Title

Predictors of Repeat Sexually Transmitted Infections and the Efficacy and Economic Impact of a Financial Incentive Program for Sexually Transmitted Infection/HIV Testing Among Men-Who-Have-Sex-with-Men

Author

Anderson, Laura Jane

Publication Date

2018

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Predictors of Repeat Sexually Transmitted Infections and the Efficacy and Economic Impact of a Financial Incentive Program for Sexually Transmitted Infection/HIV Testing Among Men-Who-Have-Sex-with-Men

A dissertation submitted in partial satisfaction of the

requirements for the degree of Doctor of Philosophy

in Epidemiology

by

Laura Jane Anderson

2018

ABSTRACT OF THE DISSERTATION

Predictors of Repeat Sexually Transmitted Infections and

the Efficacy and Economic Impact of a Financial Incentive Program for

Sexually Transmitted Infection/HIV Testing Among Men-Who-Have-Sex-with-Men

by

Laura Jane Anderson

Doctoral in Philosophy in Epidemiology

University of California, Los Angeles, 2018

Professor Marjan Javanbakht, Chair

The incidence of sexually transmitted infections (STIs) has increased dramatically over the last decade in Los Angeles County (LAC), with men-who-have-sex-with-men (MSM) bearing a disproportionate burden of disease. STIs are not only responsible for significant morbidity and potential long-term sequelae but strong evidence indicates STI infection promotes HIV transmission and acquisition among MSM. Given the relationship between STIs and HIV incidence, it follows that MSM who repeatedly contract STIs may disproportionately contribute

to both STI and HIV transmission. Thus, understanding predictors of repeat STI infection is important for the development of targeted prevention efforts. Accordingly, **Chapter 2** of this dissertation sought to identify the rate and socio-demographic predictors of repeat gonorrhea and/or chlamydia infection in a clinic-based population of predominantly men-who-have-sex-with-men (MSM) in Los Angeles County.

Given the rising rates of STIs among MSM identifying not only predictors of infection but effective methods of prevention is crucial for infection control. Modeling studies have indicated that increased testing frequency could significantly reduce transmission of HIV and quell the rise of STIs. However, despite its demonstrated value, STI testing rates among MSM remain extremely low. Conventional methods such as education and awareness campaigns have demonstrated limited success in prompting STI testing in MSM populations and thus it is important that innovative testing strategies are developed and their impact evaluated both in terms of clinical effectiveness and cost. As such, **Chapter 3** of this dissertation evaluates the impact of an MSM-focused financial incentive program for STI and HIV testing on testing frequency and STI positivity. **Chapter 4** assesses the cost-effectiveness of a financial incentive program to encourage MSM to undergo STI and HIV testing.

The dissertation of Laura Jane Anderson is approved.

Pamina M. Gorbach

Sung-Jae Lee

Arleen Leibowitz

Marjan Javanbakht, Committee Chair

University of California, Los Angeles

2018

DEDICATION

To my parents, William and Deborah Anderson. To my sister, Ellen Sue. And to my nieces, Winifred & Marianne.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ACRONYMS

STI = Sexually Transmitted Infection

HIV = Human Immunodeficiency Virus

CDC = Centers for Disease Control and Prevention

MSM = Men-who-have-sex-with-men

LAC = Los Angeles County

P&S = Primary and Secondary

EL = Early Latent

GC = Gonorrhea

CT = Chlamydia

HR = Hazard Ratio

aHR = Adjusted Hazard Ratio

CI = Confidence Interval

OR = Odds Ratio

aOR = Adjusted Odds Ratio

RPR = rapid plasma regain

TPPA = Treponema Pallidum Particulate Agglutination

NAAT = Nucleic Acid Amplification Test

ACKNOWLEDGEMENTS

A sincere thank you to my Committee Chair, Dr. Marjan Javanbakht, for your guidance, patience and levity throughout this process.

A resounding thank you to my Doctoral Committee, Dr. Arleen Leibowitz, Dr. Sung-Jae Lee, and Dr. Pamina Gorbach. May I be as insightful and kind as each of you one day.

To AIDS Healthcare Foundation (AHF), especially Mark McGrath, Lauren Natoli, and Sagar Amin, an emphatic THANK YOU for being the source of my data; for always picking up the phone and patiently answering my questions; and treating me like one of your own. You are doing great things.

My truest gratitude to my mentor, boss, and role model, Dr. Teryl Nuckols. Your belief in me has sustained me throughout these last 6.5 years.

To my boyfriend, Daniel Whitmore for your endless love and support.

And to mom, dad, Teach, SueBee, and JoeBlo- thanks for being the best family anybody could ask for.

VITA

EDUCATION

The University of California Los Angeles, Los Angeles, CA

Jonathan and Karin Fielding School of Public Health

Master of Public Health, Epidemiology, March 2013

The University of North Carolina at Chapel Hill, Chapel Hill, NC

Bachelor of Arts, Economics; Chemistry Minor, May 2006

RESEARCH EXPERIENCE

Cedars Sinai Medical Center, Los Angeles, CA

Clinical Research Data Specialist, 2014-present

AIDS Healthcare Foundation, Los Angeles, CA

Public Health Consultant, 2014-2017

The University of California Los Angeles Department of Medicine, Los Angeles, CA

Graduate Student Researcher, 2012-2014

RESEARCH PAPERS IN PUBLICATION

Anderson LJ, Shekelle P, Keeler E, Uscher-Pines L, Shanman R, Morton S, Aliyev G, Nuckols TK. The Cost of Interventions to Increase Influenza Vaccination: A Systematic Review. Am J Prev Med. 2018 Feb;54(2):299-315

Nuckols TK, Keeler E, Morton S, **Anderson L**, Doyle BJ, Pevnick J, Booth M, Shanman R, Arifkhanova A, Shekelle P. Economic Evaluation of Quality Improvement Interventions Designed to Prevent Hospital Readmission: A Systematic Review and Meta-analysis. JAMA Internal Medicine. 2017 May 30

Nuckols TK, Keeler E, Morton SC, **Anderson L**, Doyle B, Booth M, Shanman R, Grein J, Shekelle P. Economic Evaluation of Quality Improvement Interventions for Bloodstream

Infections Related to Central Catheters: A Systematic Review. JAMA Internal Medicine. 2016 Dec 1;176(12):1843-1854

Bristow CC, Larson E, **Anderson LJ**, Klausner JD. Cost-effectiveness of HIV and syphilis antenatal screening: a modelling study. Sex Transmitted Infections. 2016 Aug: 92(5):340-6

Nuckols TK, Asch S, Patel V, Keeler E, Buntin MB, **Anderson L**, Escarce J. The Cost-Effectiveness of Computerized Physician Order Entry in U.S. Hospitals from the Societal Perspective. The Joint Commission Journal on Quality and Patient Safety. 2015 Aug: 41(8):341-50

Nuckols, TK, Smith-Spangler C, Morton S, Asch S, Patel V, **Anderson L**, Deichsel E, Shekelle P. The Effectiveness of Computerized Order Entry at Reducing Preventable Adverse Drug Events and Medication Errors in Hospital Settings: A Systematic Review and Meta-Analysis. Systematic Reviews. 2014 June: 3:56

Javanbakht M, Boudov M, **Anderson L**, Malek M, Smith LV, Chien M, Guerry S. Sexually Transmitted Infections among Incarcerated Women: Findings from a decade of screening in a
Los Angeles County Jail, 2002-2012. American Journal of Public Health. 2014 Nov. 104(11):e103-9

Nuckols TK, **Anderson L**, Diamant A, Popescu I, Chou R. Opioid Prescribing: A Systematic Evaluation and Critical Appraisal of Recent Guidelines. Annals of Internal Medicine. 2014 Jan: 160(1):38-47

Chapter 1. Introduction

1.1 Rates of STIs Among MSM

Rates of sexually transmitted infections (STIs) have increased dramatically over the last decade in Los Angeles County (LAC), with men who have sex with men (MSM) disproportionally contributing to infection. Between 2009 and 2016 rates of primary and secondary (P&S) syphilis increased 109% in LAC from 7.6 to 15.9 cases per 100,000.[1] During the same time period early latent (EL) syphilis infections rose nearly 117% from 8.3 to 18.0 cases per 100,000.[1] Importantly, MSM account for the majority of syphilis cases; in fact, over 80% of P&S syphilis cases nationwide in 2016 occurred among MSM.[1] Accordingly, rates of syphilis among MSM exceed those of heterosexual men and women. The 2016 rate of P&S syphilis among MSM in California was estimated to be 450.7 per 100,000 MSM- over 115 times higher than the rate among women.[1]

Similar upward trends also exist for gonorrhea (GC) and chlamydia (CT). Between 2010 and 2015, GC incidence among MSM attending STD Surveillance Network clinics in several large US cities increased an estimated 151% (from 1,369 cases per 100,000 MSM to 3,435 cases per 100,000 MSM).[1] Over the same period gonorrhea rates among women and men-who-have-sex-with-women increased but by a significantly smaller margin (39.8% and 31.7%, respectively).[1] The Centers for Disease Control and Prevention (CDC) estimated an increase from 13.0% in 2010 to 16.0% in 2015 in the overall prevalence of chlamydia among MSM attending these clinics.[1]

1.2 Relationship between STIs and Incident HIV

STIs are not only responsible for significant morbidity and potential long-term sequelae, such as neurosyphilis and disseminated gonococcal infection, but strong evidence indicates STI infection

promotes HIV transmission and acquisition among MSM.[2-4] A 2015 study of MSM in Atlanta, GA reported that after adjusting for time-varying risk behaviors a prior diagnosis of rectal CT or GC was significantly associated with incident HIV (adjusted hazard ratio (aHR) = 2.7; 95% confidence interval (95% CI): 1.2-6.4).[4] Similarly, a 2010 study of MSM in San Francisco, CA found that after controlling for behavioral risk factors, having two or more rectal CT or GC infections within two years increased the likelihood of HIV diagnosis by almost 9-fold (aHR = 8.85, 95% CI: 2.57-30.40).[2] Finally, in a 2010 study of MSM in Sydney, Australia authors reported a significant association between rectal GC and HIV acquisition (aHR= 7.12, 95% CI: 2.05-24.79).[3]

1.3 Targeting High-Risk MSM for Focused Prevention Efforts

Given the well-established relationship between STIs and HIV incidence it follows that MSM who repeatedly contract STI infections may disproportionately contribute to both STI and HIV transmission. As such, identifying risk factors for repeat STI infection is important for the development of focused prevention efforts among MSM. And, with the international emergence of gonococcal resistance to antibiotics, targeted prevention efforts in MSM may be increasingly crucial in halting disease propagation. Several prior studies have examined characteristics associated with repeat STIs in this population.[5-7] Two studies reported significant associations between HIV-infection and repeat syphilis infection; however, both studies failed to control for sexual risk behaviors, presumably strong confounding variables.[6,7] In a third study authors found HIV-infection (aOR = 1.65, 95% CI: 1.14-2.37) along with black race (aOR = 1.84, 95% CI:1.12-3.04) and having 10 or more sexual partners (aOR = 1.99, 95% CI: 1.12-3.50) to be significant predictors of repeat syphilis infection after controlling for sexual risk behaviors.[5] While the depth of the literature focused on predictors of repeat syphilis infection is shallow,

studies examining risk factors for repeat CT and GC among MSM remains even more limited. Indeed, there have been no prior published studies evaluating associated risk factors of repeat CT and/or GC infection among MSM. To address the dearth of literature, the objective of **Chapter 2** is to identify socio-demographic predictors of repeat CT and/or GC testing among MSM.

1.4 Testing and Treatment as a Method of Prevention

Identifying not only predictors of infection but effective methods of prevention is crucial for infection control. Enhanced testing and treatment is a promising strategy for STI prevention. In fact, prior modeling studies suggest that increased frequency of STI screening in MSM could significantly reduce transmission of HIV and help mitigate outbreaks of STIs.[8,9] Specifically, a 2010 study found that increasing the frequency of syphilis testing among MSM to twice per year has the potential to reduce syphilis prevalence by 61% and as much as 84% if the increased testing was targeted to MSM with 10 or more partners or those who reported group sex.[8] Tuite and colleagues examined the marginal effect of increased frequency versus increased coverage of syphilis screening using an agent-based, network model of syphilis transmission. Authors reported that increasing the frequency of syphilis screening to every three months in a small fraction of the population was more effective at reducing reported and incident syphilis infections than just increasing the proportion of MSM screened.[9]

1.5 Suboptimal Testing Rates Among MSM

Current CDC guidelines advise annual screening for all sexually active MSM, with more frequent screening (every 3-6 months) among those who report high risk behaviors.[10] Despite these recommendations, evidence suggests that testing rates have been suboptimal among MSM including HIV-infected MSM.[11-14] Hoover and colleagues evaluated screening practices at 8 large HIV clinics in 6 US cities and found that rectal CT and rectal and pharyngeal GC annual

screening rates ranged from 2.3% to 8.5% and the annual screening rate for syphilis ranged from 66.0% to 75.8%.[12] A 2010 study examined STI screening in an HIV-positive cohort of MSM and reported that only 49% of patients enrolled had ever been tested for an STI.[11] Likewise, in a community-recruited sample of HIV-unidentified black MSM, only 40% reported having been screened for an STI in the past 2 years.[13] Given the low uptake of STI screening and the benefit to infected individuals and their partners, development of new and effective methods to promote regular testing is crucial.

1.6 Financial Incentives to Motivate Behavior Change

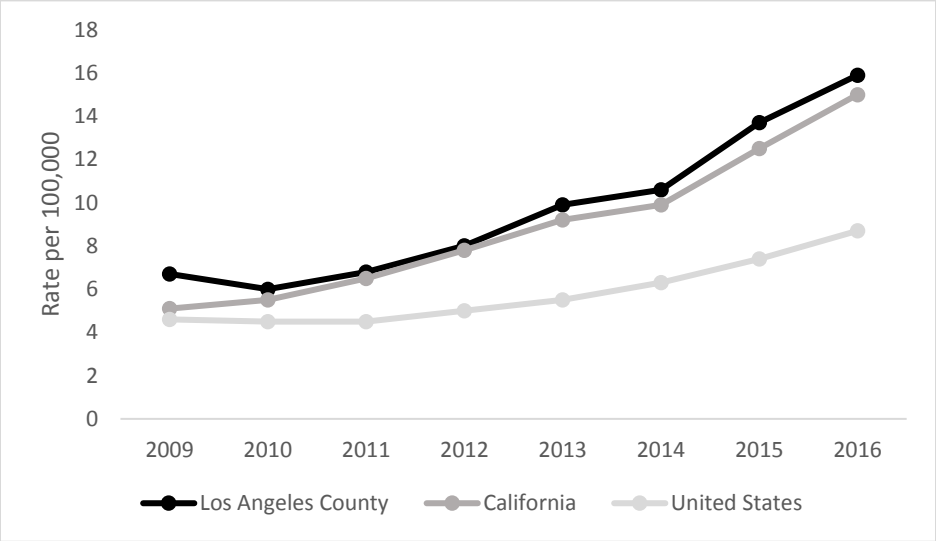
Developed in part as a response to the limitations of conventional economics, behavioral economics is a relatively new field which integrates classic economic thought with psychology in trying to explain when and why people make self-harming decisions.[15] These ideas may be extended to the field of public health to help characterize patterns of individual behavior that often undermine one's own health. For example, individuals typically place a disproportionate weight on present relative to future costs and benefits; this is known as present-biased preferences.[16] The idea of present-biased preferences may be used to help individuals from making seemingly irrational decisions by altering immediate costs and benefits. For public health that means making healthy behaviors more convenient (less immediately costly) and unhealthy behaviors less convenient (more immediately costly). The use of financial incentives builds on this theory; monetary rewards serve as short-term benefits for engaging in activities with short-term costs (e.g., using a condom and getting tested) and benefits that accrue in the long term (e.g. staying disease-free).

A growing body of evidence has indicated that financial incentives have been successful in motivating behavior change and improving health outcomes in a variety of settings. Studies have revealed that monetary incentives may improve smoking cessation[17], reduce drug-addictive behaviors[18-20], increase tuberculosis skin test reading compliance[21,22] and amend poor dietary habits.[23]

Given the demonstrated effectiveness in other areas of health, financial incentives have started to gain popularity as tools for encouraging STI and HIV testing and their effectiveness and acceptability is under evaluation. A recent systematic review investigated the impact of incentives on HIV and STI testing uptake and reported that all included studies (n=7) demonstrated higher rates of uptake in an incentivized group compared to a non-incentivized group.[24] Further, a 2012 study of men and women in rural Tanzania utilized cash payments of $10 or $20 per negative test result to encourage safer sexual behaviors; individuals enrolled in the $20 cash payment arm were significantly less likely than the control group to test positive for any STI over a one year period (aOR=0.73, 95% CI: 0.47 to 0.99) whereas STI results for those in the $10 cash payment arm were not statistically any different from those in control (aOR=1.06, 95% CI: 0.75 to 1.38).[25] Another study examined the acceptability of a hypothetical monetary incentive based program among Mexican males 18-25 years of age and found that most individuals in the study were highly accepting of a program where cash payments were contingent on attendance in STI education talks, STI testing, and negative test results.[26] Interestingly, a 2015 study compared the impact of doxycycline prophylaxis versus financial incentives on contracting any bacterial STI. Authors reported that HIV-positive MSM who took doxycycline were less likely to test positive for any bacterial STI after 48 weeks than individuals who received incentives (OR= 0.27; 95% CI: 0.09-0.83).[27] While the literature surrounding the

feasibility and effectiveness of financial incentives to promote testing and prompt behavior seems promising, there has been only one study carried out in an MSM population in a developed country. However, this study was limited by a small sample size (n=30) and lacked a standard-of-care control group.[4] To address this gap in knowledge, **Chapters 3 and 4** of this dissertation evaluate both the clinical and economic impact (respectively) of a financial-incentive program to promote uptake of STI and HIV testing in a clinic-based population of MSM in Los Angeles County.

Figure 1.1. Primary and Secondary Syphilis Rates: US, California and Los Angeles County, 2009-2016



Chapter 2. Predictors of Repeat Gonorrhea and/or Chlamydia Infection in a Population of Predominantly Men-Who-Have-Sex-With-Men (MSM) in Los Angeles County

2.1 Abstract

Background: Repeat infection with gonorrhea and/or chlamydia may significantly contribute to onward transmission of HIV and other sexually transmitted infections.

Objective: To identify the rate and socio-demographic predictors of repeat gonorrhea and/or chlamydia infection in a clinic-based population of predominantly men-who-have-sex-with-men (MSM) in Los Angeles County.

Methods: We constructed a retrospective cohort of men attending a not-for-profit STI clinic in Los Angeles, CA. Subjects were available for study inclusion if they were: male and presented to the clinic with an initial case of gonorrhea or chlamydia at any site (urethral, rectal, or pharyngeal) between October 1, 2011 and September 30, 2015. Kaplan-Meier survival curves and Cox regression models were used identify socio-demographic predictors of repeat infection defined as any gonorrhea or chlamydia at any site (urogenital, rectal, or pharyngeal) detected within up to four years of prior infection and 30 days after verified treatment.

