

Seroadaptive behaviors among Seattle men who have sex with men (MSM):
a shift in operationalization, trends, and association with HIV/STI

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Abstract

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Many men who have sex with men (MSM) engage in seroadaptive behaviors – i.e., chose their sex partners, selectively use condoms, or adopt a sexual role based on their partner’s HIV sero-status. Some of these behaviors may protect against HIV, but the complexity in measuring seroadaptive behaviors has made it difficult to develop messages about the practice.

In a retrospective records review of MSM attending the Public Health – Seattle & King County (PHSKC) STD clinic and Gay City Health Project (GCHP), we examined trends in sexual behaviors and HIV test positivity between 2002 and 2013. We used log binomial regression to assess the risk of HIV/STI test positivity for serosorting (condomless anal intercourse [CAI] only with HIV-concordant partners) relative to non-concordant CAI (CAI with partners of discordant or

unknown status) and no CAI. For an ongoing cross-sectional seroadaptive behaviors study, we developed a computer-based method to automatically recruit and enroll MSM PHSKC clinic patients into the study. We describe the proportion of men who enroll in the study and how these men differ from those who decline to enroll, to gauge the representativeness of our study sample. Using data from the population of enrolled men, we compared the prevalence and agreement (kappa statistic) of four seroadaptive behaviors using two definitions: a behavioral definition (men are classified as engaging in seroadaptive behaviors based on their reported sexual history) versus a purposely-adopted definition (men are specifically asked if they purposely adopted certain behaviors based on their partner's HIV status, to reduce the risk of HIV acquisition or transmission).

We found that the proportion of men who report serosorting in the prior year increased substantially (by 15%) between 2002 and 2013, and in 2013 nearly one-third to one-half of MSM reported the behavior. Among HIV-negative MSM, these increases were concurrent with significant declines in the proportion of MSM who reported NCCAI, indicating a shift toward generally safer behaviors. Serosorting was associated with a lower risk of HIV than NCCAI (adjusted relative risk [aRR]=0.53; 95% confidence interval [CI]=0.45-0.62) but a higher risk than no CAI (aRR=1.98; 95% CI=1.61-2.44). The absolute risk of testing newly positive for HIV declined for all men (from 3.5% to 1.4%; $P=0.001$), regardless of reported behavior. In our cross-sectional seroadaptive behaviors study, we enrolled men at 2,661 (54%) of 4,994 eligible clinic visits during an 18-month period in 2013-2014, including 1,748 unique MSM. Enrolled men were broadly representative of all MSM in the clinic but compared to non-enrolled men,

they reported a higher number of male sex partners (11 vs. 8; $P < 0.001$) and were more likely to report methamphetamine use in the prior year (15% vs 8%; $P < 0.001$). However, the HIV test positivity of enrolled and non-enrolled men was similar (1.9% vs. 2.0%; $P = 0.8$). Among 3,410 visits by men enrolled in the study 2013-2015, pure serosorting (choosing partners based on HIV status) was the most commonly reported behavior (31%-47%), regardless of the definition used. We found that the agreement between the two definitions for the four behaviors was only slight to moderate (kappa range: 0.11-0.43) and the concordance varied by behavior – between 15% and 70% who were classified as engaging in seroadaptive behaviors per the behavioral definition also reported purposely-adopting the behaviors based on their partners' HIV status.

Results from this dissertation suggest that seroadaptive behaviors are common and are increasing. We confirmed prior studies that found that these behaviors represent an intermediate level of HIV risk – they are associated with a lower risk of HIV than NCCAI but a higher risk than no CAI. Thus, these behaviors may be an effective HIV prevention strategy for some men. However, we also noted that using a behavioral definition to measure seroadaptive behaviors likely includes men who did not purposely adopt these behaviors; therefore, additional work is needed to further describe how use of a purposely-adopted definition may effect these risk estimates in order to appropriately counsel men about the risks and/or benefits of these behaviors. Finally, our novel approach to recruitment holds promise for future studies to efficiently recruit or screen a somewhat young and relatively high-risk population of MSM into HIV prevention research.

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CHAPTER 1. Introduction

HIV epidemic among men who have sex with men

Since the beginning of the HIV epidemic in the United States (US), men who have sex with men (MSM) have been, and continue to be, the most heavily impacted risk group. In 2013, nearly 32,000 MSM were diagnosed with HIV and approximately 660,000 MSM have been diagnosed with AIDS since the beginning of the epidemic [1]. MSM represent 67% of all new HIV diagnoses in the US (84% of new HIV diagnoses where risk information is available) [1], despite accounting for only an estimated 3-7% of the US population [2]. Since 2000, MSM are the only risk group for whom HIV incidence has not declined [3], and the HIV diagnosis rate has even increased in certain sub-groups of MSM (e.g., young black MSM)[4].

