good candidates for PrEP may feel like they are not at risk of HIV, thus emboldening them to have more risky sex. Therefore, this algorithm may make individuals more mindful or may backfire if individuals who score low with this algorithm decide to have riskier sex. Subsequent analyses will be needed to determine the ramifications of utilizing this score in the general testing population. As with any advance, there are also likely to be differences in response based on the population analyzed (e.g., meth users versus individuals in serodiscordant couples) and these differences should be elucidated with further study.

Lastly, while this algorithm is timely as of this writing, the circumstances for HIV infection will most certainly change over the coming decades. Advances in technology, changes in drug use behavior, and other biomedical innovations like long-lasting injectable PrEP may significantly change the HIV epidemiological landscape. Provided such an algorithm is used in practice, it is imperative that the algorithm be implemented in a dynamic way in order to account for new and emerging risk factors for HIV infection.

Implementation in Other Jurisdictions

If implemented in other jurisdictions, there are numerous factors that all agencies should consider and other factors that may not apply to all agencies. This sub-section will first discuss the factors that everyone should consider followed by those that only a select few may need to consider.

First, this analysis as well as studies by Menza and Smith have showed that certain variables are consistently related to HIV infection across MSM populations: receptive anal sex, history of STIs, methamphetamine use, and number of sex partners. These variables should be asked about in all populations seeking to replicate this algorithm. However, other variables such as race/ethnicity of last two sexual partners and nitrates use were not consistent across populations when analyzing statistical significance as well as coefficient magnitude. Therefore, other variables may need to be more thoroughly vetted to determine which variables are most appropriate for different subsets of MSM.

Second, we learned that mental health factors potentially play a greater role than once previously thought. The significant finding of HIV infection among Hispanic MSM who reported IPV was novel, and this is just a further validation of the Syndemics framework. In our opinion, other jurisdictions should use this framework as not only a way to craft their own HIV risk algorithm but also holistically update HIV prevention efforts.

Third, other jurisdictions may consider HIV prevalence and community viral load in determining additional population factors that may influence score adjustment. Community viral load is a concept that defines the proportion of individuals who are HIV-positive and are adherent to treatment: lower values indicate more medication adherence and thus more control of the virus in the population. In contrast, higher values indicate less medication adherence and less control of the virus in the population. Populations with a higher prevalence of HIV and a higher

community viral load will need an adjustment to a lower cut-point for PrEP candidacy to cover more individuals since the probability for infection is higher. Environments where HIV prevalence is low and community viral load is low will need an adjustment to a higher cut-point for PrEP candidacy since the probability for infection is lower.

Fourth, medication-related factors should also be considered before prescription of PrEP. The iPrEx study showed that PrEP was only completely efficacious if nearly every dose was taken (Grant et al. 2010). However, the efficacy waned as an individual missed PrEP doses. Provided this risk score is implemented, we recommend the use of a short medication adherence scale such as the 8-item Morisky Medication Adherence Scale (Morisky et al. 2008). This scale has a high reliability with a Cronbach's alpha measure of 0.83 (Morisky et al. 2008). Although originally developed for hypertension (Morisky et al. 1986), this scale has shown to be useful in measuring TB medication adherence (Coly & Morisky 2004) and HIV medication adherence (DiIorio 2008 et al.).

If an individual is not sure of their PrEP candidacy, meets the algorithm criteria for PrEP, and has a high likelihood for medication adherence as shown by a medication adherence scale, we recommend PrEP initiation. For MSM with a lower probability of adequate medication adherence, quarterly testing is suggested if PrEP is initiated. This condition would be used to ensure early viral detection provided the patient contracts the virus due to low medication adherence. This requirement could be as simple as only prescribing 90 days of PrEP medication at a time and requiring a return in three months as a prerequisite for filling the next prescription. Provided the patient does not test HIV-positive after three months, a new prescription for PrEP can be provided. Accounting for such medication adherence factors will further maximize the effectiveness of this algorithm.