Results: Of the 2,293 male patients entered in the cohort, 14% (n=296) presented with a repeat gonorrhea and/or chlamydia infection within four years. The mean age was 31.5 years (standard deviation = 8.8). Most men were either white (39.1%) or Hispanic (36.1%), followed by black (12.0%), Asian (9.0%), and other race/ethnicity (3.9%). HIV positivity at baseline was 13.5% with the majority of men identifying as either bisexual or homosexual (82.2%). The reinfection rate was estimated at 11.5% (95% CI, 10.1%-12.9%) within one year and 32.6% within four years. In a multivariable model, repeat infection was independently associated with: being aged 30-39 (compared with 16-19 years; adjusted hazard ratio (AHR) = 4.81; 95% CI, 1.14-20.32);

being black (compared with white; AHR = 1.85; 95% CI, 1.17-2.93); and self-identifying as bisexual (compared with heterosexual; AHR = 3.08; 95% CI, 1.65-5.75), homosexual (AHR = 2.46; 95% CI, 1.47, 4.12), or declining identification of sexual orientation (AHR = 4.24; 95% CI, 1.13, 15.92).

Discussion: Our study revealed that racial and sexual minorities are more likely to experience repeat gonorrhea and/or chlamydia infection. STI prevention and elimination efforts focused on individuals repeatedly infected may help reduce disease burden, including HIV.

2.2 Background

Rates of sexually transmitted infections (STIs) have increased dramatically in the U.S. over the last decade with men who have sex with men (MSM) bearing a disproportionate burden of disease. Gonorrhea incidence among MSM attending STD Surveillance Network clinics increased an estimated 151% (from 1,369 cases per 100,000 MSM to 3,435 cases per 100,000 MSM) between 2010 and 2015.[1] Over the same period gonorrhea rates among women and men-who-have-sex-with-women increased but by a significantly smaller margin (39.8% and 31.7%, respectively). Similar upward trends also exist for chlamydia infections. The Centers for Disease Control and Prevention (CDC) estimated an increase from 13.0% in 2010 to 16.0% in 2015 in the overall prevalence of chlamydia among MSM.[1]

STIs are not only responsible for significant morbidity and potential long-term sequelae in men, such as disseminated gonococcal infection, but strong evidence indicates STI infection promotes HIV transmission and acquisition. [2-4,28-31] In fact, a recent study found that MSM with a prior diagnosis of rectal gonorrhea or chlamydia were almost three times more likely to test positive for HIV in the future, after controlling for time-varying risk behaviors and demographic characteristics.[4] Another study found that after adjusting for number of sexual partners, MSM

with a history of 2 additional prior rectal infections had an 8-fold increased risk of incident HIV infection.[8]

As such, repeat infection with STIs may disproportionately contribute to both STI and HIV disease propagation. An understanding of the social and demographic predictors of repeat infection would help identify higher-risk individuals and serve to inform tailored prevention efforts. And, with the international emergence of gonococcal resistance to antibiotics, focused primary prevention efforts in MSM may be increasingly crucial in halting the spread of disease.

Previous studies have examined risk factors associated with repeat syphilis infection in MSM and reported HIV-infection,[5-7] black race/ethnicity,[5] and having 10 or more sex partners[5] as significant predictors. However, no prior studies have evaluated risk factors associated with repeat gonorrhea and/or chlamydia infection in this population. The objective of this study is to identify socio-demographic predictors of repeat gonorrhea and/or chlamydia in clinic-based predominantly-MSM population in Los Angeles County.

2.3 Methods

Study Population

We constructed a retrospective cohort of men attending AIDS Healthcare Foundation (AHF) Men's Wellness Clinic in Los Angeles, California from October 1, 2011 to September 30, 2015. The clinic offers free STI and HIV testing and treatment services to members of the Hollywood neighborhood and surrounding area. The clinic operates on weekday evenings and all day on Saturday.

Subjects were available for study inclusion if they were: male and presented to the clinic with an

initial laboratory confirmed case of gonorrhea or chlamydia at any site (urethral, rectal, or pharyngeal) between October 1, 2011 and September 30, 2015. Exclusion criteria included participation in an incentivized testing program which was implemented in the clinic from October 1, 2013 to September 30, 2015. Patients enrolled in this program were excluded from the study as these individuals were selected into the program due to their high-risk status and were strongly motivated to seek regular testing and treatment.

Data Source and Predictor Variables

Data from the clinic's electronic medical records were extracted and utilized in our analysis. Medical record data contained self-reported demographic information collected by clinic staff at intake, including: sex, age, race/ethnicity, homelessness, marital status, and sexual orientation. We determined HIV status at baseline (HIV positive or HIV negative) via baseline HIV testing results. To capture socioeconomic status, zip codes for each study subject were linked to 2013 US Census data of median household income and 2014 Census estimates of education attainment. Information on sexual risk behaviors was largely missing from the dataset and was not utilized in this analysis. No data on substance use were available.

Outcome Variable

The outcome measure for our analysis was repeat gonorrhea and/or chlamydia infection at any site (urogenital, rectal, or pharyngeal). Because there is no standard definition in the medical literature for categorizing a repeat STI infection within a specific time, we defined a repeat infection as a second infection within four years of initial infection and 30-days after verified treatment, as our dataset allowed for such a substantial time frame.

Statistical Analysis

Descriptive statistics for demographic characteristics were calculated for all patients in our

dataset at baseline (i.e., date of entry into cohort), patients with one or more repeat infections over follow-up, and patients without one or more repeat infections over follow-up. Frequencies and percentages were calculated for categorical variables and means and standard deviations were calculated for continuous variables.

Kaplan–Meier survival curves were used to estimate the time to repeat infection. To account for multiple repeat infections within a single individual, each reported case of a treated infection within the same individual was considered a separate event. In addition to survival for the entire cohort, separate survival curves were constructed and compared across several predictor variables. For each predictor variable, we identified differences in survival functions over strata by testing the universal null hypothesis that all survival curves were identical using a log-rank test. For variables with more than two strata (i.e. age category and race/ethnicity), we additionally performed pairwise comparisons whereby each individual stratum was compared to every other stratum. We adjusted for multiple comparisons using the Tukey-Cramer adjustment.

Cox regression models were used to estimate predictors of repeat STI. To account for multiple repeat infections from a single individual, each repeat infection was treated as a distinct observation. To correct for dependence among of observations within individuals, the modified sandwich estimator approach (i.e. robust variance estimator approach) was used. This method allows for a correction in standard error due to dependence within individuals without making assumptions about the nature or structure of the dependence.[32]

Univariable Cox regression models estimated hazard ratios (HRs) for groups defined by the following variables: HIV status at baseline, age category, race/ethnicity, sexual orientation, homelessness, marital status, median household income of zip code and education attainment of zip code. Unadjusted hazard ratios (UHR) and corresponding 95% confidence intervals (95%

CI) were calculated.

Multivariable Cox regression models estimated independent associations between each of the predictor variables and repeat gonorrhea and/or chlamydia infection. Variables selected for inclusion as covariates in the multivariable model were based on significance of associations in univariable models and a priori knowledge. Adjusted hazard ratios (AHR) and 95% confidence intervals were reported.

2.4 Results

Study Population

Of the 15,202 men attending the clinic during the study period 2,187 (14%) presented with an initial laboratory confirmed case of gonorrhea or chlamydia at any site and were eligible for inclusion in the study cohort. Table 1 reflects demographic characteristics for the entire study cohort, individuals with repeat STI, and individuals without repeat STI. Fourteen percent of men (296/2,293) presented with a repeat gonorrhea and/or chlamydia infection during follow-up. The mean age of the cohort at baseline was 31.5 years (standard deviation = 8.8). Most men were either white (39.1%) or Hispanic (36.1%), followed by black (12.0%), Asian (9.0%), and other race/ethnicity (3.9%). HIV positivity at baseline was 13.5% and most men identified at either bisexual or homosexual (10.6% and 71.6%, respectively; 82.2% combined).

Kaplan Meier Survival Curves

The Kaplan-Meier survival curves for the overall cohort and by predictor variables may be found in Figure 1. The overall rate of reinfection was estimated at 11.5% (95% CI, 10.1%-12.9%) within one year, 19.0% (95% CI, 17.1%-20.9%) within two years, 25.7% (95% CI, 23.2%-28.1%) within three years, and 29.4% (95% CI, 26.2%-32.6%) within four years. The median time to reinfection was 3.09 years (95% CI, 3.03-3.15).

Survival curves by HIV status at baseline were not significantly different over the course of follow-up (p=0.66). Survival functions for each race/ethnicity category were not identical (p<0.01); specifically, those in the black category (p<0.01), Hispanic category (p=0.05), Asian category (p=0.02) and other race/ethnicity category (p<0.01) were significantly more likely to present with repeat infection when compared whites. Survival curves for age category were also found to be non-identical (p<0.01)); those aged 16-19 were less likely to re-attend with a repeat infection compared to those aged 30-39 (p<0.01). Non-identical survival curves for sexual orientation (p<0.01) revealed that men identifying as bisexual were significantly more likely to present with a repeat infection compared to heterosexuals (p<0.01) and those who declined to identify sexual orientation (p=0.02). Interestingly, the survival curve for those identifying as homosexual was not significantly different than the curve for those identifying as heterosexual (p=0.17), bisexual (p=0.69), and those who declined (p=0.96). Survival curves for educational attainment of zip code were not identical either (p<0.01). More specifically, it was discovered that men living in a zip code where >95% of men graduated high school (i.e., most educated group) were significantly less likely to present with a repeat infection compared to men living in zip codes where 90%-95% (p=0.2), 80%-90%% (p<0.01), 70%-80% (p<0.01), and 70% or less (p<0.01) of men received a high school diploma (i.e., less educated groups). One- and four-year rates of repeat infection by age and zip code education attainment may be found in Figure 2.

Cox Regressions

In univariable regression modeling, repeat infection was positivity associated with being aged 30-39 years (HR = 3.92; 95% CI, 1.22, 12.60); being of black race/ethnicity (HR = 1.78; 95% CI, 1.17-2.72); being of Hispanic race/ethnicity (HR = 1.44; 95% CI, 1.08-1.92); self-identifying as bisexual (HR = 3.02; 95% CI, 1.81-5.02) or homosexual (HR = 2.11; 95% CI, 1.40-3.17); and

living in a zip code where the average median income is $55,000-$64,999 compared to >$75,000 (HR=2.11, 95% CI, 1.30-3.41). Men reporting a marital status of "other" were also less likely to experience a repeat infection when compared to single men (HR = 0.12; 95% CI, 0.02-0.89). Lastly, men living in zip codes with high school graduation rates of 80%-90% (HR = 2.42; 95% CI, 1.68-3.49), 70%-80% (HR = 1.93; 95% CI, 1.31-2.85), and 70% or less ($p<0.01$) were more likely to present with a repeat infection compared to men residing in zip codes with a rate greater than 95%.

In the multivariable model, repeat infection was independently associated with: being aged 30-39 (compared with 16-19 years; adjusted hazard ratio (AHR) = 4.81; 95% CI, 1.14-20.32); being black (AHR = 1.85; 95% CI, 1.17-2.93); self-identifying as bisexual (AHR = 3.08; 95% CI, 1.65-5.75), homosexual (AHR = 2.46; 95% CI, 1.47, 4.12), or declining identification of sexual orientation (AHR = 4.24; 95% CI, 1.13, 15.92) (Table 2).

2.5 Discussion

Our study used survival analysis techniques to examine the rate and socio-demographic predictors of repeat gonorrhea and/or chlamydia infection among an MSM-predominant cohort in Los Angeles County. We found that 11.5% of men presented with a repeat infection within one year and 29.4% within four years. In a multivariable analysis, being black and self-identifying as a sexual minority placed men at an increased risk for repeat infection.

Our findings are not consistent with prior studies which have all found significant positive associations between HIV-positivity and repeat STI infections in MSM.[5-7] This lack of association may be explained by HIV positive men in our study having also been enrolled in HIV care which was provided by the same facility during daytime hours. It is conceivable that these HIV positive men were more likely to have received prior STI testing and treatment, as once-

yearly testing is included in the HIV clinic's standard-of-care practice. However cross-study comparisons are limited as previous studies have focused exclusively on syphilis reinfection. One study in MSM, however did find black race to be significantly associated with repeat syphilis infection,[5] a characteristic we also found to be significant.

Studies that have looked at gonorrhea and chlamydia reinfection have largely been carried out in populations of either both males and females or exclusively females. Findings from these studies have generally reported reinfection occurs at a younger age,[33] however our study did not support this finding. In fact, our study found that men 30-39 were the most at-risk for presenting with a repeat gonorrhea and/or chlamydia infection when compared to men in a younger age group. Several studies have found positive associations between sexual minorities and repeat infections, results which are in accordance with ours.[34-36] These somewhat varying results highlight the importance of identifying predictors of repeat STI infection by STI-type and patient population for better-designed and implemented preventions efforts.

The positive association between black race and repeat infection in this study may be explained by the higher prevalence of STIs among black MSM when compared to white MSM, despite similar self-reported sexual risk behaviors such as unprotected anal intercourse and commercial sex work.[37] Disparities in prevalence between black and white MSM may be attributed to differences sexual network structure such as size and patterns of sexual mixing[38,39] and societal determinants such as levels of poverty, access to care, and literacy.[40] This study attempted to control for social environmental factors by adjusting for average income and education attainment by zip code, however understanding the degree to which racial disparities of repeat infection are explained by differences in sexual networks and social characteristics is an important area for future study.

This study also found strong associations between male sexual minorities (individuals self-reporting as homosexual or bisexual) and repeat gonorrhea and/or chlamydia infection when compared to heterosexual men. This discrepancy may owe to not only a higher STI prevalence within this population, but a higher likelihood of reported sexual risk behaviors as well as known differences in socioeconomic status, mobility, and access to health care.

While average high school education attainment of zip code was not significant in the multivariable model, strong significant associations were present in unadjusted analyses. It was found that living in neighborhoods where men were less educated significantly increased the likelihood of presenting with a repeat infection. Prior studies have also used community level socioeconomic status data to assess the impact of neighborhood conditions on risk for HIV and other STIs and reported similar findings.[41-44] In fact, a recent study indicated exposure to neighborhood poverty during adolescence increased the likelihood of contracting chlamydia during young adulthood (AOR = 1.23, 95 % CI = 1.06, 1.42).[42] This link between neighborhood socioeconomic status and heightened risk for repeat infection may be attributable to social and structural determinants such as poorer access to quality health care, heightened stigma surrounding STI testing and treatment, and increased social and physical neighborhood disorder; or, may simply reflect the heightened risk of exposure due to higher prevalence of STIs within neighborhoods of lower socioeconomic status. A better understanding of the mechanisms by which neighborhood socioeconomic status contributes to STI and HIV risk is warranted.

This study was subject to several limitations. First, our analysis likely underestimated the actual rates of repeat gonorrhea and/or chlamydia infection in our cohort, as we only captured reinfections from a single STI clinic in Los Angeles County. Our inability to account for undiagnosed cases and infections diagnosed in other clinics may also lead to bias in the hazard

ratio estimates. Next, due to data scarcity we were unable to control for sexual risk behaviors which in previous studies have been significantly associated with repeat STI.[5,34] Such unmeasured and uncontrolled confounding may induce bias in the point estimates of our multivariable model. Furthermore, our data lacked detail regarding gender which limited our ability to ascertain risk by gender-identity. Finally, this study was done in a population consisting mostly of self-identifying homosexual and bisexual men; the results may not be generalizable to populations outside of ours.

Repeat infection of gonorrhea and chlamydia is common among sexual and racial minorities. Knowledge of characteristics of those likely to have repeat infection is important as providers often do not ask about risk behaviors directly. Targeted screening and other tailored prevention efforts may help diminish infection persistence.

Table 2.1. Baseline Characteristics for Clinic-Based Cohort of Men by Repeat Gonorrhea and/or Chlamydia Infection Status, 2011-2014

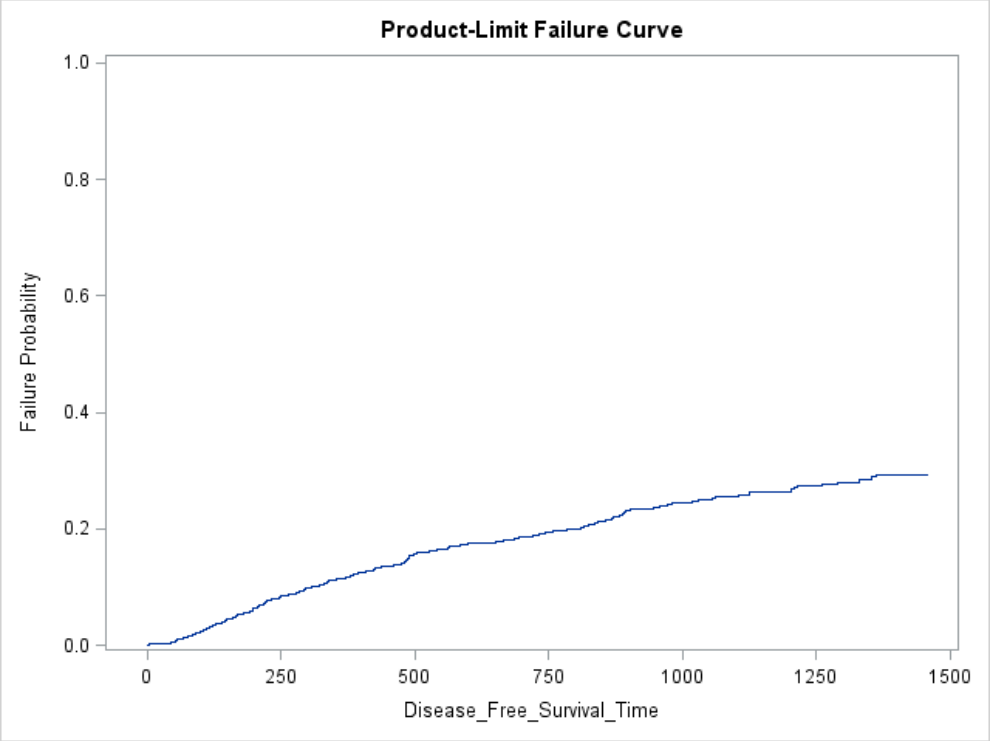
	Overall		Repeat Infection		No Repeat Infection		P Value
Characteristic	n	%	n	%	n	%	
Total	2,187	100	296	100	1,891	100	
Age, mean [sd]	31.5 [8.8]	--	31.8 [7.9]	--	31.4 [8.9]	--	0.44
Age Category							
16-19	52	2.4	3	1.0	49	2.6	0.04
20-24	424	19.4	44	14.9	380	20.1	
25-29	648	29.6	91	30.7	557	29.5	
30-39	671	30.7	107	38.8	564	29.8	
40+	391	17.9	51	17.2	340	18.0	
Race/Ethnicity							
White	748	39.1	94	32.6	654	40.3	0.18
Black	229	12.0	37	12.9	192	11.8	
Hispanic	690	36.1	114	39.6	576	35.5	
Asian	172	9.0	29	10.1	143	8.8	
Other	74	3.9	14	4.9	60	3.7	
HIV Status at Baseline							
Negative	1,337	86.5	187	88.6	1,150	86.1	0.33
Positive	209	13.5	24	11.4	185	13.9	
Homeless							
No	1,868	98.7	284	98.3	1,584	98.7	0.51
Yes	25	1.3	5	1.7	20	1.3	
Sexual Orientation							
Heterosexual	320	16.6	28	9.6	292	17.9	<0.01
Bisexual	204	10.6	43	14.8	161	9.8	
Homosexual	1380	71.6	217	74.6	1,163	71.1	
Declined	23	1.2	3	1.0	20	1.2	
Marital Status							
Single	1,725	90.7	270	93.1	1,455	90.3	0.41
Domestic Partner	78	4.1	9	3.1	69	4.3	
Married	47	2.5	7	2.4	40	2.5	
Separated/Divorced	15	0.8	2	0.7	13	0.8	
Widowed	4	0.2	1	0.3	3	0.2	
Other	32	1.7	1	0.3	31	1.9	
Median Household Income of Zip Code							
> $75,000	252	13.1	29	10.1	223	13.6	0.01
$65,000-$74,999	206	10.7	25	8.7	181	11.1	
$55,000-$64,999	159	8.3	24	8.4	135	8.3	
$45,000-$54,999	429	22.3	57	19.9	372	22.7	
$35,000-$44,999	541	28.1	90	31.4	451	27.6	