The HIV epidemic in King County, Washington parallels that of the US. Between 2011 and 2013, 87% of all new HIV diagnoses in King County (where risk information is available) were among MSM; there were 181 MSM newly HIV diagnosed in 2013 [5]. An estimated 13-18% of King County MSM have diagnosed HIV infection, compared to <1% of non-MSM, non-injection drug-using King County residents. However, HIV prevention efforts in King County have demonstrated success. There were nearly 6,000 publicly-funded HIV tests performed among MSM in 2013, which represents a 31% increase since 2007. During the same 7-year period (2007-2013), the HIV test positivity among MSM declined from 2.8% to 2.0% [5].

HIV prevention research

In the last decade, behavioral HIV prevention interventions have taken a back seat to biomedical prevention strategies, since the latter have demonstrated an ability to reduce HIV infection [6-9] while the former have shown an ability to reduce risk behavior among MSM but not necessarily reduce new HIV infections [10-14]. However, behavioral approaches to HIV prevention are essential to supplement or enhance biomedical strategies, and are a key component of the National HIV/AIDS Strategy for the United States [15]. From a methodologic perspective, recruiting large numbers of MSM into HIV prevention research is critical for studies with an HIV outcome, but behavioral interventions in particular have suffered from small sample sizes, which have led to a call for better practices to recruit MSM into behavioral HIV prevention research [16].

Seroadaptive behaviors

For at least the last 25 years, many MSM have adopted their sexual behaviors based on their partners' perceived HIV status to reduce the risk of HIV acquisition or transmission [17-20]. These "seroadaptive behaviors" refer to behaviors in which an individual chooses his partners, selectively uses condoms or adopts a sexual role based on the perceived HIV status of his partner. Although seroadaptive behaviors may be an HIV prevention strategy for some men, their effectiveness depends on accurate HIV status disclosure between an individual and his partner, which, in turn, depends on how recently an individual has been tested for HIV. Because of these limitations, seroadaptive behaviors are not recommended as HIV prevention strategies

by the Centers for Disease Control and Prevention (CDC) [21]. Although the commonness of these behaviors in MSM communities merits a better understanding of their pervasiveness and biological impact, the absence of a standard definition and method to measure seroadaptive behaviors have made it challenging to create evidence-based guidelines to either recommended or discourage the practice.

This dissertation uses data from MSM patients at the Public Health – Seattle and King County (PHSKC) STD clinic and Gay City Health Project to evaluate the risks, trends, and operationalization (i.e., defining the measurement) of seroadaptive behaviors. We begin by presenting trends in the prevalence of seroadaptive behaviors over time and their association with testing newly positive for HIV and bacterial sexually transmitted infections (STI) (Chapter 2). Next, we describe a computer-based approach to recruiting MSM into a cross-sectional behavioral risk study to determine if this novel approach is a feasible method to effeciently recruit large numbers of MSM into behavior research. We also characterize the differences between men who enroll and those who do not to determine if we are able to recruit a representative sample of MSM using this new recruitment method (Chapter 3). Finally, we present results from a cross-sectional study in which we compare the prevalence and agreement of two definitions of seroadaptive behaviors (Chapter 4). We conclude by summarizing the findings of these studies and discussing their implications (Chapter 5).

CHAPTER 2: Trends in serosorting and the association with HIV/STI risk over time among men who have sex with men (MSM)

ABSTRACT

Background: Serosorting among men who have sex with men (MSM) is common but recent data to describe trends in serosorting are limited. How serosorting affects population trends in HIV and other sexually transmitted infection (STI) risk depends on serosorting's association with HIV and STI risk and whether serosorting is replacing high-risk or low-risk behaviors.

Methods: We collected data as part of routine care from MSM attending an STD clinic (2002-2013) and a community-based HIV/STD testing center (2004-2013) in Seattle, Washington. MSM were asked about condom use with HIV-positive, HIV-negative and unknown-status partners in the prior 12 months. We classified behaviors into four mutually exclusive categories: no anal intercourse (AI); consistent condom use (always used condoms for AI); serosorting (condomless anal intercourse [CAI] only with HIV-concordant partners); and non-concordant CAI (CAI with HIV-discordant/unknown-status partners; NCCAI).

Results: Behavioral data were complete for 49,912 clinic visits. Serosorting increased significantly among both HIV-positive and HIV-negative men over the study period. Among HIV-negative men, the increase in serosorting was concurrent with a decrease in NCCAI, and among HIV-positive men, the increase in serosorting was concurrent with a decrease in consistent condom use and a decrease in abstinence from anal sex. Adjusting for time since last negative HIV test, the risk of testing HIV positive during the study period decreased among MSM who

reported NCCAI (7.1% to 2.8%; P=0.02), serosorting (2.4% to 1.3%; P=0.17) and no CAI (1.5% to 0.7%; P=0.01). Serosorting was associated with a 47% lower risk of testing HIV positive compared to NCCAI (adjusted relative risk [aRR]=0.53; 95% CI=0.45-0.62).

Conclusion: Serosorting increased and NCCAI decreased among Seattle MSM between 2002 and 2013, a period during which HIV test positivity among MSM also declined.