As discussed previously, there are also factors that may not apply to all clinics but bear mentioning. Financial factors (e.g., insurance coverage, grant funding) may further influence the algorithm cut-point if implemented in other jurisdictions. Certain jurisdictions may have a high proportion of uninsured (e.g., undocumented immigrants) where funding is only available to prescribe PrEP to the most at-risk. In this case, the score would need to be adjusted upward (i.e., be more selective). In contrast, other jurisdictions may have a high proportion of insured and therefore third-party billing may allow for complete coverage. Similar to the biological and medication adherence factors, insurance/funding levels must also be taken into consideration when deciding what cut-point is ideal for a given organization and jurisdiction.

Second, while this sample had a high proportion of racial/ethnic minorities, Latinos made up a majority of this minority (see what I did there?). If implemented in places like Baltimore or Atlanta that have a high proportion of African-Americans, other cultural-specific factors should be considered. In contrast, if implemented in places like South Dakota or Nebraska, or places with a high proportion of White individuals, racial/ethnic networks may not be as important.

Third, population density may be another important consideration. Los Angeles is the second largest city in the United States, and the socialization patterns may differ from places like Dubuque, Iowa. Population density may affect partnering patterns, and this is another factor to consider in jurisdictions that still serve MSM clientele but have populations much smaller than Los Angeles.

While the HIV PrEP Algorithm will need to be adapted if implemented in other jurisdictions, we believe that this tool will hopefully be one more additional tool in the HIV prevention arsenal.

Conclusions

The field of HIV prevention has changed substantially over the past two decades, initially with the implementation of nPEP and then with the implementation of PrEP. Although nPEP usage has been limited, nPEP and PrEP usage are likely to increase given the standardized education with the new risk assessment and proposal for implementation of the HIV Risk Algorithm at the Los Angeles LGBT Center.

While the dataset used to develop the algorithm has numerous limitations, the sample size, breadth of variables, theoretical basis and length of follow-up are robust. This tool will hopefully be one more effective tool in the HIV prevention arsenal. By quantifying risk and assessing nPEP and PrEP candidacy, sexual health providers can intervene quicker for MSM already exposed and more accurately inform the needs for MSM who may undergo consistent exposure. There is no magic bullet for the HIV epidemic, but with this algorithm in addition to our existing toolkit, we can hopefully move one step closer to a world free of HIV.

Appendix I – Risk Assessment

Client Identification

Race/Ethnicity:

- White/Caucasian
- Hispanic/Latino(a)
- Black/African-American
- Asian
- American Indian/Alaskan Native
- Native Hawaiian/Pacific Islander
- Don't Know
- Declined
- Other Race

Orientation:

- Gay, lesbian, queer, or homosexual
- Bisexual
- Heterosexual
- Client does not know
- Other

Current Gender:

- Male
- Female
- Transgender Male to Female
- Transgender Female to Male
- Other

Current genitalia same as birth:

- Yes
- No
- N/A

Homeless Status:

- Not Homeless
- Homeless Outdoor
- Homeless Shelter
- Homeless Car
- Homeless No Detail
- No Response

Highest level of education:

- 8th grade or below
- Some high school
- High school graduate/GED
- Some college
- College degree
- Post-graduate study/degree

How did you learn about out services:

- Friend
- Publication
- Health education workshop
- Radio/TV ad
- Billboard
- LAGLC website
- Other website
- Other

Today's appointment set via text message:

- Yes
- No
- N/A

STI Counseling/Testing/Treatment

West Hollywood affiliation:

- Not affiliated
- Resident
- Employed
- Own real property
- Own a business
- Attend school
- Homeless and spend time

Test Site:

- Schrader screening
- Schrader treatment
- SPOT screening
- SPOT treatment
- POW

Screening Test:

- STD Only
- HIV Only
- STD & HIV
- Not testing
- Did not take

Type of test:

- Anonymous Test
- Confidential Test
- Did not state
- Not applicable

Reason for STI testing:

- Symptoms
- Screening
- Vaccination
- Tested positive
- Referred by partner (internet)
- Referred by partner (in person)
- Referred by health department
- Referred by InSpot
- Referred by other
- Other (please specify in a note)

Reason for HIV/STI testing:

- Just wanted to know
- Risky behavior
- STI related
- Starting a new relationship
- Reconfirming HIV+ result
- has HIV+ partner(s)
- had HIV+ partner(s)
- AIDS like symptoms
- Not testing
- Other (please specify in a note)

Number of prior HIV tests:

Date of last HIV test:

The result of the last HIV test result was::

- Negative
- Positive
- Pending
- Indeterminate
- Did not return for results

Vaccination history:

- Vaccinated for HEP A
- In progress for HEP A vaccination
- Not vaccinated for HEP A
- Does not know if vaccinated for HEP A
- Vaccinated for HEP B
- In progress for HEP B vaccination
- not vaccinated for HEP B
- Does not know if vaccinated for HEP B
- Other vaccines in the last 3 months

STI Symptoms

Discharge:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Burning:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Itching:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Bleeding:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Pain:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Lesion:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Rash:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Swelling:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Warts:

- None
- Urethral area
- Vaginal area
- Anus
- Throat
- Other (please specify in a note)
- Duration

Rectal urgency:

- None
- Duration

Frequent urination:

- Yes
- No
- N/A

Other:

STI History

Chlamydia:

- Never
- Past Year
- Ever

Gonorrhea:

- Never
- Past Year
- Ever

Herpes:

- Never
- Past Year
- Ever

Warts:

- Never
- Past Year
- Ever

Hepatitis A:

- Never
- Past Year
- Ever

Hepatitis B:

- Never
- Past Year
- Ever

Hepatitis C:

- Never
- Past Year
- Ever

Syphilis:

- Never
- Past Year
- Ever

Syphilis treatment:

Clinic treated

Date of treatment

City

State

Last Sexual Experience

Last sexual experience:

Partner #1 age:

Partner #1 gender:

- Male
- Female
- Transgender Male to Female
- Transgender Female to Male
- Intersex

Partner #1 ethnicity:

- Hispanic/Latino(a)
- Non-Hispanic
- Unknown/Unreported

Partner #1 race:

- American Indian/Alaskan Native
- Asian
- Black/African-American
- Caucasian
- Hawaiian/Pacific Islander
- More than one race
- Unknown/Unreported

Partner #1 sex risks:

- IDU
- Anonymous
- HIV status unknown
- HIV/AIDS infected
- Sex worker
- Partner found through the internet
- N/A

Partner #1 insert anal:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #1 receive anal:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #1 give oral:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #1 receive oral:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #1 vaginal:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #1 other sexual activities:

- Mutual masturbation
- Fisting
- Toy play
- Water sports

Prior Last sexual experience:

Partner #2 age:

Partner #2 gender:

- Male
- Female
- Transgender Male to Female
- Transgender Female to Male
- Intersex

Partner #2 ethnicity:

- Hispanic/Latino(a)
- Non-Hispanic
- Unknown/Unreported

Partner #2 race:

- American Indian/Alaskan Native
- Asian
- Black/African-American
- Caucasian
- Hawaiian/Pacific Islander
- More than one race
- Unknown/Unreported

Partner #2 sex risks:

- IDU
- Anonymous
- HIV status unknown
- HIV/AIDS infected
- Sex worker
- Partner found through the internet
- N/A

Partner #2 insert anal:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #2 receive anal:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #2 give oral:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #2 receive oral:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #2 vaginal:

- No
- Yes with condom
- Yes without condom
- N/A

Partner #2 other sexual activities:

- Mutual masturbation
- Fisting
- Toy play
- Water sports

# of sex partners in the last 30 days:

Sexual Activity in the Last 3 Months

Number of sex partners:

Do you have a main partner:

- Yes
- No
- N/A

Do you use condoms with your main partner:

- Yes, condom use always
- Yes, condom use mostly
- Yes, condom use sometimes
- No
- N/A

Insertive anal activity:

- No
- Yes, condom use always
- Yes, condom use mostly
- Yes, condom use sometimes
- Yes, condom use never

Receptive anal activity:

- No
- Yes, condom use always
- Yes, condom use mostly
- Yes, condom use sometimes
- Yes, condom use never

Give oral activity:

- No
- Yes, condom use always
- Yes, condom use mostly
- Yes, condom use sometimes
- Yes, condom use never

Receive oral activity:

- No
- Yes, condom use always
- Yes, condom use mostly
- Yes, condom use sometimes
- Yes, condom use never

Vaginal activity:

- No
- Yes, condom use always
- Yes, condom use mostly
- Yes, condom use sometimes
- Yes, condom use never

Met sexual partner(s) at:

- None
- Bar/club
- Street
- Private sex parties
- Bathhouse/sex club
- Gym
- Circuit parties
- Internet: www.manhunt.com
- Internet: www.adam4adam.com
- Internet: www.craigslist.com
- Internet: www.bareback.com
- Internet: www.dudesnude.com
- Internet: Other:
- Phone app: Grindr
- Phone app: Scruff
- Phone app: Jack'd
- Phone app: Recon
- Phone app: Other
- Through a friend
- Other (please specify in a note)
- Refused

Sexual Activity in the last 12 Months

Risk factors in the last 12 months:

- N/A
- Vaginal or anal sex with a male
- Oral sex with a male
- Vaginal or oral sex with a female
- Oral sex with a female
- Sex without a condom
- Sex with a person who is an IDU
- Sex with a person who is a MSM (female only)
- Sex with a person of unknown HIV status
- Sex with a person who is HIV+

IDU past 12 months:

- N/A
- Client used injection drugs
- Client shared IDU equipment

Substance Use in the last 3 months

Ecstasy:

- No
- Yes
- Yes before/during sex
- Refused/declined

Methamphetamines:

- No
- Yes
- Yes before/during sex
- Refused/declined

Nitrates/poppers:

- No
- Yes
- Yes before/during sex
- Refused/declined

Viagra/Cialis/Levitra:

- No
- Yes
- Yes before/during sex
- Refused/declined

Cocaine:

- No
- Yes
- Yes before/during sex
- Refused/declined

Crack:

- No
- Yes
- Yes before/during sex
- Refused/declined

Heroin:

- No
- Yes
- Yes before/during sex
- Refused/declined

GHB:

- No
- Yes
- Yes before/during sex
- Refused/declined

Alcohol:

- No
- Yes
- Yes before/during sex
- Refused/declined

How many times have you had 5 or more drinks at one time in the last 3 months:

STI Risk Assessment

Sex with male:

- Past 3 months
- Past Year
- Ever
- Never

Sex with female:
- Past 3 months
- Past Year
- Ever
- Never

Sex with transgender/transsexual:
- Past 3 months
- Past Year
- Ever
- Never

Used methamphetamines:
- Past 3 months
- Past Year
- Ever
- Never

Used injection drugs:
- Past 3 months
- Past Year
- Ever
- Never

Sex with IV drug user:
- Past 3 months
- Past Year
- Ever
- Never

Sex with anonymous partner:
- Past 3 months
- Past Year
- Ever
- Never

Sex with person with HIV/AIDS:
- Past 3 months
- Past Year
- Ever
- Never

Sex with sex worker:
- Past 3 months
- Past Year
- Ever

- Never

Sex for drugs or money:
- Past 3 months
- Past Year
- Ever
- Never

Performed in the Adult Film Industry in last 3 months:
- Yes
- No
- N/A

Victim of Domestic Violence:
- Past 3 months
- Past Year
- Ever
- Never

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