$25,000-$34,999	277	14.4	58	20.2	219	13.4	
< $25,000	59	3.1	4	1.4	56	3.4	
Percentage of Men With High School Diploma in Zip Code							
> 95% (most educated)	588	26.9	51	17.2	537	28.4	<0.01
90%-95%	310	14.2	40	13.5	270	14.3	
80%-90%	521	23.8	91	30.7	430	22.7	
70%-80%	483	22.1	67	22.6	416	22.0	
< 70% (least educated)	285	13.0	47	15.9	238	12.6	

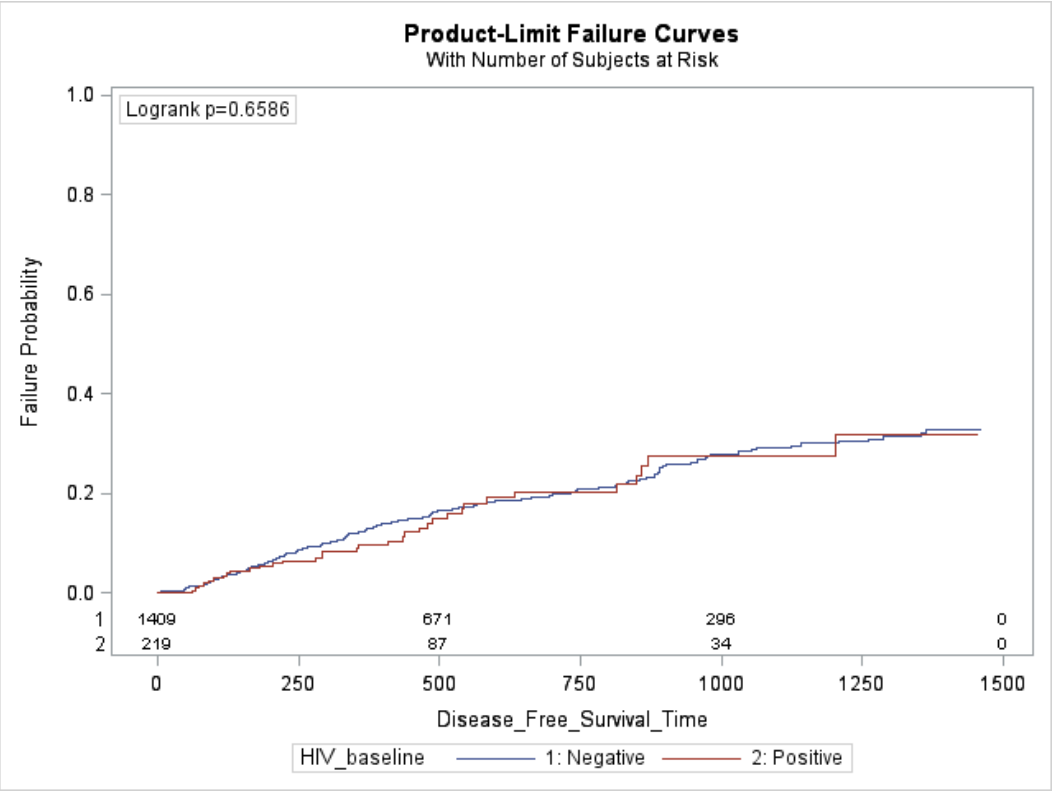
Note: sd = standard deviation

Figures 2.1A-2.1F. Kaplan Meier Survival Curves for Repeat Gonorrhea and/or Chlamydia Infection by Patient Characteristics. (2.1A) Entire Cohort, (2.1B) HIV Status at Baseline, (2.1C) Age Cateogry, (2.1D) Race/Ethnicity Category, (2.1E) Sexual Orientation, (2.1F) Education Attainment of Zip Code

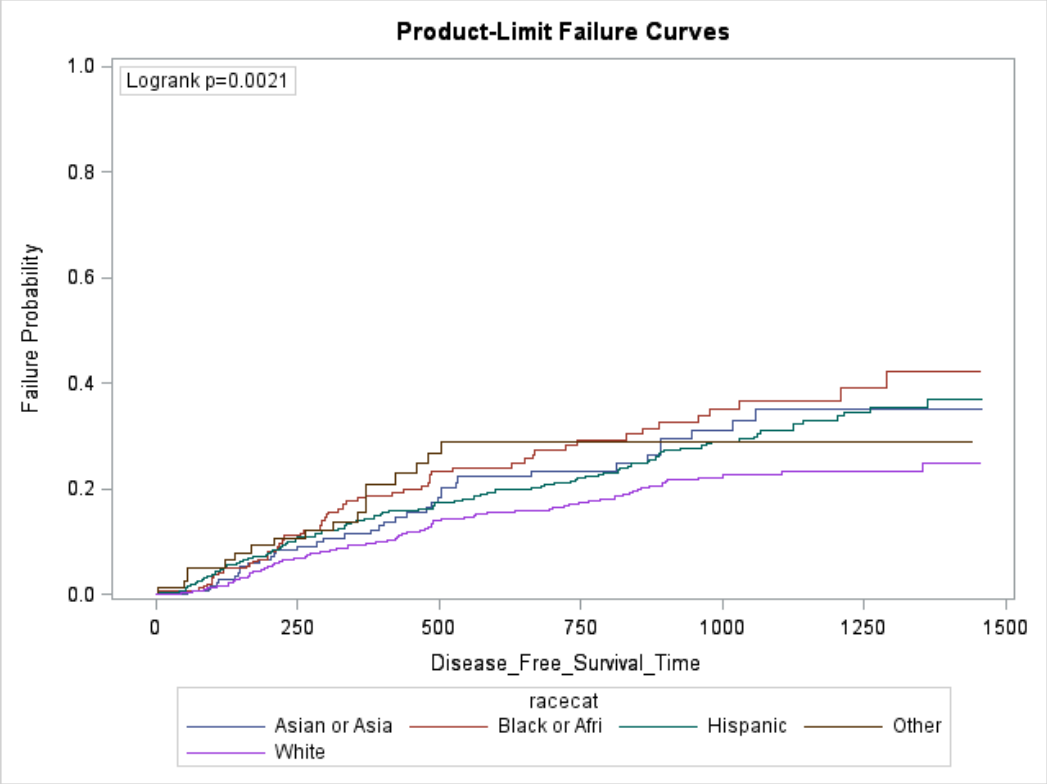
2.1A. Entire Cohort



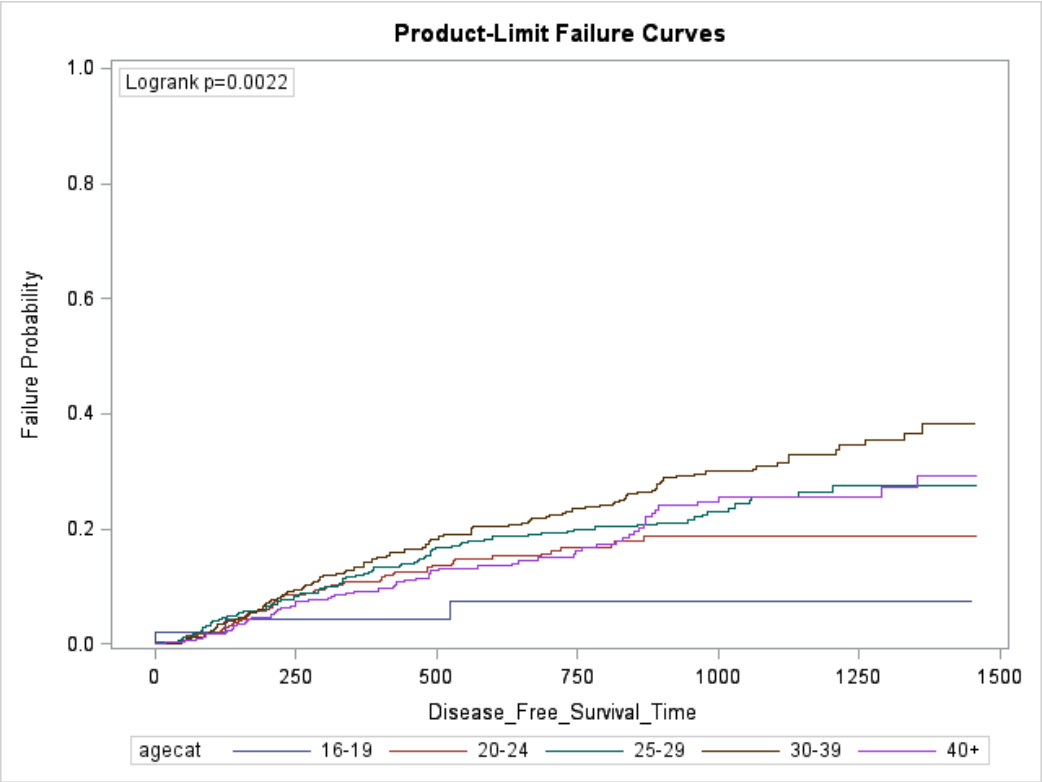
2.1B. HIV Status at Baseline



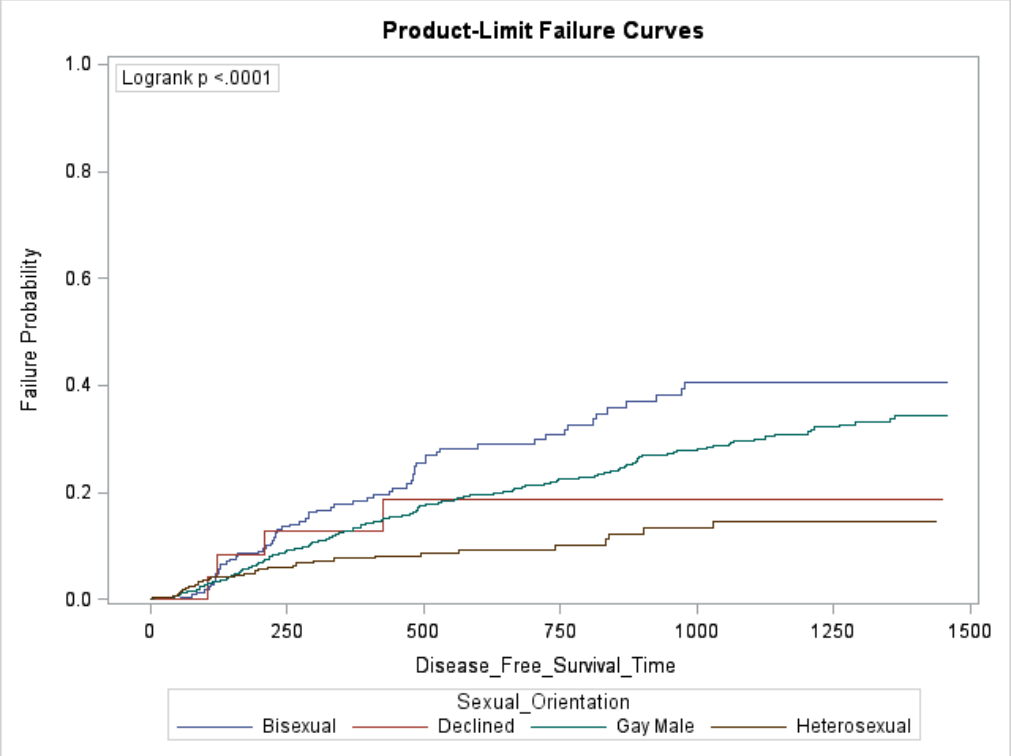
2.1C. Race/Ethnicity Category



2.1D. Age Category



2.1E. Sexual Orientation



2.1F. Education Attainment of Zip Code

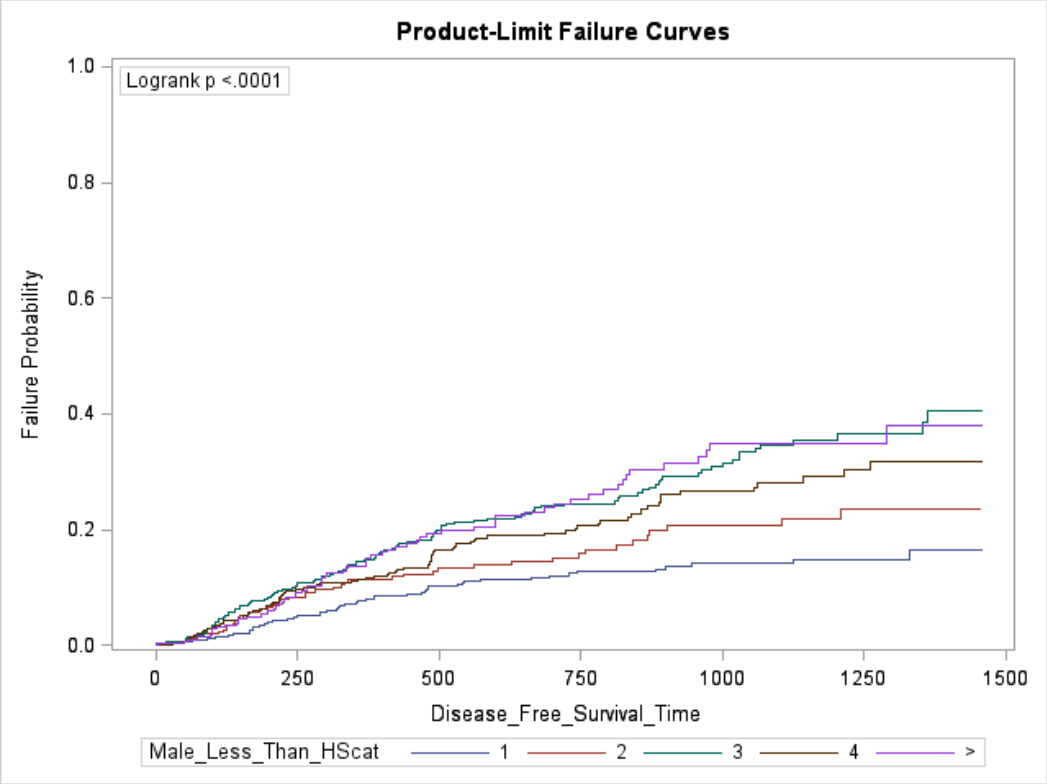
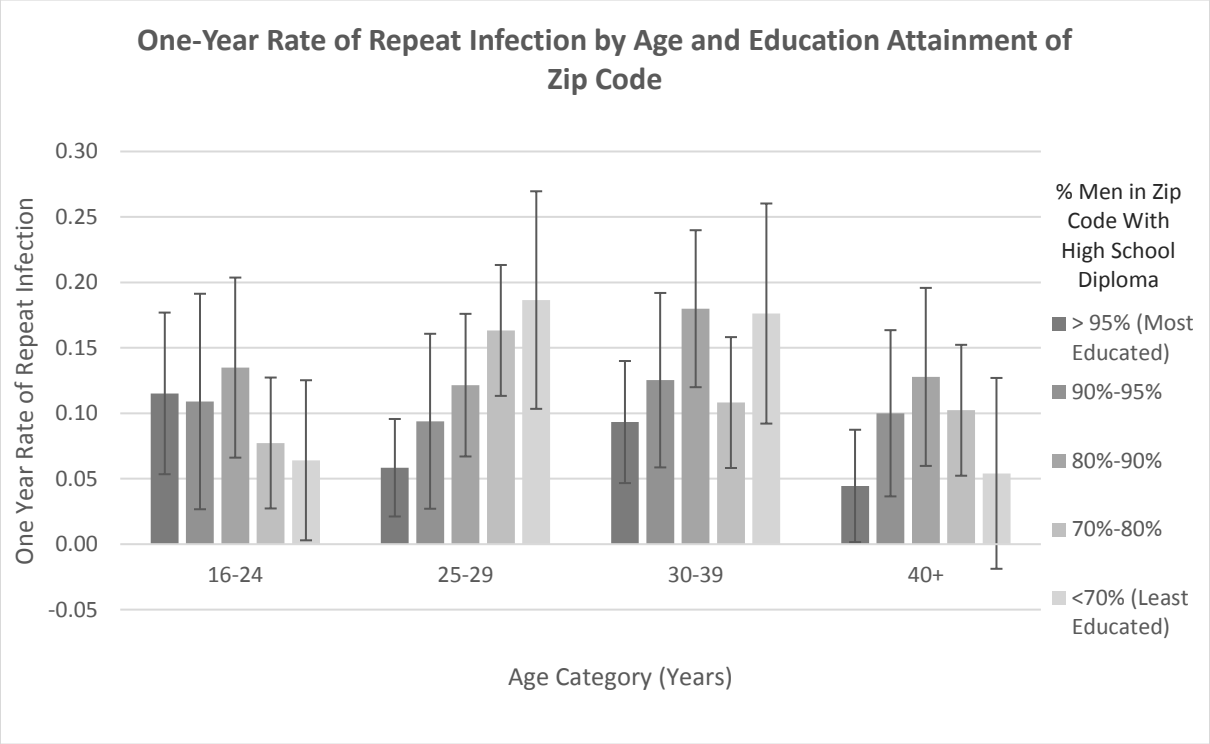