INTRODUCTION

Since at least the early 1990s, many men who have sex with men (MSM) have modified their sexual practices based on their partners' perceived HIV status [17-19]. Serosorting refers to the practice of choosing sex partners or selectively using condoms based on a partner's perceived HIV status, while strategic or seropositioning refer to selectively practicing insertive or receptive anal sex based on a partner's HIV status. These behaviors and others, collectively referred to as seroadaptive behaviors, are common among MSM [22-27]. Data from the early 2000s suggested that the proportion of MSM who reported serosorting was on the rise [28-30] and recent data from San Francisco MSM through 2011 [27] suggest that these increases have continued.

The effect of seroadaptive behaviors on HIV and sexually transmitted infection (STI) risk is somewhat controversial. Mathematical models suggest that serosorting can either increase or decrease a person's risk of acquiring HIV depending on the accuracy of HIV status disclosure, which largely depends on the population's HIV testing frequency [31-33]. Empiric evidence indicates that seroadaptive behaviors represent an intermediate level of HIV risk – they are associated with a lower risk of HIV acquisition than non-concordant condomless anal intercourse (NCCA) but a higher risk than consistent condom use [23, 28, 34-36]. Serosorting may also increase STI risk, but the magnitude is dependent on one's HIV status and the type and anatomic site of STI [30, 37, 38]. Because of this, an increase in serosorting has been hypothesized to explain the concurrent increase in bacterial STI rates and in some places, declines in HIV incidence [37]. However, whether serosorting increases or decreases

population-level HIV/STI rates depends, in part, on how the frequency of serosorting changes and what behaviors it replaces.

We have collected detailed sexual behavior data from MSM patients attending the Public Health – Seattle and King County (PHSKC) STD clinic since 2001. We previously reported that serosorting among HIV-negative and HIV-positive MSM increased between 2001 and 2007, and that NCCAI decreased during that same time period [28]. The extent to which these trends have continued in the subsequent six years – a period during which HIV testing frequency has increased [39] and antiretroviral therapy (ART) use has risen dramatically – is unclear. Further, important questions remain about the effect of serosorting on HIV and bacterial STI risk, and how these risks may have changed in the last decade in light of expanding HIV prevention efforts. The goals of this study were to: (1) examine trends in serosorting and other seroadaptive behaviors among Seattle MSM from 2001-2013; (2) evaluate the association between serosorting and HIV and bacterial STIs; and (3) determine if the risk of serosorting has changed over time.

METHODS

Study design and population

This is a secondary data analysis of records from two sources: (1) MSM who attended the PHSKC STD clinic from October 1, 2001 to December 31, 2013; and (2) MSM who attended Gay City Health Project (GCHP), a community-based organization with a publicly funded HIV/STI testing program, from February 2, 2004 to December 31, 2013. The start dates for the study reflect the dates when the collection of detailed sexual behavior information was initiated at

the two sites. We defined MSM to be men who reported a male sex partner in the prior 12 months and restricted analyses to men who had complete sexual behavior data.

Data collection and measures

All data were collected as part of routine clinical care. At the STD clinic until October 2010, clinicians conducted face-to-face interviews (FTFI) with patients to collect information on sexual behaviors, drug use, and HIV testing history. These data were recorded on standardized paper forms and subsequently entered into the clinic's electronic medical record database. In October 2010, the STD clinic initiated a computer-assisted self-interview (CASI) system to collect these data from English-speaking patients. FTFI continued to be conducted during this time for patients who did not speak English or were unable or unwilling to use a computer, when the computer system was not functioning, and in some instances to improve patient flow through the clinic. At GCHP, clients were asked to complete standardized paper questionnaires that solicited information on demographics, sexual behavior, drug use, and HIV testing history. FTFI were conducted for partner-level condom data and for any patients who did not speak English. Data were subsequently entered in GCHP's electronic databases.

Sexual behavior information collected at the STD clinic and GCHP were identical. Men were asked about the gender of their sex partners, if they had insertive or receptive anal intercourse with partners who were HIV-positive, HIV-negative, or of unknown status, and how often they used condoms with partners (always/usually/sometimes/never), stratified by sexual role (insertive or receptive) and partner HIV status. All sexual behavior questions were asked about partners in aggregate and referenced the prior 12 months. We used these data to

construct the following mutually exclusive sexual behavior categories: (1) No anal sex: men who did not report having anal sex with their male partners; (2) consistent condom use: men who reported having anal sex but always used condoms with all partners; (3) serosorting: men who reported having condomless anal intercourse (CAI) with HIV concordant partners and either did not have HIV-discordant/unknown-status anal sex partners or reported always using condoms with discordant/unknown-status partners; and (4) NCCAI: men who reported inconsistent or no condom use for anal sex with HIV-discordant/unknown-status partners. Because NCCAI includes several behaviors that confer different levels of HIV risk [23, 40], we further stratified HIV-negative men who reported NCCAI into the following categories: (1) insertive NCCAI (NCCIAI): men who had condomless insertive anal sex with HIV-positive/unknown-status partners and did not have any receptive anal sex with these partners; (2) condom seropositioning: men who always used condoms for receptive anal sex with HIV-positive/unknown-status partners and who used condoms inconsistently or never for insertive anal sex with these partners; (3) receptive NCCAI (NCCRAI): men who reported inconsistent or no condom use for receptive anal sex with HIV-positive/unknown-status partners.

HIV and STI Testing

HIV testing was recommended to all STD clinic and GHCP patients who had not previously tested HIV positive. Rapid HIV antibody tests were offered to MSM at high risk for HIV. We used OraQuick (OraSure Technologies Inc., Bethlehem, PA) until 2013 when both sites switched to INSTI (bioLytical Laboratories, British Columbia). Patients who agreed to a blood draw were tested using a second-generation HIV EIA (Vironostika HIV-1 Microelisa System; bioMerieux,

Durham, NC or rLAV Genetic System; Bio-Rad Laboratories, Hercules, CA) until 2010, at which time we replaced this assay with a third-generation EIA (Genetic Systems HIV1/2 Plus O EIA, Biorad Laboratories, Redmond, WA). We performed pooled HIV RNA testing for all MSM who agreed to a blood draw beginning in 2003 at the STD clinic and 2006 at GCHP [41-44].

Urethral specimens (swab or urine) for gonorrhea and chlamydia culture or nucleic acid amplification testing (NAAT) were obtained from STD clinic patients with signs/symptoms of urethritis or who reported exposure to a partner with gonorrhea or chlamydia. At GCHP, urine testing for urethral gonorrhea and chlamydia began in March 2011 and was performed via NAAT. We obtained rectal specimens from MSM who reported receptive anal sex in the prior year. At the STD clinic, rectal specimens were tested for gonorrhea and chlamydia using culture until September 2010 and NAAT thereafter. GCHP used culture to test rectal specimens from November 2006 to December 2007 and began NAAT testing in March 2011. There were no rectal specimens tested at GCHP in 2008-2010. Our laboratory performed gonorrhea cultures on modified Thayer-Martin media, chlamydial culture on McCoy cell culture, and NAAT testing using APTIMA Combo 2 (GenProbe Diagnostics, San Diego, CA). All MSM who agreed to have a blood sample obtained were tested for syphilis using the rapid plasma regain (RPR) test. A single, experienced disease investigational specialist (DIS) reviews all cases of syphilis in King County and assigns a stage based on laboratory and clinical findings. This information became available in our electronic databases beginning in 2006. For MSM tested for syphilis before that time, we defined early syphilis (primary, secondary, or early latent) as: (1) a clinical diagnosis of early syphilis with a positive RPR test and positive *Treponema pallidum* particle agglutination assay (TPPA), or (2) no clinical diagnosis and no history of syphilis with an RPR titer $\geq 1:32$ and a

positive TPPA, or (3) no clinical diagnosis and no history of syphilis with a VDRL \geq 1:8 and a positive TPPA.

Statistical analysis

We examined differences in demographic, behavioral and clinical characteristics of patients attending the two sites using chi-square tests for categorical variables and t-tests for continuous variables. To examine secular trends in sexual behavior, we restricted the analysis to each man's first visit to the STD clinic or GCHP in a calendar year and used linear regression to assess the statistical significance of linear trends over time. Because we had STD clinic data for only three months in 2001, we combined 2001 with 2002 data. Due to the small number of HIV-positive men attending GCHP (the site is primarily an HIV testing venue), we only used data from the STD clinic to examine behavioral trends among HIV-positive men. We used multivariate log binomial regression models to estimate the relative risk (RR) of the association between sexual behaviors and HIV or bacterial STIs (urethral gonorrhea or chlamydia, rectal gonorrhea or chlamydia, and early syphilis). The unit of analysis for regression models was a clinic visit; we clustered by participant and used robust variances in the regression models to account for multiple visits by the same individual. For the multivariate models we combined two sexual behavior categories, "consistent condom use" and "no anal sex" into one category ("no CAI"). Models included the following pre-specified confounders of the association between serosorting and HIV/bacterial STIs: age, race/ethnicity, methamphetamine use (ever/never), clinic, number of sex partners in the past 12 months, calendar year, and time since last HIV test (included in the HIV outcome model only; the variable included "missing" as a category due to a

high proportion of missing values). To examine if calendar year modified the association between sexual behavior and HIV or bacterial STIs (i.e., if the relative risk of serosorting compared to NCCAI varied by year), we used a likelihood ratio test to examine the statistical significance of a year*sexual behavior interaction term. All regression analyses were limited to men who were tested for HIV or bacterial STIs at the clinic visit. Two-sided statistical tests were performed at a significance level (α) of 0.05. This study was reviewed and approved by the University of Washington Institutional Review Board.