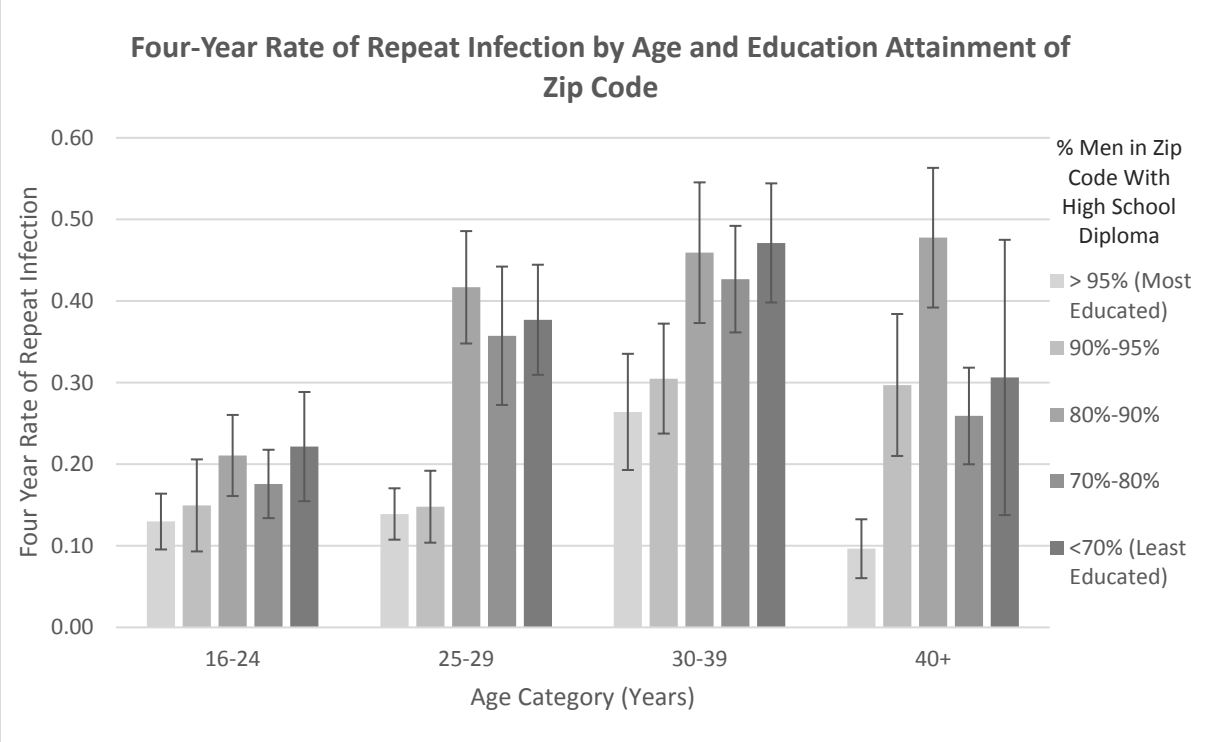
Table 2.2. Risk Factors for Repeat Gonorrhea and/or Chlamydia Infection in a Clinic-Based Cohort of Men, 2011-2014

Characteristic	Crude Hazard Ratio (95% CI)	Adjusted Hazard Ratio (95% CI)
Age Category		
16-19	Ref	Ref
20-24	2.45 (0.74, 8.07)	2.34 (0.53-10.29)
25-29	3.14 (0.98, 10.12)	3.94 (0.92, 16.84)
30-39	**3.92 (1.22, 12.60)**	**4.81 (1.14, 20.37)**
40+	2.81 (0.86, 9.22)	3.16 (0.72, 13.84)
Race/Ethnicity		
White	Ref	Ref
Black	**1.78 (1.17, 2.72)**	**1.85 (1.17, 2.93)**
Hispanic	**1.44 (1.08, 1.92)**	1.31 (0.92-1.86)
Asian	1.50 (0.95, 2.24)	0.89 (0.49, 1.63)
Other	1.52 (0.84, 2.75)	1.61 (0.86, 3.01)
HIV Status at Baseline		
Negative	Ref	Ref
Positive	0.92 (0.59, 1.46)	0.86 (0.54, 1.36)
Homeless		
No	Ref	
Yes	0.74 (0.30, 1.81)	
Sexual Orientation		
Heterosexual	Ref	Ref
Bisexual	**3.02 (1.81, 5.02)**	**3.08 (1.65, 5.75)**
Homosexual	**2.11 (1.40, 3.17)**	**2.46 (1.47, 4.12)**
Declined	1.78 (0.51, 6.24)	**4.24 (1.13, 15.92)**
Marital Status		
Single	Ref	
Domestic Partner	0.60 (0.29, 1.21)	
Married	0.94 (0.45, 1.98)	
Separated/Divorced	0.69 (0.16, 2.94)	
Widowed	**2.97 (1.43, 6.14)**	
Other	**0.12 (0.02, 0.89)**	
Median Household Income of Zip Code		
> $75,000	Ref	
$65,000-$74,999	0.47 (0.16, 1.38)	
$55,000-$64,999	**2.11 (1.30, 3.41)**	
$45,000-$34,999	1.49 (0.96, 2.32)	
$35,000-$44,999	1.15 (0.72, 1.84)	
$25,000-$34,999	1.52 (0.86, 2.68)	
< $25,000	1.03 (0.58, 1.83)	
Percentage of Men With High School Diploma in Zip Code		
> 95% (most educated)	Ref	Ref
90%-95%	1.46 (0.94, 2.25)	0.70 (0.41, 1.20)
80%-90%	**2.42 (1.68, 3.49)**	1.47 (0.95, 2.28)
70%-80%	**1.93 (1.31, 2.85)**	1.08 (0.67, 1.74)
< 70% (least educated)	**2.39 (1.54, 3.71)**	1.40 (0.86-2.28)

Note: HR = Hazard Ratio; CI = Confidence Interval
*Other includes: American Indian, Alaskan Native, Native Hawaiian, or Other

Figure 2.2 One- and Four-Year Rates of Repeat Infection, by Age and Education Attainment of Zip Code





Note: Error bars represent 95% confidence intervals

Chapter 3. Efficacy of a Financial Incentive Program for STI and HIV Testing Among Men Who Have Sex With Men (MSM) in Los Angeles County

3.1 Abstract

Background: Despite continuous efforts to stall the rise of sexually transmitted infections (STI), the past decade has seen a dramatic increase in STI rates in men who have sex with men (MSM) both in Los Angeles County and nationwide. Given the established link between STI infection and subsequent HIV seroconversion and limitations of conventional prevention methods, innovative STI testing and treatment strategies targeting high-risk individuals are warranted in this population. Financial incentive programs have demonstrated success in motivating behaviors in a variety of other settings.

Objective: To evaluate the impact of an MSM-focused financial incentive program for STI and HIV testing on three primary outcomes: 1.) number of testing clinic visits; 2.) adherence to STI and HIV testing recommendations issued by the Centers for Disease Control and Prevention; and 3.) STI positivity.

Methods: The study took place in a free STI clinic in Los Angeles, CA. Men were eligible if they were 18 years of age or older and had one or more diagnoses of rectal chlamydia, rectal gonorrhea, and/or syphilis in the past two years. Two hundred and eight men were enrolled at baseline and matched to 208 controls on the basis of race/ethnicity and age who received standard-of-care. Intervention group participants were tested for bacterial STIs (rectal gonorrhea (GC), urethral GC, pharyngeal GC, rectal chlamydia (CT), urethral CT and syphilis) and HIV upon enrollment and were asked to return to the clinic for re-testing every three months, for one year. Intervention participants received $50 gift card at baseline and each return testing visit; an additional $50 electronic gift card was provided if they were STI- and HIV-free after each testing

visit. In addition to financial incentives, intervention participants also received a clinic priority card, a "welcome package", and testing reminders via text message and email. To assess the impact of the intervention on STI infections, a pre-post design compared STI positivity for intervention participants at baseline and 3 months to positivity after one year of follow-up. We also examined the number of testing visits for program participants versus matched-controls. Multivariable logistic regression was utilized to examine factors associated with adherence to CDC testing guidelines.

Results: When assessing STI positivity among intervention participants over time, significant declines were observed between baseline and 12 months in any STI (46.2% vs. 14.3%, $p<0.01$); subanalyses revealed significant reductions in rectal CT (32.5% vs. 3.6%, $p<0.01$), rectal GC (17.3% vs. 4.3%, $p=0.01$), and pharyngeal GC (11.4% and 4.4%, $p=0.04$). There were also significant declines in STI between 3 months and 12 months; subanalyses indicated declines in rectal CT (11.4% vs. 3.6%, $p<0.01$) and rectal GC (10.8% vs. 4.3%, $p=0.03$). During the one-year follow-up period, intervention group participants returned to the clinic for testing a median of 4 times (IQR: 3-5) compared to 1 time (IQR: 0-2) for the matched-control group ($p <0.01$). In the multivariable logistic model, intervention participants were significantly more likely to comply with CDC STI and HIV testing recommendations than individuals in the matched-control group (adjusted odds ratio=43.2, 95% confidence interval: 20.4-91.7).

Discussion: Financial incentive programs can be effective strategies to encourage STI and HIV testing and to maintain lower STI positivity among high-risk MSM. Further research involving randomization and evaluations of the financial impact of these programs is warranted.

3.2 Background

Rates of sexually transmitted infections (STIs) have increased dramatically over the last decade in Los Angeles County (LAC), with men who have sex with men (MSM) bearing a disproportionate burden of disease.[16,45,46] STIs are not only responsible for significant morbidity and potential long-term sequelae, but strong evidence indicates STI infection promotes HIV transmission and acquisition among MSM.[2-5,28-30] As such, prevention efforts aimed at reducing STI incidence may also serve to limit the spread of HIV.

Modeling studies have indicated that increased testing frequency, one method of STI prevention, could significantly reduce transmission of HIV and help mitigate outbreaks of STIs among MSM.[8,9,47] Current CDC guidelines advise annual screening for all sexually active MSM, with more frequent screening (every 3-6 months) among those who report high risk behaviors.[10] However, despite the demonstrated value of STI testing and the current standards for screening, testing rates among MSM remain abysmally low.[11-13]

Conventional methods such as education and awareness campaigns have demonstrated limited success in prompting STI testing in MSM populations and thus it is important that innovative testing strategies are developed and their effectiveness evaluated. A growing body of evidence has indicated that financial incentives have been successful in motivating behavior change and improving health outcomes in a variety of public health settings.[17-21,23,48,49] The use of financial incentives builds on the behavioral economics theory of present-biased preferences which describes the human tendency to place a disproportionate emphasis on immediate costs and benefits while overly discounting future costs and benefits. Financial incentives may exploit this bias by serving as short term benefits for engaging in healthy behaviors with short term costs (e.g. condom-use) and benefits that accrue in the long term (e.g. staying STI-free).[15]

Given the demonstrated effectiveness in other areas of health, financial incentives have started to gain popularity as tools for encouraging STI testing and staying STI-free and their effectiveness and feasibility is under evaluation. A 2014 systematic review investigated the impact of incentives on HIV and STI testing uptake and reported that all included studies (n=7) demonstrated higher rates of uptake in an incentivized group compared to a non-incentivized group.[24] While most of the included studies were conducted in developed countries (n=5), none of the studies were evaluated in MSM. However, one more recent 2015 pilot study compared the impact of doxycycline prophylaxis to financial incentives on contracting any bacterial STI among a population of HIV-positive MSM. Authors revealed that individuals who were assigned doxycycline were less likely to test positive for any bacterial STI after 48 weeks than individuals who received incentives (UOR (unadjusted odds ratio)= 0.27; 95% CI: 0.09-0.83).[27] While this study provided valuable insight into the feasibility of financial incentives and their performance relative to a drug prophylaxis, it is of value to understand the effectiveness of these programs compared to a status-quo scenario.

Accordingly, we sought to assess the efficacy of a financial incentive program targeted at high-risk MSM in Los Angeles County on three primary outcomes: 2) number of clinic testing visits; 2.) adherence to STI and HIV CDC testing recommendations; and 3.) STI positivity.

3.3 Methods

Setting and Study Population

We conducted a quasi-experimental study at AIDS Healthcare Foundation (AHF) Wellness Clinic a free not-for-profit STI and HIV testing clinic in Los Angeles, California. Patients were screened upon intake and were eligible for enrollment if the following inclusion criteria were

met: 1.) 18 years of age or older; 2.) male; and 3.) one or more diagnoses of rectal chlamydia, rectal gonorrhea, and/or syphilis in the past two years. The enrollment period extended from October 1, 2013 to Sept 30, 2014 and all participants were followed-up for one year.

To serve as a comparison, a matched-control group was constructed using the clinic's electronic medical record data. The matched-control group consisted of men who presented to the clinic during the enrollment period and who met the inclusion criteria for the program but were not offered enrollment due to program staff scheduling availability, which was largely random. Matched-control group individuals were individually matched to intervention group participants on the basis of age (plus or minus five years) and race/ethnicity at a ratio of 1:1.

Intervention

The intervention comprised three objectives: 1.) to increase frequency of HIV/STI testing; 2.) to reduce STI burden; and 3.) to encourage safer sexual behaviors.

The first objective, increasing frequency of HIV/STI testing, was based on evidence from prior modeling studies that have demonstrated increased frequency of STI screening in MSM can significantly reduce transmission of HIV and help mitigate outbreaks of STIs.[8,9,47] The rationale for the second objective, reducing STI burden among high-risk MSM, was based on the clinic's organizational mission of lessening community disease burden through increased testing and treatment, supported by prior research linking STI infection to HIV seroconversion.[2-5,28-30,50] The last objective, encouraging safer sexual behaviors, was built on widely-established evidence indicating certain sexual behaviors, such as unprotected sex and sex with anonymous partners, place an individual at heightened risk for both HIV and STI contraction.

Upon patient check-in a trained program staff member reviewed each patient's medical chart to identify those who qualified for inclusion. Patients who met inclusion criteria were called by their first name (consistent with clinic protocol) and lead into a vacant clinical exam room by a program staff member and asked to verify their identity. The program staff described the content of the program and assessed the patient's willingness to participate. For patients who agreed, a consent form was signed and an initial baseline questionnaire was administered via face-to-face interview. The questionnaire contained 20 sexual behavior and substance use questions and typically took around 5 minutes to complete. Intervention group participants were then given a $50 Target gift card for their first testing session and led back to the waiting room to complete STI testing. The enrollment procedure typically took around 15 minutes with minimal disruption of clinic workflow.

Intervention group participants completed STI and HIV testing upon enrollment (baseline) and were asked to return to the clinic for re-testing every three months, for one year. At each testing session intervention group participants were instructed to complete a full STI panel, including the following tests: chlamydia (rectal and urethral), gonorrhea (rectal, urethral, and pharyngeal), syphilis, and HIV. Patients did not receive testing for pharyngeal chlamydia as no FDA-approved test was available and such screening was not recommended by the CDC during the period of program implementation.[51] Participants received a $50 electronic Target gift card for each return visit, and an additional $50 electronic Target gift card if they were STI- and HIV-free after each testing visit. The electronic gift cards were sent via email which program administrators had the ability to manage and track. Intervention group participants had the potential to earn up to $500 in Target gift cards over a one year period.

In addition to financial incentives for testing and remaining STI- and HIV-free, intervention group participants also received other types of incentives and testing reminders. In the month following program enrollment participants received a "welcome package" mailed to their home address which contained: one 12-oz bottle of premium water based lubricant, 50 condoms, candy, and standard AHF educational brochures regarding STI- and HIV-risk. Participants also received a priority card which could be used to expedite clinic wait times during their return visits. Finally, program staff notified intervention group participants when it was time to test via SMS text messages and/or email reminders. Reminders were typically sent 4 weeks before testing was due and provided participants with an encouraging message and the clinic's address and hours.

Individuals in the matched-control group received the clinic's standard of care which included standard STI/HIV risk assessment and counseling, free STI and HIV testing available on first-come-first-serve basis, and counseling to return for retesting as set forth in the CDC STD testing and treatment guidelines including advising on annual screening for all sexually active MSM, with more frequent screening (every 3-6 months) among those who report high-risk behaviors.[10,52,53]

Data Collection

Study related data elements including demographic information, sexual risk behavior data, and STI/HIV testing results were abstracted from the patient's electronic medical record. In accordance with standard clinic procedure, demographic information including race/ethnicity, occupation, marital status, and sexual orientation was collected for all patients via self-administered paper questionnaires upon intake and entered in the electronic medical records system by clinic staff. To capture socioeconomic status, postal zip codes for each study subject

were linked to 2013 US Census data of median household income. Additionally, trained counselors performed a routine risk-assessment via a face-to-face interview; this consisted of several sexual risk behavior questions (such as number of sexual partners in last 12 months, sex of partner(s), type of sex engaged in, % anonymous sexual partners, and % anal encounters using a condom). Patients were also questioned about their STI, HIV, and vaccination (Hepatitis A and B) history and their reason for visit.

Electronic medical record data also reflected HIV and STI screening results for the following tests: INSTI HIV1/HIV2 rapid antibody test, 4th generation antigen/antibody HIV test, nucleic acid amplification (NAAT) HIV test, rapid plasma regain (RPR) test for syphilis, RPR syphilis titer, T pallidum particle agglutination (TPPA) syphilis antibody test, and tests for pharyngeal gonorrhea, rectal gonorrhea, urethral gonorrhea, rectal chlamydia, and urethral chlamydia. Information regarding any treatment(s) administered by an AHF medical provider were also available from the electronic medical records. Data for individuals were abstracted one year prior to baseline and up to one year after baseline enrollment.

Outcome Measures

We examined three primary outcomes: 1.) number of testing clinic visits; 2.) adherence to STI and HIV testing recommendations issued by the CDC; and 3.) STI positivity. We defined a testing visit as a clinic visit where at least one STI or HIV test was performed. For instance, if an individual sought testing for rectal gonorrhea only, this clinic visit would still constitute a testing visit even if a full STI panel was not performed. Adherence to STI and HIV testing recommendations were based on CDC guidelines that advise annual screening for all sexually active MSM, with more frequent screening (every 3-6 months) among those who report high-risk

behaviors, such as multiple, anonymous partners, unprotected anal intercourse.[10,52,53] For this analysis, we have assumed both the intervention and control group participants to be "high-risk." This assumption is based on several factors. First, the responses to sexual risk behavioral questions collected at baseline intake indicated that both the matched control and intervention group participants were likely to engage in risky sexual behaviors. Second, as a condition of enrollment, all men in both the matched control and intervention groups had tested positive for a rectal infection (gonorrhea or chlamydia) or syphilis in the past two years- indicative of unprotected receptive anal intercourse- indicative of risky sexual behaviors. As such, we defined adherence to the CDC STI and HIV testing recommendations as receiving testing at least once for each STI (urethral, rectal, and pharyngeal gonorrhea; urethral and rectal chlamydia; and syphilis) and HIV within a year of the initial baseline testing session. STI positivity was defined as the percentage of individuals testing positive for syphilis, gonorrhea (rectal, urethral, or pharyngeal), and/or chlamydia (rectal or urethral) at each testing visit. We ascertained new syphilis infections by consulting medical records for testing and treatment history as well as antibody titer levels.[54]

Statistical Methods

We examined the number of testing visits in the year prior to enrollment and the year after enrollment for both intervention and matched-control groups. We compared the median number testing visits in the pre-enrollment period between the intervention and matched-control groups using the Wilcoxon Rank-Sum Test; we utilized the same statistical test to compare the median number of testing visits in the post-enrollment period between the two groups.

Simple and multivariable logistic regression models were built to assess factors associated with CDC STI and HIV testing recommendation adherence. Simple logistic models first assessed associations between intervention group, demographics, and other potential baseline predictors and adherence to CDC STI/HIV testing recommendations. Next, a multivariable logistic regression model was constructed to estimate the association between being in the intervention group and adherence to CDC STI and HIV testing recommendations, controlling for several potential confounding factors. Covariates were entered the multivariable model based on statistical significance of simple logistic models and prior knowledge of confounding variables.

A pre-post design was used to compare STI positivity among intervention group patients at baseline and follow-up visits. That is, the presence of any STI (gonorrhea, chlamydia or syphilis) at any site (urethra, rectum or throat) at baseline was compared to the presence of any STI at one year of follow-up for all intervention group participants; similarly, STI-positivity after 3 months of follow-up was compared to STI-positivity after one year of follow-up. Differences in positivity by STI type and site of infection over the one year enrollment period were also assessed. McNemar's Test for dependent data was used to detect any statistically significant differences between time-periods.

3.4 Results

Baseline Demographic and STI Status

Over a one year period research staff offered program enrollment to 243 eligible patients, 208 (86%) of which agreed to participate. Intervention participants were matched with 208 control

subjects on the basis of age (+/- 5 years) and race/ethnicity; those patients who declined the intervention were not eligible for control group selection.

The average age of participants was 30 years, with 41% identifying as Hispanic/Latino, followed by white/Caucasian (36%), and Black/African American (10%) (Table 1). No statistically significant differences were observed betwee2n the intervention and matched-control groups at baseline for the following variables: race/ethnicity, age, HIV-status, STI test results (including pharyngeal, urethral, and rectal gonorrhea, urethral and rectal chlamydia, and new syphilis infections) and reason for visit. The percentage of individuals who were HIV-positive at baseline was 12.0% for the intervention group and 12.8% for the matched-control group. Rectal infections were the most common at baseline with 17.3% of the intervention group and 25.3% of the matched-control group testing positive for rectal gonorrhea and 32.5% of the intervention group and 29.5% of the matched-control group testing positive for rectal chlamydia. When zip code was linked to median household income based on 2013 US Census data, a significantly greater proportion of the intervention group reported living in a zip code with median household income of over $75,000 when compared to matched-control group (7.1% vs. 15.1%, respectively; p= 0.01).

Receipt of Program Incentives

The number of incentives paid by type may be found in Table 2. Over a two-year period, 796 incentives for testing and 586 incentives for being STI-free were received by intervention group individuals. On average, participants received 3.8 incentives for testing and 2.8 incentives for remaining STI-free. The percentage of individuals attending the clinic for testing who also

received an additional incentive for remaining STI-free were 54%, 74%, 80%, 84%, and 86% over the 5 testing intervals (baseline, 3 months, 6 months, 9 months, and 12 months).

Impact of Intervention on STI Testing

In the 1-year pre-enrollment period the median number of testing visits for both the intervention and matched-control group was 3 (interquartile range (IQR), intervention group: 2-5; IQR, matched-control group: 2-5; p=0.06). During the one-year follow-up period, intervention group participants returned to the clinic for testing a median of 4 times (IQR: 3-5) compared to 1 time (IQR: 0-2) for the matched-control group ($p < 0.01$). In the post-intervention period, 92.3% of intervention group participants returned to the clinic for at least one testing visit compared to 49.5% of matched-control group individuals. The percentage of intervention group participants returning for follow-up testing at 3, 6, 9, and 12 months was 77.4%, 73.1%, 64.9%, and 67.3%, respectively.

Results from the simple and multivariable logistic regressions may be found in Table 2. In an unadjusted model, intervention group participants were significantly more likely to comply with CDC STI and HIV testing recommendations when compared to individuals in the matched-control group (crude OR = 28.9 95% confidence interval (95% CI): 16.4-50.9). After controlling for age, race, HIV-status at baseline, STI-status at baseline, number of testing visits in the year prior to baseline, and median income of zip code, being in the intervention group was still significantly associated with adherence to CDC STI/HIV testing recommendations (adjusted OR (AOR) = 43.2; 95% CI: 20.4-91.7). Additionally, having 3 or more testing visits in the year prior to enrollment was predictive of adherence to testing guidelines (AOR = 5.34; 95% CI: 1.57-18.09).

Impact of Intervention on STI Positivity for Intervention Participants

Positivity estimates at baseline, 3 months, 6 months, 9 months, and 12 months of follow-up are reflected in Figure 1. At baseline, 46.2% of all intervention group participants tested positive for any STI (rectal, urethral, or pharyngeal gonorrhea, rectal or urethral chlamydia, or new syphilis) compared to 14.3% after 12 months of follow-up ($p<0.01$) (Table 3). Three-month positivity for any STI (26.1%) was also compared to positivity after 12 months of follow-up (14.3%) and the difference was also found to be statistically significant ($p<0.01$). When sub-analyses were performed to examine changes in STI positivity by STI type and infection site statistically significant reductions in STI positivity between baseline and 12 months were observed for: rectal chlamydia (32.5% vs. 3.6%, $p<0.01$), rectal gonorrhea (17.3% vs. 4.3%, $p=0.01$), and pharyngeal gonorrhea (11.4% and 4.4%, $p=0.04$); and between 3 months and 12 months for: rectal chlamydia (11.4% vs. 3.6%, $p<0.01$) and rectal gonorrhea (10.8% vs. 4.3%, $p=0.03$).

Missing STI positivity data was a potential concern with 67% (140/208) of intervention participants receiving testing after 12 months of follow-up. To address this, we compared baseline demographic characteristics and baseline test result data for intervention participants with and without missing test results at one year. There were no observed statistically significant differences between the two groups (Figure 4)

3.5 Discussion

In this quasi-experimental study we assessed the preliminary effectiveness of a financial incentive program for STI and HIV testing on STI positivity, frequency of STI testing, and adherence to CDC recommendations for STI and HIV testing in a clinic-based population of MSM in Los Angeles County. We found that positivity of any STI fell significantly over one

year of follow-up among intervention group participants. During the follow-up period, individuals in the intervention group visited the clinic for testing more often than those in the matched-control group. Finally, the intervention group was significantly more likely to comply with CDC STI and HIV testing recommendations for high-risk MSM.

Our findings are generally aligned with results from a body of literature that has reflected financial incentives to be an effective strategy for encouraging STI and HIV testing;[22,24,55-58] however, the depth of this literature is relatively limited. In fact, a recent systematic review found only 5 studies conducted in developed countries which aimed to estimate the impact of financial incentives on STI or HIV testing.[24] All five studies were promising, demonstrating higher rates of testing uptake in an incentivized group,[22,55-58] with three of these studies reporting statistically significant improvements.[56-58]

A more robust body of literature on the use of financial incentives to influence behavior change is available in other areas of health and social sciences. In particular, studies have reported that monetary incentives can improve: smoking cessation;[17] drug-addictive behaviors;[18-20,49] adherence to tuberculosis skin test reading;[21,48] and dietary habits.[23]

Given the demonstrated effectiveness of financial incentives to prompt healthy practices, it follows that such strategies may be useful in the domain of sexual health, in particular STI and HIV testing. However, such tactics are fairly uncommon. Instead, traditional behavioral intervention strategies, such as education and awareness campaigns, are more typical despite their history of limited success. This lack of uptake of strategies involving financial incentives may be attributed to several factors. First, financial incentives require upfront program costs, which can be a barrier to implementation given the funding bodies for these programs (e.g.

health care providers) may not be the entities realizing the downstream financial benefits (e.g. public or private payers). Second, there has been doubt surrounding long-term effectiveness of such strategies. In fact, several studies examining medication adherence interventions involving financial incentives in HIV-positive patients have reported a lack of sustained effectiveness.[59-61] Finally, interventions involving financial incentives have elicited skepticism due to ethical concerns of bribery, coercion, and potential for the erosion of personal and intrinsic motivation.

To this end, implementing and evaluating the effectiveness (including both the short-term and long-term impact) as well as investigating and quantifying the start-up, maintenance, and downstream costs of financial incentive programs compared to more conventional strategies for STI and HIV testing is warranted. Further, understanding the optimal conditions in which to implement these interventions along with the specific intervention components, including the size, delivery, communication strategy, duration, timing and frequency of the incentive, are crucial aspects to explore. For example, data shows that individuals are often more motivated by the fear of possibly losing a benefit than by the anticipation of gaining a benefit;[62] so, program implementers may want to consider framing messages to communicate a loss of incentives for not testing rather than receiving incentives for testing. In the case of the intervention we evaluated, a multi-component approach was used which incorporated not only financial incentives but included the addition of a personal pass to expedite clinic wait times and a "welcome package" sent to participants' homes. Teasing out the incremental impact of additional components that may enhance access or build rapport with study subjects is important for future scale-up and implementation.

Our analyses were subject to several limitations. While a high percentage of participants in the intervention group came back for testing at least once in the follow-up period, the proportion of

those returning for follow-up visits at each testing interval was much lower. It is conceivable that those individuals who failed to come back to the clinic for testing were of different risk, thereby producing misestimations of STI and HIV positivity. Missingness of test result data at baseline was also of concern for members of the matched-control group. Such severe missingness, especially for rectal testing and syphilis, exposes the baseline positivity estimates to bias if those not testing were more or less likely to test positive. Validity of the outcome measures, number of testing visits and adherence to CDC HIV and STI testing recommendations, is a concern as we only accounted for visits to the study clinic. Because matched-control group subjects were not incentivized to return to the study clinic, these individuals were perhaps less likely to revisit this particular clinic as opposed to another free community clinic, conceivably biasing our results away from the null. Finally, the intervention was implemented in a population of high-risk MSM in an urban environment and results may not be easily generalizable to other groups and settings such as rural locations where access to public transportation and proximity to community clinics may be limited.

STI and HIV testing is crucial for infection control and understanding how to improve uptake of regular screening practices, especially among high-risk populations, is critical in stalling the rise of such diseases. Traditional behavioral prevention approaches in subpopulations with persistently high rates of STI and HIV, such as MSM, have been met with moderate success. Our study, along with a limited body of evidence, has demonstrated interventions utilizing financial incentives to be promising. As such, further evaluation of the effectiveness, cost, and optimization of these strategies is important so that we may fully understand their application and usefulness as new tools for prevention.

Table 3.1. Baseline Characteristics of Intervention and Matched-Control Groups, October 2013 - September 2014

	Matched-Control Group		Intervention Group		
Characteristic	n	Col %	n	Col %	p-value
Total	208	100.0	208	100.0	--
Age, mean [sd]	30.7	[7.3]	29.6	[7.3]	0.11
Age Categories					
18-19	1	0.5%	3	1.4%	0.32
20-24	37	17.8%	50	24.0%	0.12
25-29	69	33.2%	75	36.1%	0.54
30-39	71	34.1%	56	26.9%	0.11
40+	30	14.4%	24	11.5%	0.38
Race/Ethnicity					
White	73	35.6%	76	36.7%	0.82
Black	20	9.8%	21	10.1%	0.90
Hispanic	85	41.5%	85	41.1%	0.93
Other*	27	13.2%	25	12.1%	0.74
Median Household Income of Zip Code					
Under $25,000	10	5.1%	5	2.4%	0.17
$25,000-$34,999	28	14.1%	33	16.1%	0.58
$35,000-$44,999	55	27.8%	57	27.8%	0.99
$45,000-$54,999	43	21.7%	40	19.5%	0.58
$55,000-$64,999	24	12.1%	17	8.3%	0.20
$65,000-$74,999	24	12.1%	22	10.7%	0.66
Over $75,000	14	7.1%	31	15.1%	**0.01****
HIV Status at Baseline					
Positive	24	12.8%	25	12.0%	0.81
Negative	163	87.2%	183	88.0%	--
Syphilis at Baseline					
Positive	4	4.3%	4	2.0%	0.27
Negative	90	95.7%	195	98.0%	--
Rectal Gonorrhea at Baseline					
Positive	37	25.3%	33	17.3%	0.07
Negative	109	74.7%	158	82.7%	--
Urethral Gonorrhea at Baseline					
Positive	15	8.6%	12	6.0%	0.32
Negative	159	91.4%	189	94.0%	--
Pharyngeal Gonorrhea at Baseline					
Positive	26	15.5%	23	11.4%	0.26
Negative	142	84.5%	178	88.6%	--
Rectal Chlamydia at Baseline					
Positive	43	29.5%	62	32.5%	0.55
Negative	103	70.5%	129	67.5%	--
Urethral Chlamydia at Baseline					
Positive	11	6.4%	7	3.5%	0.19
Negative	162	93.6%	195	96.5%	--
Reason for Visit					

Testing	75	42.6%	84	48.8%	0.24
Symptoms	12	6.8%	8	4.7%	0.39
Treatment / Return Visit	78	44.3%	69	40.1%	0.54
Partner Contact	6	3.4%	4	2.3%	0.55
Other	5	2.8%	7	4.1%	0.53

*Other includes: American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, Asian or Other

** Matched-Control and intervention groups significantly different at a $p<0.05$

‡ = Excluding HIV

Table 3.2. Receipt of Program Incentives, By Incentive Type and Time Period

Incentive Type	Baseline	3 Months	6 Months	9 Months	12 Months	Total
Testing Incentive, n (% receiving incentive of those enrolled)	208 (100%)	161 (77%)	152 (73%)	135 (65%)	140 (67%)	796 (77%)
STI-Free Incentive, n (% receiving incentive of those tested)	112 (54%)	119 (74%)	121 (80%)	114 (84%)	120 (86%)	586 (74%)

Table 3.3. Logistic Regression Analysis of the Association Between Adherence to CDC STI and HIV Testing Recommendations and Intervention Group, Demographic Characteristics, and STI and HIV Testing Characteristics

	Crude OR	95% CI	AOR‡	95% CI
Treatment Group				
Matched Control (Ref)	1.00	--	1.00	--
Intervention	**28.90**	**16.42-50.89**	**43.21**	**20.37-91.66**
Age	1.01	0.98-1.04	1.02	0.97-1.07
Race/ethnicity				
White (Ref)	1.00	--	1.00	--
Black	0.63	0.31-1.27	0.44	0.14-1.33
Hispanic	0.53	0.34-0.84	0.31	0.15-0.67
Other*	0.70	0.36-1.35	0.53	0.19-1.49
HIV Status at Baseline				
Negative (Ref)	1.00	--	1.00	--
Positive	0.87	0.48-1.57	0.77	0.29-2.08
STI Status at Baseline				
No STI (Ref)	1.00	--	1.00	--
≥1	**0.63**	**0.42-0.96**	0.52	0.27-1.02
Testing Visits Year Prior to Baseline				
0 (Ref)	1.00	--	1.00	--
1	0.62	0.31-1.26	1.29	0.39-4.31
2	0.98	0.47-2.02	2.19	0.61-7.84
≥ 3	1.94	0.99-3.81	**5.34**	**1.57-18.09**
Median Household Income of Zip Code				
≥ $75,000 (Ref)	1.00	--	1.00	--
$65,000-$74,999	0.53	0.22-1.26	0.97	0.25-3.75
$55,000-$64,999	**0.35**	**0.14-0.86**	0.71	0.19-2.74
$45,000-$54,999	0.78	0.36-1.73	1.91	0.60-6.23
$35,000-$44,999	0.47	0.22-0.99	0.81	0.26-2.53
$25,000-$34,999	0.65	0.29-1.50	1.08	0.30-3.86
Under $25,000	0.61	0.18-2.06	2.05	0.34-12.41

*Other includes: American Indian, Alaskan Native, Native Hawaiian, Pacific Islander, Asian or Other

‡ Adjusted age, race/ethnicity, HIV status at baseline, STI status at baseline, and median income of zip code

Table 3.4. STI Positivity at Baseline, 3 Months of Follow-up, and 12 Months of Follow-up, Intervention Participants (n=208)

	Baseline	3 Months	12 Months		
	Positivity (%)	Positivity (%)	Positivity (%)	P value*, Baseline vs. 12 Mos	P value*, 3 Mos vs. 12 Mos
Syphilis	4/199 (2.0%)	3/159 (1.9%)	0/140 (0.0%)	--	
Gonorrhea					
All sites	44/204 (21.6%)	26/160 (16.3%)	12/137 (8.8%)	**0.01**	**0.02**
Rectal	33/191 (17.3%)	17/158 (10.8%)	6/138 (4.3%)	**0.01**	**0.03**
Urethral	12/201 (6.0%)	5/159 (3.1%)	2/140 (1.4%)	0.26	0.18
Pharyngeal	23/201 (11.4%)	14/156 (9.0%)	6/137 (4.4%)	**0.04**	0.05
Chlamydia					
All sites	65/202 (32.2%)	20/161 (12.4%)	11/137 (8.0%)	**<0.01**	0.25
Rectal	62/191 (32.5%)	18/158 (11.4%)	5/138 (3.6%)	**<0.01**	**0.01**
Urethral	7/202 (3.5%)	3/160 (1.9%)	7/140 (5.1%)	0.56	0.26
Any STI‡	96/208 (46.2%)	42/161 (26.1%)	20/140 (14.3%)	**<0.01**	**<0.01**

*= P value for difference in positivity using McNemar's Test for dependent data

‡ = Excluding HIV

Figure 3.1. Chlamydia and Gonorrhea Positivity Estimates at Each Testing Period for Intervention Group, by Anatomical Site