RESULTS

During the study period there were 38,192 new problem visits made by 16,718 MSM at the STD clinic, and 18,375 visits made by 10,072 MSM at GHCP. Eighty-nine percent (N=34,254) of STD clinic visits and 85% of GHCP visits (N=15,658) had complete behavioral data and were included in this analysis. Men attending the STD clinic were older, more likely to have ever used methamphetamine and more likely to report having tested for HIV in the prior 12 months compared to men attending GHCP (Table 1.1). The majority (99%) of GHCP patients were HIV-negative compared to 87% at the STD clinic. Men at the STD clinic more often reported NCCAI (29%) than men at GHCP (22%) but were also more likely to report not having anal sex in the prior 12 months (11% vs. 1%, respectively). The proportion of men testing newly positive for HIV or bacterial STIs was significantly higher at the STD clinic compared to GHCP.

Trends in serosorting over time

Figure 1.1 presents trends in sexual behavior among HIV-negative MSM's first visit to either site in a given year (N=35,547). At the STD clinic, the proportion of visits where sexual behavior data were collected via CASI was 16%, 77%, 52%, and 82% for the years 2010-2013, respectively. The proportion of visits where HIV-negative MSM reported serosorting increased significantly over the study period at GCHP ($P<0.001$) and at the STD clinic among men who completed a FTFI in 2002-2010 ($P=0.001$) or the CASI ($P=0.008$). NCCAI declined at GCHP ($P<0.001$), at the STD clinic in 2002-2010 ($P=0.004$) and after 2010 among men completing a CASI ($P=0.11$). The proportion reporting no anal sex declined somewhat at the STD clinic (FTFI: $P=0.001$; CASI: $P=0.09$) but consistent condom use remained relatively stable (FTFI: $P=0.58$; CASI: $P=0.64$). At GCHP, there were no significant linear decreases in the proportion reporting consistent condom use ($P=0.25$) or no anal sex ($P=0.24$).

Among HIV-positive MSM at the STD clinic (N=3,460 visits; Figure 1.2), serosorting increased among men who completed a FTFI ($P=0.008$) or the CASI ($P=0.35$) while consistent condom use (FTFI: $P=0.001$; CASI: $P=0.68$) and no anal sex (FTFI: $P=0.20$; CASI: $P=0.61$) declined. NCCAI reported via FTFI significantly decreased in 2002-2008 ($P=0.002$) but did not decline after that time, and did not decline among men who completed the CASI ($P=0.76$). During the study period, the proportion of HIV-positive MSM at the STD clinic who self-reported ART use increased from 50% to 83% ($P<0.001$); this increase was similar for all HIV-positive MSM regardless of reported sexual behavior (data not shown).

Among HIV-negative men at the STD clinic and GCHP who reported NCCAI (N=11,536), 33% reported only NCCIAI, 8% reported condom seropositioning and 59% NCCRAI. In relation to

the entire population of HIV-negative men (N=44,961), the proportion reporting these behaviors was 8%, 2%, and 15%, respectively. At visits (first in calendar year) where HIV-negative MSM reported NCCAI from 2002-2013, NCCIAI increased significantly (26% to 34%; P=0.001) while NCCRAI decreased significantly (67% to 60%; P=0.02). The proportion reporting condom seropositioning was stable (7% to 7%; P=0.15). Using the entire population of HIV-negative MSM as a denominator, the comparable proportions were (6% to 7%, 17% to 13%, and 2% to 2%, respectively).

Association between sexual behavior and HIV/STIs

Men tested newly positive for HIV at 823 (2.1%) of 38,845 clinic visits (Table 1.2). Men who reported serosorting in the prior 12 months had a 47% lower risk of testing newly positive for HIV relative to men reporting NCCAI (aRR=0.53; 95% CI=0.45-0.64), but a 2-fold higher risk of testing positive for HIV compared to men who did not have CAI (aRR=1.98; 95% CI=1.61-2.44). Compared to men who reported NCCAI, HIV-negative men who reported serosorting had a 24% lower risk of early syphilis (aRR=0.76; 95% CI=0.62-0.92) but a similar risk of urethral and rectal gonorrhea/chlamydia. Among HIV-positive men, syphilis risk was similar for HIV-positive serosorters compared to those who reported NCCAI (aRR=1.02; 95% CI=0.81-1.30). Serosorting was associated with a significantly higher risk of each bacterial STI relative to no CAI for both HIV-negative and HIV-positive men.

Change in the risk of serosorting over time

From 2002-2013, the risk of testing newly positive for HIV declined overall from 3.5% to 1.4%. Adjusting for time since last HIV test, we observed declines in the proportion of men testing newly positive for HIV among men who reported NCCAI ($P=0.02$), serosorting ($P=0.14$) and no CAI ($P=0.01$) (Figure 1.3). These P-values did not appreciably change without adjustment for time since last HIV test (data not shown). The association (aRR) between serosorting and HIV (relative to NCCAI) for each year of the study period ranged from a low of 0.33 (95% CI: 0.13, 0.85) in 2003 to a high of 0.89 (95% CI: 0.49, 1.61) in 2005; there was no statistical evidence for a change in the aRR over time (P-value for year*sexual behavior interaction = 0.48). There was also no statistical evidence for a change in the association between serosorting and bacterial STI risk over time for HIV-negative men or HIV-positive men (data not shown).