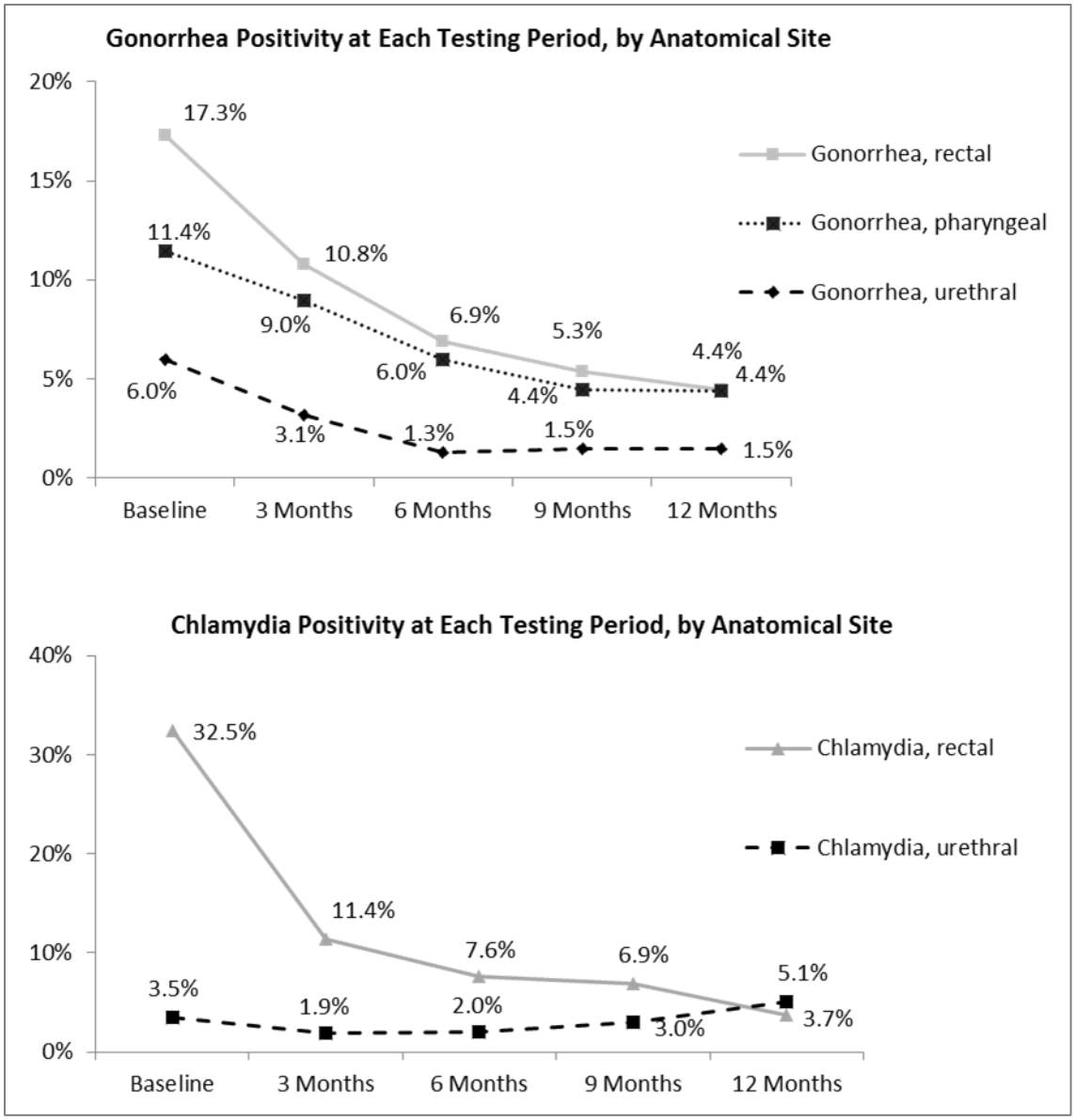


Table 3.5. Baseline Characteristics and Test Results for Intervention Participants, by Missingness at 12 Months

	Intervention Group – Missing at 12 Mos		Intervention Group – Not Missing at 12 Mos		
Characteristic	n	Col %	n	Col %	p-value
Total	68	100%	140	100%	
Age Categories					
18-19	0	0	3	2.1%	--
20-24	17	25.0%	33	23.6%	0.82
25-29	23	33.8%	53	37.9%	0.57
30-39	22	32.4%	34	24.3%	0.22
40+	6	8.8%	17	12.1%	0.47
Race/Ethnicity					
White	19	28.4%	57	40.7%	0.08
Black	6	9.0%	15	10.7%	0.69
Hispanic	34	50.8%	51	36.4%	0.0501
Other*	8	11.9%	17	12.1%	0.97
HIV Status at Baseline					
Positive	13	19.1%	15	10.7%	0.10
Negative	55	80.9%	125	89.3%	--
Rectal Gonorrhea at Baseline					
Positive	14	23.3%	19	14.5%	0.13
Negative	46	76.7%	112	85.5%	--
Urethral Gonorrhea at Baseline					
Positive	7	10.8%	5	3.7%	0.06
Negative	58	89.2%	131	96.3%	--
Pharyngeal Gonorrhea at Baseline					
Positive	7	10.8%	16	11.8%	0.84
Negative	58	89.2%	120	88.2%	--
Rectal Chlamydia at Baseline					
Positive	25	41.7%	37	28.2%	0.07
Negative	35	58.3%	94	71.8%	--
Urethral Chlamydia at Baseline					
Positive	2	3.0%	5	3.7%	0.99
Negative	64	97.0%	131	96.3%	--

*Other includes: American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, Asian or Other

** Groups significantly different at a $p<0.05$

Chapter 4. Cost-Effectiveness of a Financial Incentive Program for STI and HIV Testing Among Men Who Have Sex With Men (MSM) in Los Angeles County

4.1 Abstract

Background: Financial incentives that encourage patients to undergo HIV and STI testing are feasible and effective. However, less is known about the cost of such strategies relative to the potential benefits.

Objective: To analyze from the clinic perspective the cost-effectiveness of a financial incentive program to encourage men-who-have-sex-with-men (MSM) to undergo STI and HIV testing at a free clinic in Los Angeles, CA.

Methods: We compared the financial incentive program with the clinic's standard-of-care. To evaluate effectiveness, we compared STI testing and treatment for 208 program patients and 208 controls, matched based on race/ethnicity and age. Using a micro-costing approach and deriving quantities and costs from administrative records, we calculated the average cost to the clinic per patient enrolled, per patient adherent to CDC testing recommendations, and per STI treated over two years. Incremental cost effectiveness ratios (ICERs) included the cost per additional patient adherent to CDC testing recommendations and the cost per additional STI treated.

Results: Individuals in the intervention group were significantly more likely than the control group to adhere to CDC STI and HIV testing recommendations in the one-year period following enrollment (91% (189/208) vs. 25% (53/208), $p<0.01$) and were treated for significantly more STI infections (205 vs. 84, $p<0.01$) over the two-year data collection period compared to the matched-control group. The average cost per individual enrolled was $1,442 for the intervention group and $133 for the matched-control group. Costs averaged $1,587 per individual adherent to CDC STI and HIV testing recommendations for one year in the intervention group versus $521

in the matched-control group. Per STI treated, the average cost in the intervention group was $1,463 compared to $329 in the matched-control group. The cost per additional patient adherent with CDC STI and HIV testing recommendations was $2,002 and the cost per additional treated STI was $2,250.

Discussion: Financial incentive programs for STI and HIV testing may be very effective for encouraging STI testing and treatment. Due largely to the cost of program implementation and incentives, STI-related costs were 10-fold higher in the intervention group. Further research appraising the impact on HIV-infections averted, patient time and productivity loses is of interest.

4.2 Background

Despite continuous efforts to stall the rise of infections, the past decade has seen an increase in rates of sexually transmitted infections (STIs) among men who have sex with men (MSM) in both Los Angeles County and nationwide.[63,64] In fact, primary and secondary syphilis rates increased by 42% between 2009 and 2013 in Los Angeles, with the majority of cases in MSM.[63,64] Trends in gonorrhea and chlamydia infections reflect a similar upward trajectory. Between 2010 and 2015 the median site-specific prevalence among MSM attending STD Surveillance Network clinics increased from 15.5% to 19% for gonorrhea and from 13% to 16% for chlamydia.[65,66] The implications of rising STI rates extend beyond their significant morbidity and potential long-term health sequelae. Importantly, strong evidence has indicated STI infection may promote both HIV transmission and acquisition. [2-5,28-30]

Increased STI screening and treatment are widely recognized as effective methods for the prevention of HIV and other STIs. The Centers for Disease Control and Prevention (CDC)

guidelines advise annual screening for all sexually active MSM, with more frequent screening (every 3-6 months) among those who report high-risk behaviors, such as unprotected anal intercourse and sex with anonymous partners.[10] Despite these recommendations, however, testing rates are far below goals among MSM including HIV-infected MSM.[11-13,67]

As such, the development of affordable and effective strategies to encourage STI screening is key to sustainable infection-control. A growing body of evidence has indicated financial incentives to be successful in motivating behavior change by patients and improving health outcomes in a variety of settings. [17-21,23,48,49] Given this demonstrated effectiveness, financial incentives have started to gain popularity as tools for encouraging STI and HIV testing and studies evaluating their effectiveness have been promising. In fact, a recent systematic review investigated the impact of incentives on HIV and STI testing uptake and reported that all included studies (n=7) demonstrated higher rates of testing uptake in an incentivized group compared to a non-incentivized group.[24]

While the body of evidence assessing the effectiveness of financial incentives to promote STI and HIV testing is growing, current literature evaluating the cost of these programs is sparse. Because the success of a program is determined not only by its effectiveness, but by its affordability to the implementing entities bearing the costs, it is crucial to understand the financial implications of such strategies. Accordingly, the aim of the present study was to evaluate, from the clinic's perspective, the cost-effectiveness of a financial incentive program for STI and HIV testing compared to the clinic's status-quo.

4.3 Methods

This cost-effectiveness analysis is reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.[68]

Setting and Study Population

The program was implemented in the AIDS Healthcare Foundation (AHF) Men's Wellness Clinic, a free not-for-profit STI and HIV testing clinic in Los Angeles, California. Patients were screened for program eligibility upon intake; inclusion criteria included: 1.) being male; 2) being 18 years or older; and 3.) having one or more diagnoses of rectal chlamydia, rectal gonorrhea, and/or syphilis in the past two years. The enrollment period extended from October 1, 2013 to Sept 30, 2014 and all participants were followed-up for one year.

To serve as a comparison, a concurrent matched-control group was constructed from the clinic's electronic medical record data. The matched-control group consisted of men who presented to the clinic during the enrollment period and who met the inclusion criteria for the program but were not offered enrollment due to program staff scheduling availability, which was largely random. Matched-control group individuals were individually matched to intervention group participants on the basis of age (plus or minus five years) and race/ethnicity at a ratio of 1:1.

Intervention Group

Details of the intervention have been described fully elsewhere [cite paper 1]. In brief, intervention group participants completed STI and HIV testing upon enrollment (baseline) and were asked to return to the clinic for re-testing every three months, for one year. At each testing session intervention group participants completed a full STI panel: participants were screened for chlamydia (rectal and urethral), gonorrhea (rectal, urethral, and pharyngeal), syphilis and HIV. Participants received a $50 Target card at enrollment, a $50 Target electronic gift card for each

return testing visit, and an additional $50 electronic Target gift card if they were completely HIV- and STI-free after each testing visit. Intervention group participants had the potential to earn up to $500 in Target gift cards over a one year period.

In addition to financial incentives, intervention group participants also received other types of non-financial incentives as well as testing reminders. In the month following program enrollment participants received a "welcome package" mailed to their home address which contained: one 12-oz bottle of premium water based lubricant, 50 condoms, candy, and standard AHF informational brochures regarding STI- and HIV-risk. Participants also received a priority card which could be used to expedite clinic wait. Finally, program staff notified intervention group participants of when it was time to test via SMS text messages and/or email reminders.

Control Group

The intervention was compared to a status-quo scenario. The status-quo of the clinic included standard STI and HIV risk assessment and counseling, free STI and HIV testing available on first-come-first-serve basis, and counseling to return for retesting as set forth in the CDC STI testing and treatment guidelines [10,52,53]. The clinic did not provide incentives (financial or non-financial) or reminders of any type to non-intervention patients during this period.

Perspective and Measurement of Cost

The cost-effectiveness analysis was conducted from the clinic perspective. We considered three major categories of cost incurred by the clinic: implementation costs, cost of STI and HIV laboratory testing, and STI treatment costs. Costs were calculated using the micro-costing approach whereby total economic costs are calculated by multiplying total quantities of goods and services by their respective unit prices.[69]

Implementation Costs. Costs associated with program implementation included labor, supplies, and financial incentives. Labor costs attributable to program planning and development, implementation, administrative support, and database management were calculated from the actual 2013/2014 salaries of program staff. Hourly wage rates were multiplied by time spent on tasks in support of the intervention for each program staff member. Supply costs including clinic priority cards and welcome packages were derived from internal program records. Costs related to financial incentives were estimated from actual program expenditures.

Cost of STI and HIV Testing. Costs associated with STI and HIV testing comprised the cost of laboratory tests plus the cost of clinic personnel for specimen collection. The cost of STI and HIV laboratory tests were based on the actual number of tests administered for intervention and control groups multiplied by the price paid for each test by the clinic. Quantities of HIV screening tests, including the rapid HIV-1/HIV-2 antibody test and HIV p-24 antigen test, were also based on actual utilization. However, the quantity of confirmatory nucleic acid amplification (NAAT) tests administered were based on standard HIV testing algorithms instead of actual use as NAAT tests during this period were run in parallel with HIV rapid tests as part of an unrelated project. Clinic personnel costs associated with STI and HIV testing were calculated by multiplying the actual number of testing visits by the estimated time spent with a medical assistant and counselor during testing visits; this value was then multiplied by the respective average hourly wage rate of clinic personnel. Based on interviews with clinic management, patients spent approximately 15 minutes with a counselor who administered a risk assessment questionnaire, performed a rapid HIV-1/HIV-2 antibody test, and facilitated specimen self-collection for urethral and rectal chlamydia and gonorrhea testing. Next, patients spent another

15 minutes with a medical assistant for oral specimen collection for pharyngeal gonorrhea testing and a blood draw for syphilis testing and/or HIV confirmatory testing.

STI Medication Treatment Costs. Costs associated with STI treatment included the cost of antibiotics and the cost of clinic personnel for medication administration. The quantities of medications dispensed were based on actual clinic dispense records for both intervention and control groups. Medication quantities were then multiplied by the unit cost of each mediations. Mediations were costed from internal data reflecting the actual unit cost paid by the clinic. The cost of clinic personnel for medication administration was estimated by multiplying the number of treatment visits by the estimated time spent with a medical assistant who performed antibiotic injections and directly observed oral administration of medications; this value was then multiplied by the average hourly wage rate for medical assistants at the clinic. Based on interviews with clinic management, medical assistants spend approximately 15 minutes per patient administering medications. Individuals testing positive for HIV during follow-up were linked to HIV care; however, the costs of HIV treatment were not included, as these were exogenous to the clinic's costs and therefore outside the scope of the established perspective.

The total incremental cost of the intervention was estimated by subtracting the total cost of STI and HIV testing and STI treatment incurred by the control group from the total cost of STI and HIV testing and STI treatment in the intervention group, plus the additional labor, supply, and incentive costs associated with program start-up and maintenance. Total costs were captured and reported for the 2-year program implementation period. All costs were captured in 2013 USD and inflated to 2017 USD using the medical Consumer Price Index (mCPI) multiplier.[70]

Measurement of Effectiveness

Two primary outcome measures of effectiveness were assessed: 1.) number of patients adherent to CDC STI and HIV testing recommendations and 2.) absolute number of STIs treated. Adherence to STI and HIV testing recommendations were based on CDC guidelines that advise annual screening for all sexually active MSM, with more frequent screening (every 3-6 months) among those who report high-risk behaviors, such as multiple or anonymous partners and unprotected anal intercourse.[10,52,53] For this analysis we defined adherence the CDC STI and HIV testing recommendations as receiving testing at least twice for each STI (urethral, rectal, and pharyngeal gonorrhea; urethral and rectal chlamydia; and syphilis) and HIV within one year of enrollment. In determining the number of STIs treated, we considered treating one pathogen at one testing session within one month of a positive test result, regardless of the number of anatomical sites the infection was present, as treating one infection; for syphilis there was no time limit for treatment.

Both number of patients adherent to CDC STI and HIV testing recommendations and number of STIs treated were collected for the cohort for the two years of program implementation. We estimated the incremental effectiveness for both outcome measures by calculating the absolute difference between intervention and matched-control groups. Differences in the proportion of patients adherent to the recommendations were determined using Pearson's chi-squared test; differences in the number of STIs treated over a two-year period was determined using a poisson means test.

Measurement of Average Cost

We calculated the average cost per patient enrolled for both the intervention and the matched-control groups by dividing the total two-year cost incurred by each group by the number of

individuals enrolled over two years (n=208 for both groups). We also calculated the average cost per patient adherence to CDC testing recommendations and the average cost per STI treated for both the intervention and the matched-control groups.

Measurement of Cost Effectiveness

To calculate an incremental cost effectiveness ratio (ICER), that is the incremental cost associated with one additional unit of effectiveness, we divided the difference in total cost between the intervention and control groups (i.e. the incremental total cost) by the difference in effectiveness estimates between the intervention and control groups (i.e. the incremental effectiveness). For this analysis, we estimated two ICERs: 1.) the incremental cost per additional patient adherent to CDC STI and HIV testing recommendations; and 2.) the incremental cost per additional STI treated.

Sensitivity Analysis

One-way sensitivity analyses were undertaken to test the robustness of the cost-effectiveness estimates to uncertainty of input variable estimates. For these analyses, single variables were tested over their likely range of plausible values while all other variables were held constant; these variables included labor costs, laboratory testing costs, and medication costs. Minimum and maximum estimates for labor costs reflected 10^{th} and 90^{th} percentile nationwide hourly wage values (respectively) for each clinic position, derived from the Bureau of Labor Statistics.[71] Upper bounds for the cost of STI and HIV tests were based on national cost limits for each service/CPT code from the Centers for Medicare and Medicaid Services 2013 Clinical Diagnostic Laboratory Fee Schedule;[72] lower bounds were set at the prices paid by the clinic. Maximum values for medication costs were derived from the average wholesale price.[73] Because

the clinic participated in the Health Resources and Services Administration's 340b Drug Pricing Program, whereby eligible health organizations receive discounted drug prices, lower bounds for medication costs were reflected the actual prices paid by the clinic. Tornado diagrams (influence analyses) were constructed to reflect the primary drivers of the cost effectiveness estimates.

4.4 Results

Demographics and STI Infections at Baseline

Over a one year period research staff offered program enrollment to 243 eligible patients, 208 (86%) of whom agreed to participate. Intervention participants were matched with 208 control subjects. The average age of participants was 30 years, with 41% identifying as Hispanic/Latino, followed by white/Caucasian (36%), and Black/African American (10%) (Table 1). No statistically significant differences were observed between the intervention and matched-control groups at baseline for the following variables: race/ethnicity, age, HIV-status, STI test results (including pharyngeal, urethral, and rectal gonorrhea, urethral and rectal chlamydia, and new syphilis infections) and reason for visit. When zip code was linked to median household income based on 2013 US Census data, a significantly greater proportion of the intervention group reported living in a zip code with median household income of over $75,000 when compared to matched-control group (7.1% vs. 15.1%, respectively; $p= 0.01$).

Effectiveness

Table 2 summarizes the key results on effectiveness. Comparison between the intervention and control groups showed that individuals in the intervention group were significantly more likely than the control group to adhere to CDC STI and HIV testing recommendations in the one-year period following enrollment (91% (189/208) vs. 25% (53/208); $p<0.01$). Including baseline, the

intervention group was treated for significantly more gonorrhea infections (91 vs. 28; $p<0.01$), chlamydia infections (103 vs. 46, $p<0.01$), and total STI infections (205 vs. 84; $p<0.01$); the intervention and control groups were treated for a similar number of syphilis infections (11 vs. 10, respectively $p=0.82$).

Costs

Total Costs. The total cost over two years was $299,887 for the intervention group and $27,609 for the control group (Table 3).