DISCUSSION

In this study of nearly 50,000 clinic visits made by MSM over a 12-year period, the proportion of HIV-negative and HIV-positive men who reported serosorting increased substantially, while the proportion of HIV-negative men who reported NCCAI declined. Moreover, among HIV-negative men who reported NCCAI, there was a shift toward a larger proportion reporting only insertive NCCAI and a decline in receptive NCCAI. Concurrent with this shift in behavior, the absolute risk of HIV acquisition declined for all men regardless of reported sexual behavior. These sentinel surveillance findings suggest that Seattle's MSM population has changed its behavior over the last 12 years to adopt what are generally safer behaviors, and that this change in behavior is parallel with a decline in this population's HIV test positivity.

Our findings extend previously observed trends among STD clinic patients in Seattle [28] and largely agree with findings from previously published studies. The overall proportion of MSM who reported serosorting in this study (35%) is similar to that reported from MSM populations in the US, Europe and Australia [22, 24-26, 37] during the same time period. The steady increase in serosorting that we observed parallels increases in seroadaptive behaviors and decreases in no CAI among San Francisco MSM participating in the National HIV Behavioral Surveillance (NHBS) survey in 2004-2011 [27]. While this suggests that the trends in our study population may extend to other US MSM, the San Francisco study presented seroadaptive behavioral trends in aggregate, so it is unclear how individual seroadaptive behaviors changed in San Francisco during that time. Our findings point to increases in some seroadaptive behaviors (e.g., serosorting) but not others (e.g., condom serosorting), highlighting that uptake of different seroadaptive behaviors is not uniform.

Concurrent with increases in serosorting among HIV-negative MSM, we observed declines in NCCAI and a fairly constant proportion who reported consistent condom use or no anal sex. Taken together, these data suggest that, among HIV-negative MSM, the increase in serosorting likely resulted from a shift in behavior away from NCCAI. Although the change in data collection method at the STD clinic in 2010 and the serial cross-sectional nature of our data limits our ability to draw this conclusion with certainty, there are two explanations of the data that substantiate our interpretations. First, FTFI data through 2010 demonstrate steady increases in serosorting and decreases in NCCAI, which parallels CASI data collected after 2010. Although FTFI data collected after 2010 showed lower levels of serosorting and more NCCAI than data from before that period, these data were collected from a subset of MSM who were

dissimilar from the larger clinic population. Second, data from GCHP, where the method of data collection did not change, show steady trends throughout the study period that are similar in magnitude to the STD clinic.

Behavioral trends among HIV-positive men were somewhat dissimilar to those among HIV-negative MSM. Among HIV-positive MSM, we did not observe the consistently large decline in NCCAI as was observed with HIV-negative MSM, and there is some suggestion that NCCAI among HIV-positive men may have increased after 2008, a change that cannot be completely explained by the change in data collection method which occurred in 2010. Further, CASI data did not show declines in NCCAI after 2010. Unlike HIV-negative men, we noted relatively large declines in the proportion of HIV-positive men reporting consistent condom use and no anal sex. The reason for these trends among HIV-positive men is unclear, but may reflect behavioral disinhibition in an era of highly effective and widespread ART use or more accurate reporting over the course of the study period (i.e., declines in social desirability bias over time).

Similar to previous studies of seroadaptive behaviors and HIV risk [23, 34, 35, 45], we found that serosorting was associated with a 2-fold higher risk of HIV compared to no CAI, but a 50% lower risk of HIV compared to NCCAI. Thus, our results lend support to public health messaging that promotes consistent condom use as the best risk reduction strategy [21]. At the same time, it is likely that for populations of MSM where HIV testing is common and HIV status disclosure is high, serosorting is an effective HIV prevention strategy among MSM for whom consistent condom use is not achievable. Clinicians and counselors should consider discussing serosorting with their MSM patients (who do not consistently use condoms) as a potential strategy to be incorporated in a comprehensive HIV risk-reduction plan.

Although in no way definitive, we believe that our findings are consistent with the hypothesis that changes in the population's sexual behavior contributed to a decline in new HIV diagnoses. During the 12-year study period, we found that the risk of testing newly positive for HIV declined for all MSM regardless of sexual behavior. Though the largest absolute reduction in HIV test positivity (7.1% to 2.8%) occurred among men reporting NCCAI, the group with the highest risk of HIV infection, the relative reduction in risk was roughly similar across risk groups, varying from 46% among men who serosorted to 61% among men who engaged in NCCAI. These declines may be due to several factors, including the increase in the proportion of HIV-infected MSM in King County who were virologically suppressed [46] or the increase in HIV testing frequency [39] during this period. Regardless of the reason for behavior-specific declines, the large shift in the population's behavior from NCCAI to serosorting is a compelling factor to consider in the overall decrease in HIV test positivity that we observed.