Implementation Costs. Implementation costs were incurred only by the intervention group and totaled $208,971 over a two-year period constituting 70% of total costs. Labor comprised the largest sub-category of implementation costs, responsible for $130,803 per two years. Incentives paid to intervention participants totaled $76,923 over two-years.

Cost of STI and HIV Tests. Both intervention and control groups incurred STI and HIV testing costs. In the intervention group costs associated with STI testing, including both labor and laboratory costs, totaled $89,957 over a two-year period ($44,979 annually) which comprised 35% of total costs. Over the same two-year period, total testing costs for matched-control group subjects were $27,044 ($13,522 annually) which accounted for 98% of total costs. In both groups laboratory costs were responsible for the majority of testing costs (intervention group: 91%; matched-control: 86%). Labor costs, which included wages for counselors and medical assistants, accounted for 9% and 14% of testing costs in the intervention and matched-control groups, respectively.

STI Medication Treatment Costs. Over two-years medication and labor associated with medication administration was responsible for $959 in the intervention group compared to $565

in the matched-control group, constituting a very small percentage of total costs among both study groups (intervention group: 0.3% of total costs; matched-control group: 2%). Among medication treatments, penicillin G was the single most expensive medication type constituting 24% of all medication treatment in the intervention group and 44% of medication treatment costs in the matched-control group. Labor associated with medication administration accounted for 50% and 30% of medication treatment costs in the intervention and matched-control groups, respectively.

Average Costs and Cost-Effectiveness

Average Costs. Average costs estimates may be found in Table 4. The average cost per individual enrolled for a one year period was $1,442 for the intervention group and $133 for the matched-control group. Costs averaged $1,587 per individual adherent to CDC STI and HIV testing recommendations in the intervention group versus $521 in the matched-control group. Per STI treated, the average cost in the intervention group was $1,463 compared to $329 in the matched-control group.

Cost-Effectiveness. ICERs may be found in Table 4. The cost per additional patient adherent to CDC STI and HIV testing recommendations was estimated to be $2,002. The cost per additional treated STI was calculated to be $2,250.

Sensitivity Analysis

Results from the one-way sensitivity analyses may be found in Figure 1. Both ICERs were most sensitive to variation in: program manager salary, cost of STI and HIV tests, and research assistant salary. The incremental cost per additional individual adherent to STI and HIV testing

recommendations ranged from a minimum value of $1,844 to $2,922 The incremental cost per additional STI treated ranged from a minimum value of $2,073 to $3,284 .

4.5 Discussion

In this cost-effectiveness analysis based on retrospective matched cohort study, we determined that a financial incentive programs for STI and HIV testing was associated with higher STI testing and treatment among a population of high-risk MSM, as compared with matched controls. Over a two-year period, the cost per enrolled individual, including implementation costs, STI testing costs, and STI medication treatment costs, were approximately ten times higher in the intervention group than the matched-control group. Labor for the start-up and maintenance of the program and financial incentives were responsible for a majority of the cost difference between the two study groups. However, the intervention's effectiveness also contributed to its higher cost- that is, returning patients led to increased costs for testing and treatment. Upon examining the cost-effectiveness, we found the incremental cost per additional STI treated to be relatively modest and comparable with findings from other studies.

Prior studies have demonstrated the effectiveness of financial incentive programs for STI and HIV testing, [22,24,55-58] but evaluations of the cost of these interventions are more limited. Generally, however, our results are aligned with the current cost literature. In a 2005 cost-effectiveness study testing five interventions to encourage STI testing in both men and women, the investigators found the incremental cost per additional STI treated to be $1,620 for financial incentives when compared to the status-quo (costs were reported in 2001 USD and included program, testing and treatment costs). When inflated to 2017 USD (using the mCPI multiplier[70]) the ICER equates to $2,807—just slightly higher than our study's ICER ($2,250/additional infection treated). Interestingly, authors of the study reported both motivational counseling alone

and motivational counseling plus a phone call reminder to be both more costly and less effective than financial incentives.

While financial incentives may be more cost-effective than alternative interventions, further ways to reduce average costs may be of interest to clinic managers and public health authorities. Two significant cost categories in our analysis included labor associated with program implementation and maintenance and financial incentives. To reduce burden on human resources, incentive programs may benefit from an automated system for notifying patients when to test (via text or email) and an automated record-keeping system for determining incentive pay-outs. Additionally, implementing an incremental incentive schedule whereby the value of payouts gradually increases as participants sustain regular testing frequency may not only reduce costs but serve to better retain individuals.

Due to the size of our data we were precluded from directly measuring the impact of the program on HIV seroconversion and modeling subsequent cost of HIV treatment averted; however rudimentary estimates may be performed. Assuming a baseline annual rate of HIV in this population of 0.0385 (from clinic data); a 53% relative risk reduction of acquiring HIV among those that are not infection with gonorrhea or chlamydia,[2] and a 50% relative reduction in STD prevalence among those in the intervention group (compared to the control, based on program data) we can estimate an annual rate of HIV among those in the intervention group of 0.031. The number of HIV infections averted over the two year data collection period can be estimated by the reduction in incidence rate multiplied by the number of HIV negative men at baseline: (0.0385-0.0301)*183 = 1.54 HIV infections averted. With a discounted life-time medical cost of HIV treatment estimated at $371,579 (inflated to 2017 USD) a savings of $571,190 for averted

HIV care can be estimated. Comparing this 2-year savings to the total 2-year total cost of the program ($299,887), one may see how such a program may be cost-saving to society.

To this end, additional research appraising the economic value of financial incentives from the societal perspective is needed. That is, cost-effectiveness analyses estimating not only the costs of program start-up and maintenance, testing, and treatment is of value, but measuring and modeling the costs associated with disease sequelae (such as neurosyphilis or disseminated gonococcal infection), productivity losses, patient travel, and reduced risk for subsequent HIV seroconversion is of interest. Additionally, incorporating the effect of treatment of study subjects on transmission to future sex partners is of value, especially in higher-risk populations. Finally, a more comprehensive understanding the optimal conditions in which to implement financial incentive interventions along with the specific intervention components, including the size, delivery, communication strategy, duration, timing and frequency of the incentive, is important for future development and application.

Our analyses were subject to several limitations. Validity of our effectiveness measures, including adherence to CDC STI and HIV testing recommendations and number of infections treated, is a concern as we only accounted for visits to the study clinic. Because matched-control group subjects were not incentivized to return to the study clinic, these individuals were perhaps less likely to revisit this particular clinic as opposed to another public clinic, conceivably overestimating the impact of the program on both testing and treatment measures. Next, at baseline we noted a significantly greater proportion of the intervention group reported living in a zip code with median household income of over $75,000 when compared to matched-control group; however, this difference would likely attenuate our results as individuals with higher income are conceivable less motivated by cash incentives. Additionally, clinic personnel time

measurements, including time spent with medical assistants and counselors for testing and treatment, were crudely estimated. Future studies may seek to implement a time-in-motion study design as this would more accurately reflect labor resource requirements. However, in several sensitivity analyses, we varied medical assistant and counselor wages and found the change in ICER values to be relatively inconsequential. Furthermore, cost estimates for STI and HIV tests were relatively low due to contracting with the local county health department. In a sensitivity analysis, we varied cost of STI and HIV tests over their plausible range of values and saw a maximum increase in cost estimates of nearly 50%. As such, the generalizability of our findings outside of public health contracted sites may be limited. Finally, the intervention was implemented in a population of high-risk MSM in an urban environment and results may not be easily generalizable to other groups and settings such as rural locations where access to public transportation and proximity to community clinics may be limited. Because the cost per infection treated directly depends on disease prevalence in a population, the intervention may be less cost-effective in a group at lower-risk for STIs.

In conclusion, our study demonstrated that in addition to being feasible and effective, financial incentives programs for STI and HIV testing in MSM may also be a good economic value compared to other program alternatives. While total costs of the program were roughly ten times higher for the intervention group when compared to control subjects, mostly attributable to program labor and paid incentives, the intervention group was over 3 times as likely to adhere to CDC STI and HIV testing recommendations. Further, prior studies reporting similar incremental cost per treated infection also reported financial incentives to be both less costly and more effective than motivational counseling and phone call reminders. It is therefore crucial to not only understand the relative cost-effectiveness of incentive programs relative to the status-quo,

but in comparison to other programs which may compete for financial and human resources. Finally, a more comprehensive understanding of the effect of incentive programs on transmission to sex partners as well as the more distal costs incurred including those associated with disease sequelae, reduced risk of HIV acquisition, and productivity losses is imperative for understanding the global impact of such programs.

Table 4.1. Baseline Characteristics of Intervention and Matched-Control Groups, October 2013 - September 2014

	Intervention Group		Matched Control Group		
Characteristic	n	Col %	n	Col %	p-value
Total	208	100.0	208	100.0	--
Age, mean [sd]	29.6	[7.3]	30.7	[7.3]	0.11
Age Categories					
18-19	3	1.4%	1	0.5%	0.32
20-24	50	24.0%	37	17.8%	0.12
25-29	75	36.1%	69	33.2%	0.54
30-39	56	26.9%	71	34.1%	0.11
40+	24	11.5%	30	14.4%	0.38
Race					
White	76	36.7%	73	35.6%	0.82
Black	21	10.1%	20	9.8%	0.90
Hispanic	85	41.1%	85	41.5%	0.93
Other*	25	12.1%	27	13.2%	0.74
Median Household Income of Zip Code					
Under $25,000	5	2.4%	10	5.1%	0.17
$25,000-$34,999	33	16.1%	28	14.1%	0.58
$35,000-$44,999	57	27.8%	55	27.8%	0.99
$45,000-$54,999	40	19.5%	43	21.7%	0.58
$55,000-$64,999	17	8.3%	24	12.1%	0.20
$65,000-$74,999	22	10.7%	24	12.1%	0.66
Over $75,000	31	15.1%	14	7.1%	**0.01**
Self-Reported Male Sexual Partners					
Yes	201	96.6%	181	96.3%	0.80
No	7	3.4%	7	3.7%	--
HIV Status at Baseline					
Positive	25	12.0%	24	12.8%	0.81
Negative	183	88.0%	163	87.2%	--
New Syphilis at Baseline					
Positive	4	2.0%	4	4.3%	0.27
Negative	195	98.0%	90	95.7%	--
Rectal Gonorrhea at Baseline					
Positive	33	17.3%	37	25.3%	0.07
Negative	158	82.7%	109	74.7%	
Urethral Gonorrhea at Baseline					
Positive	12	6.0%	15	8.6%	0.32
Negative	189	94.0%	159	91.4%	--
Pharyngeal Gonorrhea at Baseline					
Positive	23	11.4%	26	15.5%	0.26
Negative	178	88.6%	142	84.5%	--
Rectal Chlamydia at Baseline					
Positive	62	32.5%	43	29.5%	0.55

Negative	129	67.5%	103	70.5%	--
Urethral Chlamydia at Baseline					
Positive	7	3.5%	11	6.4%	0.19
Negative	195	96.5%	162	93.6%	--
Reason for Visit					
Testing	84	48.8%	75	42.6%	0.24
Symptoms	8	4.7%	12	6.8%	0.39
Treatment / Return Visit	69	40.1%	78	44.3%	0.54
Partner Contact	4	2.3%	6	3.4%	0.55
Other	7	4.1%	5	2.8%	0.53

*Other includes: American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, Asian or Other

Table 4.2. Summary of Program Effectiveness

	Intervention	Control (Standard-of-Care)	Intervention minus Control
Adherence to CDC STI and HIV Testing Recommendations, 2 yrs.			
Enrolled (n)	208	208	--
Adherent (n)	189	53	--
Adherent (%)	90.9%	25.5%	+65.4%*
Treated Sexually Transmitted Infections, 2 yrs.			
Gonorrhea (n)	91	28	+63**
Chlamydia (n)	103	46	+57**
Syphilis (n)	11	10	+1
All STIs (n)[a]	205	84	+121**

*chi-squared test, p <0.01

**poisson means test, p <0.01

[a]Chlamydia + gonorrhea + syphilis

Abbreviati205ons:

CDC = Centers for Disease Control and Prevention

STI = sexually transmitted infections

Table 4.3. Estimated Two-Year Costs of Intervention by Cost Category (in 2017 USD)

	Intervention Group	Matched-Control Group
Cost Category	**Cost, 2 yrs (% of total cost)**	**Cost, 2 yrs (% of total cost)**
i.) Implementation Costs		
Labor		
Program Manager	$89,057	--
Program Assistant	$41,746	--
Supplies		
Clinic Priority Cards	$78	--
Welcome Packages	$1,167	--
Incentives		
For Testing	$44,306	--
For Remaining Infection-Free	$32,617	--
Subtotal, Implementation Costs	**$208,971 (70%)**	--
ii.) STI Testing Costs		
Gonorrhea (rectal)	$12,741	$3,306
Gonorrhea (urethral)	$13,142	$3,974
Gonorrhea (pharyngeal)	$13,025	$3,907
Chlamydia (rectal)	$12,724	$3,306
Chlamydia (urethral)	$13,175	$3,974
Syphilis, RPR	$1,883	$539
Syphilis, RPR Titer	$187	$207
Syphilis Confirmatory, TPPA	$187	$207
HIV rapid	$8,633	$1,959
HIV p24	$5,407	$1,368
HIV NAAT	$530	$681
Counselors	$4,856	$2,109
Medical Assistants	$3,468	$1,506
Subtotal, STI and HIV Testing Costs	**$89,957 (30%)**	**$27,044 (98%)**
iii.) STI Medication Treatment Costs		
Azithromycin	$68	$56
Penicillin g	$234	$247
Ceftiraxone	$146	$91
Doxycycline	$35	$5
Medical Assistant	$477	$167
Subtotal, STI Treatment Costs	**$959 (0.3%)**	**$565 (2%)**
Total Cost, 2 yrs	**$299,887**	**$27,609**

Abbreviations:
STI = sexually transmitted infection
RPR = rapid plasma reagin
TPPA = treponema pallidum particulate agglutination
NAAT = Nucleic acid amplification test

Table 4.4 Summary of Cost Effectiveness (in 2017 USD)

	Intervention	Control (Standard-of-Care)	Δ (Intervention minus Control)
Total Cost Summary			
Total Cost, 2 yrs	$299,887	$27,609	$272,278
Average Cost Summary			
Average Cost per Individual Enrolled	$1,442	$133	$1,309
Average Cost per Individual Adherent to CDC Recommendations*	$1,587	$521	$1,066
Average Cost per STI Treated	$1,463	$329	$1,134
Cost-Effectiveness Summary (ICERs)			
Incremental Cost Per Additional Individual Adherent to CDC Recommendations* (Δ$/Δn)		$272,278 / 136 = **$2,002**	
Incremental Cost Per Additional STI Treated (Δ$/Δn)		$272,278 / 121 = **$2,250**	

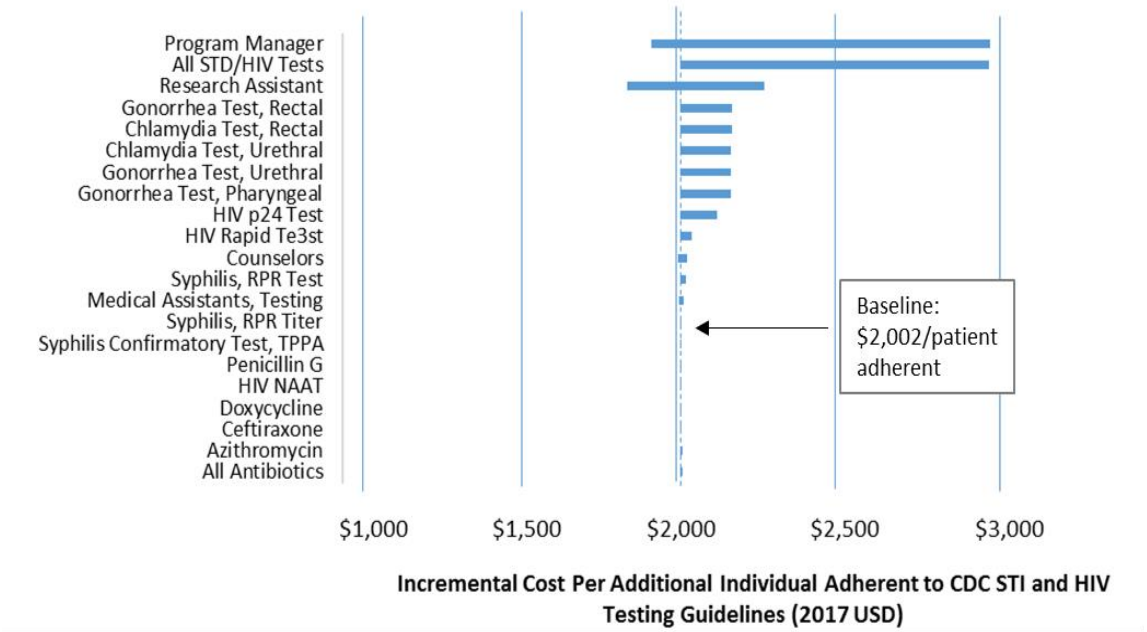
*For one year

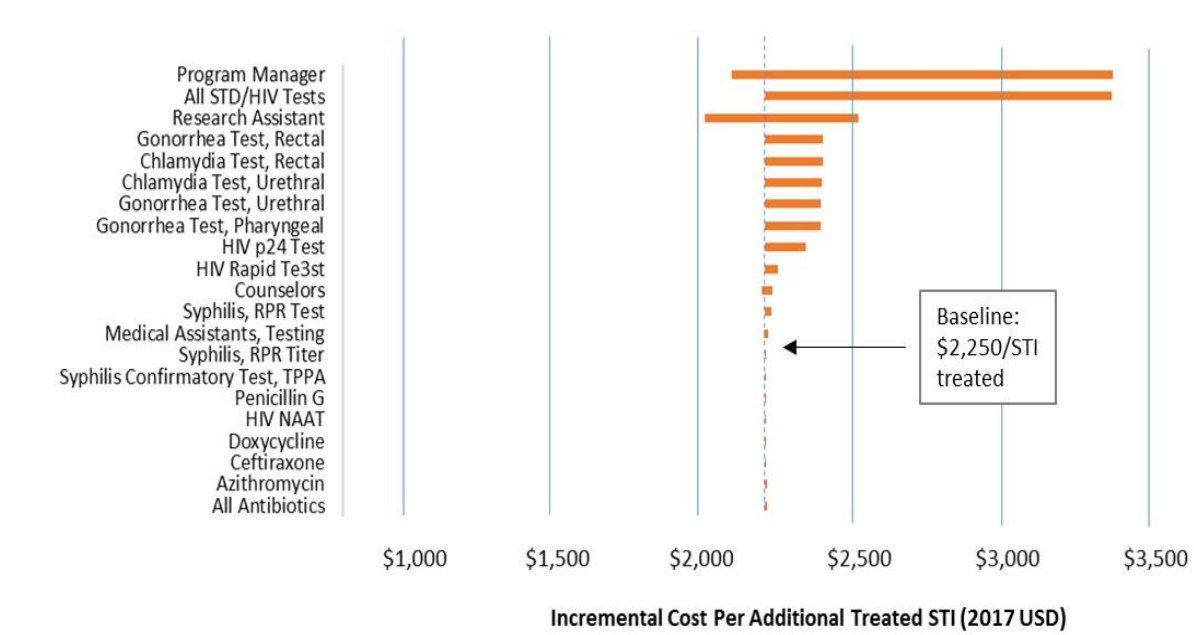
Abbreviations:

CDC = Centers for Disease Control and Prevention

STI = sexually transmitted infection

Figure 4.1. Sensitivity Analyses of Cost-Effectiveness Estimates to Variable Assumptions





Chapter 5. Concluding Remarks

Rates of STIs are high and steadily increasing among MSM.[1] STIs are responsible not only for substantial morbidity and irreversible disease sequalae but evidence suggests STI infection promotes HIV transmission and acquisition.[2-4,29] Indeed, MSM who repeatedly contact STIs may disproportionately contribute to propagation of both STIs and HIV. An understanding of risk factors for repeat STIs may serve to inform focused prevention interventions.

Increased STI testing and treatment is one prevention method that holds promise for reducing HIV transmission and stalling the rise of STIs. However, conventional strategies to encourage uptake of testing have been met with limited success. Accordingly, it is important that innovative testing strategies are developed and their impact evaluated both in terms of clinical effectiveness and cost.

The purpose of this dissertation was three-fold. First, we sought to identify predictors of repeat STIs in a population of MSM. Next, we evaluated the effectiveness of a financial incentive program for STI and HIV testing among high-risk MSM in terms of both testing frequency and STI positivity. Lastly, we assessed the affordability of the program from the perspective of an STI clinic by performing a cost-effectiveness analysis.

Chapter 2 used survival analysis techniques to identify the rate and socio-demographic predictors of repeat CT and/or GC infection in a clinic-based population of men in Los Angeles County. We found that 11.5% of men presented with a repeat infection within one year and 29.4% within four years. In a multivariable Cox regression model, being black and self-identifying as a sexual minority (either homosexual or bisexual) placed men at an increased risk for repeat infection. These findings were largely substantiated by prior studies. However, we did

not find likelihood of repeat infection to be dependent on HIV-status- perhaps owing to the likelihood that HIV-positive men were enrolled in HIV care at the same clinic (which included STI testing as standard-of-care). An understanding of the characteristics of those likely to experience repeat infection is important as providers often do not ask about risk behaviors directly. Further, this knowledge may help develop targeted prevention efforts which serve to reduce infection persistence.

Chapter 3 aimed to evaluate the impact of an MSM-focused financial incentive program for STI and HIV testing on testing frequency, adherence to CDC testing recommendations, and STI positivity. We found that individuals in the intervention group visited the clinic for testing more often than those in the matched-control group. Furthermore, the intervention group was significantly more likely to comply with CDC testing recommendations for high-risk MSM. Finally, positivity of any STI fell significantly over one year of follow-up among intervention group participants. Our results were generally aligned with a body of evidence demonstrating interventions utilizing financial incentives to be effective. However, implementation of such strategies is fairly uncommon. Instead, traditional behavioral intervention strategies, such as education and awareness campaigns, are more typical despite their history of limited success. This lack of uptake of financial incentives strategies may be attributed to doubt surrounding the long-term effectiveness of such strategies, skepticism due to ethnical concerns, and uncertainty of cost. To this end, implementing and evaluating the effectiveness (including both the short-term and sustained impact) as well as quantifying the start-up, maintenance, and downstream costs of financial incentive programs compared to more conventional strategies is warranted. Further, teasing out the incremental impact of additional components such as those that enhance access or build rapport with study subjects is important for future scale-up and implementation.

Chapter 5 examined the cost-effectiveness of a financial incentive program for STI and HIV testing from the economic perspective of an STI clinic. Over a two-year period, the cost per enrolled individual, including implementation costs, STI testing costs, and STI medication treatment costs, were approximately ten times higher in the intervention group than the matched-control group. Labor for the start-up and maintenance of the program and financial incentives were responsible for a majority of the cost difference between the two study groups. Upon examining the cost-effectiveness, we found the incremental cost per additional STI treated to be relatively modest and more cost-effective than roughly half of interventions with published results. Additional ways to reduce average costs may be of interest to clinic managers and public health authorities. For example, incentive programs may benefit from automation such as technology-mediated systems for notifying patients when to test (via text or email) and for determining incentive pay-outs. Finally, a more comprehensive understanding of the more distal costs incurred including those associated with disease sequelae, transmission to sex partners, reduced risk of HIV acquisition, and productivity losses is imperative for estimating the global impact of such programs.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Sexually Transmitted Disease Surveillance 2016. 2017.
2. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhea and chlamydia reinfection is associated with increased risk of HIV seroconversion. *Journal of acquired immune deficiency syndromes (1999).* Apr 1 2010;53(4):537-543.
3. Jin F, Prestage GP, Imrie J, et al. Anal sexually transmitted infections and risk of HIV infection in homosexual men. *Journal of acquired immune deficiency syndromes (1999).* Jan 2010;53(1):144-149.
4. Vaughan AS, Kelley CF, Luisi N, del Rio C, Sullivan PS, Rosenberg ES. An application of propensity score weighting to quantify the causal effect of rectal sexually transmitted infections on incident HIV among men who have sex with men. *BMC medical research methodology.* 2015;15:25.
5. Cohen SE, Chew Ng RA, Katz KA, et al. Repeat syphilis among men who have sex with men in California, 2002-2006: implications for syphilis elimination efforts. *American journal of public health.* Jan 2012;102(1):e1-8.
6. Katz KA, Lee MA, Gray T, Marcus JL, Pierce EF. Repeat syphilis among men who have sex with men--San Diego County, 2004-2009. *Sexually transmitted diseases.* Apr 2011;38(4):349-352.
7. Phipps W, Kent CK, Kohn R, Klausner JD. Risk factors for repeat syphilis in men who have sex with men, San Francisco. *Sexually transmitted diseases.* Jun 2009;36(6):331-335.

8. Gray RT, Hoare A, Prestage GP, Donovan B, Kaldor JM, Wilson DP. Frequent testing of highly sexually active gay men is required to control syphilis. *Sexually transmitted diseases.* May 2010;37(5):298-305.

9. Tuite AR, Fisman DN, Mishra S. Screen more or screen more often? Using mathematical models to inform syphilis control strategies. *BMC public health.* 2013;13:606.

10. Workowski KB, G. *Sexually Transmitted Diseases Treatment Guidelines, 2015.* Centers for Disease Control and Prevention; June 5, 2015 2015.

11. Berry SA, Ghanem KG, Page KR, Thio CL, Moore RD, Gebo KA. Gonorrhoea and chlamydia testing rates of HIV-infected men: low despite guidelines. *Sexually transmitted infections.* Nov 2010;86(6):481-484.

12. Hoover KW, Butler M, Workowski K, et al. STD screening of HIV-infected MSM in HIV clinics. *Sexually transmitted diseases.* Dec 2010;37(12):771-776.

13. Mimiaga MJ, Reisner SL, Bland S, et al. Health system and personal barriers resulting in decreased utilization of HIV and STD testing services among at-risk black men who have sex with men in Massachusetts. *AIDS patient care and STDs.* Oct 2009;23(10):825-835.

14. Tai E, Sanchez T, Lansky A, Mahle K, Heffelfinger J, Workowski K. Self-reported syphilis and gonorrhoea testing among men who have sex with men: national HIV behavioural surveillance system, 2003-5. *Sexually transmitted infections.* Nov 2008;84(6):478-482.

15. Loewenstein G, Brennan T, Volpp KG. Asymmetric paternalism to improve health behaviors. *Jama.* Nov 28 2007;298(20):2415-2417.

16. California Department of Public Health SCB. *Sexually Transmitted Diseases in California 2013.* January 2015 2015.

17. Cahill K, Hartmann-Boyce J, Perera R. Incentives for smoking cessation. *The Cochrane database of systematic reviews.* 2015;5:Cd004307.

18. Budney AJ, Higgins ST, Radonovich KJ, Novy PL. Adding voucher-based incentives to coping skills and motivational enhancement improves outcomes during treatment for marijuana dependence. *Journal of consulting and clinical psychology.* Dec 2000;68(6):1051-1061.

19. Lussier JP, Heil SH, Mongeon JA, Badger GJ, Higgins ST. A meta-analysis of voucher-based reinforcement therapy for substance use disorders. *Addiction (Abingdon, England).* Feb 2006;101(2):192-203.

20. Pilling S, Strang J, Gerada C. Psychosocial interventions and opioid detoxification for drug misuse: summary of NICE guidance. *BMJ (Clinical research ed.).* Jul 28 2007;335(7612):203-205.

21. Malotte CK, Hollingshead JR, Rhodes F. Monetary versus nonmonetary incentives for TB skin test reading among drug users. *American journal of preventive medicine.* Apr 1999;16(3):182-188.

22. Malotte CK, Ledsky R, Hogben M, et al. Comparison of methods to increase repeat testing in persons treated for gonorrhea and/or chlamydia at public sexually transmitted disease clinics. *Sexually transmitted diseases.* Nov 2004;31(11):637-642.

23. Purnell JQ, Gernes R, Stein R, Sherraden MS, Knoblock-Hahn A. A systematic review of financial incentives for dietary behavior change. *Journal of the Academy of Nutrition and Dietetics.* Jul 2014;114(7):1023-1035.

24. Lee R, Cui RR, Muessig KE, Thirumurthy H, Tucker JD. Incentivizing HIV/STI testing: a systematic review of the literature. *AIDS and behavior.* May 2014;18(5):905-912.

25. de Walque D, Dow WH, Nathan R, et al. Incentivising safe sex: a randomised trial of conditional cash transfers for HIV and sexually transmitted infection prevention in rural Tanzania. *BMJ open.* 2012;2:e000747.

26. Galarraga O, Sosa-Rubi SG, Infante C, Gertler PJ, Bertozzi SM. Willingness-to-accept reductions in HIV risks: conditional economic incentives in Mexico. *The European journal of health economics : HEPAC : health economics in prevention and care.* Jan 2014;15(1):41-55.

27. Bolan RK, Beymer MR, Weiss RE, Flynn RP, Leibowitz AA, Klausner JD. Doxycycline prophylaxis to reduce incident syphilis among HIV-infected men who have sex with men who continue to engage in high-risk sex: a randomized, controlled pilot study. *Sexually transmitted diseases.* Feb 2015;42(2):98-103.

28. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sexually transmitted infections.* Feb 1999;75(1):3-17.

29. Solomon MM, Mayer KH, Glidden DV, et al. Syphilis predicts HIV incidence among men and transgender women who have sex with men in a preexposure prophylaxis trial. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Oct 2014;59(7):1020-1026.

30. Pathela P, Braunstein SL, Blank S, Schillinger JA. HIV incidence among men with and those without sexually transmitted rectal infections: estimates from matching against an HIV case registry. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Oct 2013;57(8):1203-1209.

31. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. *Lancet (London, England).* 1998;351 Suppl 3:5-7.

32. Allison P. *Survival Analysis Using SAS A Practical Guide.* 2 ed. Cary, NC: SAS Institute Inc.; 2010.

33. Niccolai LM, Livingston KA, Laufer AS, Pettigrew MM. Behavioural sources of repeat Chlamydia trachomatis infections: importance of different sex partners. *Sexually transmitted infections.* Apr 2011;87(3):248-253.

34. Hughes G, Nichols T, Peters L, Bell G, Leong G, Kinghorn G. Repeat infection with gonorrhoea in Sheffield, UK: predictable and preventable? *Sexually transmitted infections.* Feb 2013;89(1):38-44.

35. Brewer TH, Peterman TA, Newman DR, Schmitt K. Reinfections during the Florida syphilis epidemic, 2000-2008. *Sexually transmitted diseases.* Jan 2011;38(1):12-17.

36. Ogilvie GS, Taylor DL, Moniruzzaman A, et al. A population-based study of infectious syphilis rediagnosis in British Columbia, 1995-2005. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Jun 1 2009;48(11):1554-1558.

37. Millett GA, Flores SA, Peterson JL, Bakeman R. Explaining disparities in HIV infection among black and white men who have sex with men: a meta-analysis of HIV risk behaviors. *AIDS (London, England).* Oct 1 2007;21(15):2083-2091.

38. Bohl DD, Raymond HF, Arnold M, McFarland W. Concurrent sexual partnerships and racial disparities in HIV infection among men who have sex with men. *Sexually transmitted infections.* Sep 2009;85(5):367-369.

39. Berry M, Raymond HF, McFarland W. Same race and older partner selection may explain higher HIV prevalence among black men who have sex with men. *AIDS (London, England).* Nov 12 2007;21(17):2349-2350.

40. Aral SO, Lipshutz J, Blanchard J. Drivers of STD/HIV epidemiology and the timing and targets of STD/HIV prevention. *Sexually transmitted infections.* Aug 2007;83 Suppl 1:i1-4.

41. Ford JL, Browning CR. Neighborhood social disorganization and the acquisition of trichomoniasis among young adults in the United States. *American journal of public health.* Sep 2011;101(9):1696-1703.

42. Ford JL, Browning CR. Neighborhoods and infectious disease risk: acquisition of chlamydia during the transition to young adulthood. *Journal of urban health : bulletin of the New York Academy of Medicine.* Feb 2014;91(1):136-150.

43. Harling G, Subramanian S, Barnighausen T, Kawachi I. Socioeconomic disparities in sexually transmitted infections among young adults in the United States: examining the interaction between income and race/ethnicity. *Sexually transmitted diseases.* Jul 2013;40(7):575-581.

44. Latkin CA, Curry AD, Hua W, Davey MA. Direct and indirect associations of neighborhood disorder with drug use and high-risk sexual partners. *American journal of preventive medicine.* Jun 2007;32(6 Suppl):S234-241.

45. Health LCDoP. *Sexually Transmitted Disease Morbidity Report 2013* Los Angeles, CA: Division of HIV and STD Programs, LA County Department of Public Health; November 2014 2014.

46. Centers for Disease Control and Prevention (CDC). *Sexually Transmitted Disease Surveillance 2012.* Centers for Disease Control and Prevention, U.S. Department of Health and Human Services;2014.

47. Wilson DP, Hoare A, Regan DG, Law MG. Importance of promoting HIV testing for preventing secondary transmissions: modelling the Australian HIV epidemic among men who have sex with men. *Sexual health.* Mar 2009;6(1):19-33.

48. Malotte CK, Rhodes F, Mais KE. Tuberculosis screening and compliance with return for skin test reading among active drug users. *American journal of public health.* May 1998;88(5):792-796.

49. Sigmon SC, Higgins ST. Voucher-based contingent reinforcement of marijuana abstinence among individuals with serious mental illness. *Journal of substance abuse treatment.* Jun 2006;30(4):291-295.

50. Buchacz K, Patel P, Taylor M, et al. Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. *AIDS (London, England).* Oct 21 2004;18(15):2075-2079.

51. Centers for Disease Control and Prevention (CDC). Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. 2015; https://www.cdc.gov/std/tg2015/screening-recommendations.htm. Accessed August 5, 2017.

52. Workowski KB, S. *Sexually Transmitted Diseases Treatment Guidelines, 2006.* Centers for Disease Control and Prevention; August 4, 2006 2006.

53. Workowski KB, S. *Sexually Transmitted Diseases Treatment Guidelines, 2010.* Centers for Disease Control and Prevention; December 17, 2010 2010.

54. Centers for Disease Control and Prevention (CDC). 2015 Sexually Transmitted Diseases Treatment Guidelines - Syphilis. 2015; https://www.cdc.gov/std/tg2015/syphilis.htm. Accessed August 8, 2017, 2017.

55. Chacko MR, Cromer BA, Phillips SA, Glasser D. Failure of a lottery incentive to increase compliance with return visit for test-of-cure culture for Neisseria gonorrhoeae. *Sexually transmitted diseases.* Apr-Jun 1987;14(2):75-78.

56. Currie MJ, Schmidt M, Davis BK, et al. 'Show me the money': financial incentives increase chlamydia screening rates among tertiary students: a pilot study. *Sexual health.* Mar 2010;7(1):60-65.

57. Geringer WM, Hinton M. Three models to promote syphilis screening and treatment in a high risk population. *Journal of community health.* Jun 1993;18(3):137-151.

58. Haukoos JS, Witt MD, Coil CJ, Lewis RJ. The effect of financial incentives on adherence with outpatient human immunodeficiency virus testing referrals from the emergency department. *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine.* Jul 2005;12(7):617-621.

59. Rigsby MO, Rosen MI, Beauvais JE, et al. Cue-dose training with monetary reinforcement: pilot study of an antiretroviral adherence intervention. *Journal of general internal medicine.* Dec 2000;15(12):841-847.

60. Rosen MI, Dieckhaus K, McMahon TJ, et al. Improved adherence with contingency management. *AIDS patient care and STDs.* Jan 2007;21(1):30-40.

61. Sorensen JL, Haug NA, Delucchi KL, et al. Voucher reinforcement improves medication adherence in HIV-positive methadone patients: a randomized trial. *Drug and alcohol dependence.* Apr 17 2007;88(1):54-63.

62. Tversky A KD. Loss Aversion in Riskless Choice: A Reference-Dependent Model. *The Quarterly Journal of Economics.* 1991;106(4):1039-1061.

63. Health LACDoP. *2014 Annual HIV/STD Surveillance Report.* 2014.

64. Centers for Disease Control and Prevention (CDC). *Sexually Transmitted Disease Surveillance 2016.* Atlanta, GA2016.

65. Centers for Disease Control and Prevention (CDC). *Sexually Transmitted Disease Surveillance 2015.* Atlanta, GA2015.

66. Centers for Disease Control and Prevention (CDC). *Sexually Transmitted Disease Surveillance 2010.* Atlanta, GA2010.

67. Landovitz RJ, Gildner JL, Leibowitz AA. Sexually Transmitted Infection Testing of HIV-Positive Medicare and Medicaid Enrollees Falls Short of Guidelines. *Sexually transmitted diseases.* Jan 2018;45(1):8-13.

68. Husereau D, Drummond M, Petrou S, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *International journal of technology assessment in health care.* Apr 2013;29(2):117-122.

69. WHO. *Making choices in health: WHO guide to cost-effectiveness analysis.* 2003.

70. Statistics BoL. Consumer Price Index, CPI Databases. 2017; https://www.bls.gov/cpi/data.htm. Accessed September 7, 2017.

71. Statistics BoL. May 2013 Occupational Profiles. 2014; https://www.bls.gov/oes/2013/may/oes_stru.htm.

72. Centers for Medicare and Medicaid Services. Clinical Laboratory Fee Schedule Files. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Clinical-Laboratory-Fee-Schedule-Files.html, 2018.

73. MeKesson. McKesson Connect.

https://connect.mckesson.com/portal/site/smo/template.LOGIN/.