Our findings lend some support to the idea that serosorting may increase the risk of STIs other than HIV. Compared to men who do not engage in CAI, HIV-negative and HIV-positive serosorters had an approximately 30%-100% higher risk of all bacterial STIs, a finding that is similar to studies in Chicago, San Francisco, and Australia [30, 37, 38]. At the population-level, the increase in serosorting we observed occurred concurrently with a nearly 3-fold increase in the rate of early syphilis among HIV-positive MSM in King County between 2001 and 2013 [47]. Although this ecological association does not definitively implicate serosorting among HIV-positive MSM as a cause of these rising syphilis rates, the significant decreases in consistent condom use and no anal sex during the same period, coupled with the higher risk of syphilis among serosorters compared to men who did not have CAI (aRR=1.4; 95% CI=1.1-1.7), lend

support to the hypothesis that increases in serosorting have contributed to the current syphilis epidemic among HIV-positive MSM in Seattle. However, the magnitude of these effects is uncertain.

This study has a number of strengths. To our knowledge, this is the largest study of serosorting trends in the US and covers a longer period of time than prior studies. It included two MSM populations with different HIV risk profiles. The two clinical/testing sites have collected sexual behavior data systematically since the early 2000s and together diagnose nearly 40% of all new HIV infections among MSM in King County, Washington. We were also able to obtain HIV and STI outcome data, biological measures of serosorting's impact. Our data are also subject to some important limitations. First, this is a cross-sectional study and it is not known if reported behaviors preceded or followed the acquisition of HIV and STIs. Second, we cannot say with certainty if the changes in behaviors we observed reflect true changes in the population's behavior or changes in the composition of the populations from which we collected data. Third, the initiation of the CASI at the STD clinic in 2010 limited our ability to understand how sexual behavior trends truly changed during that time. Fourth, our findings are subject to social desirability bias and recall bias. Fifth, multivariate models were adjusted for known confounders but imperfect measurement of these factors may have resulted in residual confounding. Sixth, these data represent reported sexual history and do not include behavioral intent, therefore it is unclear if MSM whose sexual behaviors were consistent with serosorting intended to engage in this behavior as an explicit HIV risk-reducing strategy. Finally, these data are specific to men attending an STD clinic and an HIV/STI testing center in Seattle, and it is not

known how these findings may extend to populations outside testing centers or outside Seattle. However, as discussed above, similar trends have been observed in at least some other cities.

In conclusion, we observed significant increases in serosorting concurrent with declines in NCCAI among Seattle MSM. Given the protective effect of serosorting relative to NCCAI, our findings suggest that serosorting may have contributed to overall declines in HIV incidence in Seattle and highlight how the behavior, while not ideal from a public health perspective, represents a step toward greater safety for some men.

TABLES AND FIGURES

Table 1.1. Demographic, behavioral and HIV/STI test positivity of MSM visits at the Public Health – Seattle & King County STD clinic and Gay City Health Project 2002-2013, by site (N=49,912)

	Total N = 49,912	STD Clinic N = 34,254	Gay City N = 15,658	
Characteristic	N (%)	N (%)	N (%)	P-Value
Age				
<25	9,593 (19)	6,167 (18)	3,426 (22)	<0.001
25-34	18,270 (37)	12,034 (35)	6,236 (40)	
35-44	12,706 (25)	9,140 (27)	3,566 (23)	
≥45	9,336 (19)	6,912 (20)	2,424 (15)	
Race/Ethnicity				
White, NH	34,275 (69)	23,728 (69)	10,547 (67)	<0.001
Black, NH	3,127 (6)	2,552 (7)	575 (4)	
Asian/Pacific Islander, NH	3,823 (8)	2,382 (7)	1,441 (9)	
Other, NH	2,952 (6)	1,897 (6)	1,055 (7)	
Hispanic	5,735 (11)	3,695 (11)	2,040 (13)	
HIV status				
Negative	44,961 (91)	29,454 (87)	15,507 (99)	<0.001
Positive	4,647 (9)	4,496 (13)	151 (1)	
Ever used methamphetamine				
	8,408 (17)	5,986 (17)	2,422 (15)	<0.001
Time since last HIV test				
Within 1 year	23,742 (48)	17,083 (50)	6,659 (43)	<0.001
1-2 years ago	5,726 (11)	4,095 (12)	1,631 (10)	
> 2 years ago	5,391 (11)	4,515 (13)	876 (6)	
Missing	15,053 (30)	8,561 (25)	6,492 (41)	
Number of male sex partners, past 12 months (mean±SD)				
	12 (<u>+41</u>)	14 (<u>+48</u>)	8 (<u>+18</u>)	<0.001
Sexual repertoire, past 12 months				
Non-concordant CAI	13,432 (27)	9,964 (29)	3,468 (22)	<0.001
Serosorter	17,502 (35)	10,778 (31)	6,724 (43)	
Consistent condom use	15,097 (30)	9,826 (29)	5,271 (34)	
No anal sex	3,881 (8)	3,686 (11)	195 (1)	
HIV/STI test positivity at visit*				
HIV	823 (2.1)	595 (2.5)	228 (1.5)	<0.001
Rectal chlamydia	2,000 (9)	1,729 (10)	271 (8)	<0.001
Rectal gonorrhea	1,620 (7)	1,524 (8)	96 (3)	<0.001
Urethral chlamydia	1,365 (5)	1,280 (5)	85 (2)	<0.001
Urethral gonorrhea	1,719 (7)	1,706 (8)	13 (0.4)	<0.001
Early syphilis	951 (2)	876 (3)	75 (1)	<0.001

CAI, condomless anal intercourse; NH: non-Hispanic; SD, standard deviation

*Of those tested

Figure 1.1. Secular trends in sexual behavior reported at the first visit in a calendar year by HIV-negative MSM attending the Public Health – Seattle & King County STD clinic and Gay City Health Project 2002-2013, by site and method of data collection (N = 35,547)

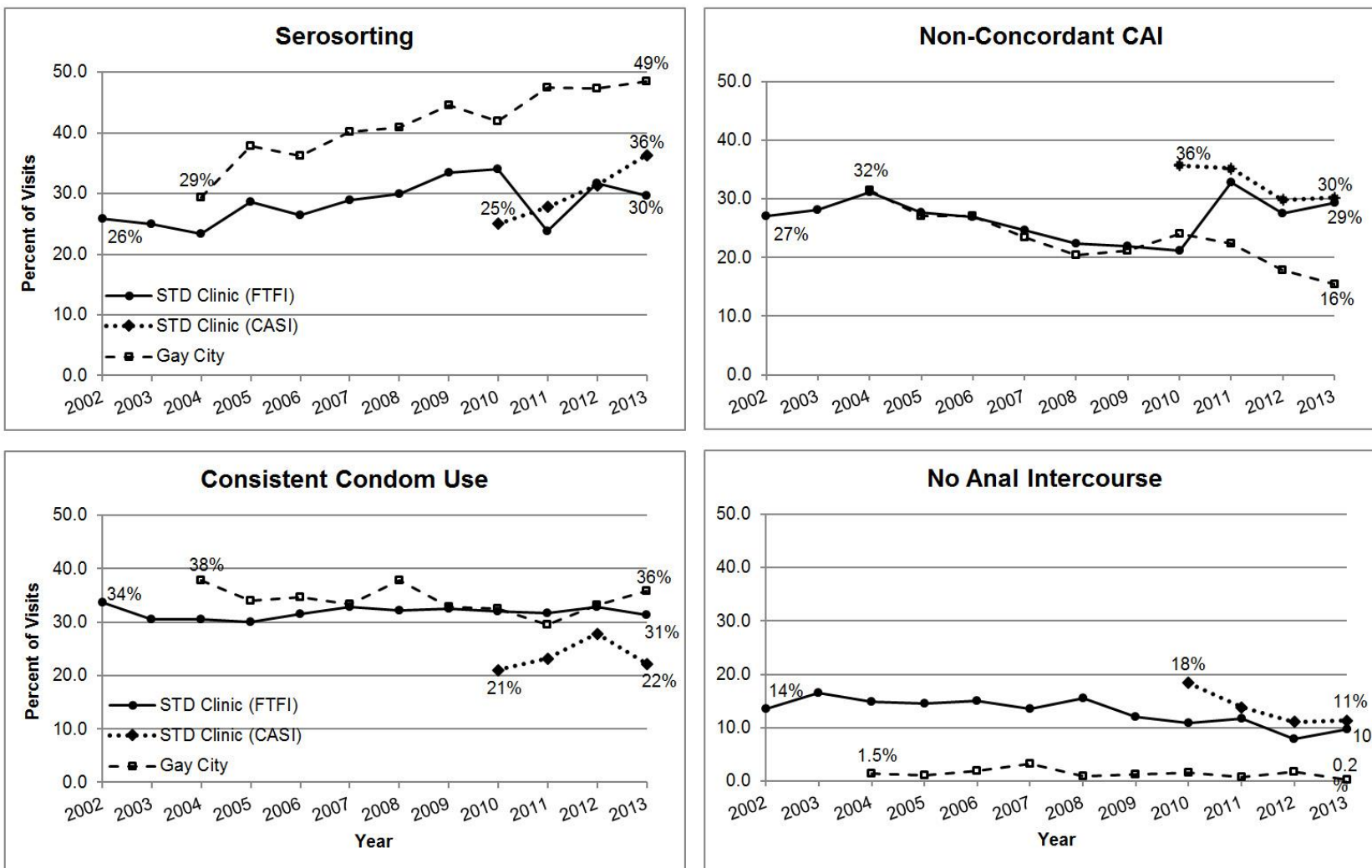


Figure 1.2. Secular trends in sexual behavior reported at the first visit in a calendar year by HIV-positive MSM attending the Public Health – Seattle & King County STD clinic 2002-2013, by method of data collection (N = 3,460)

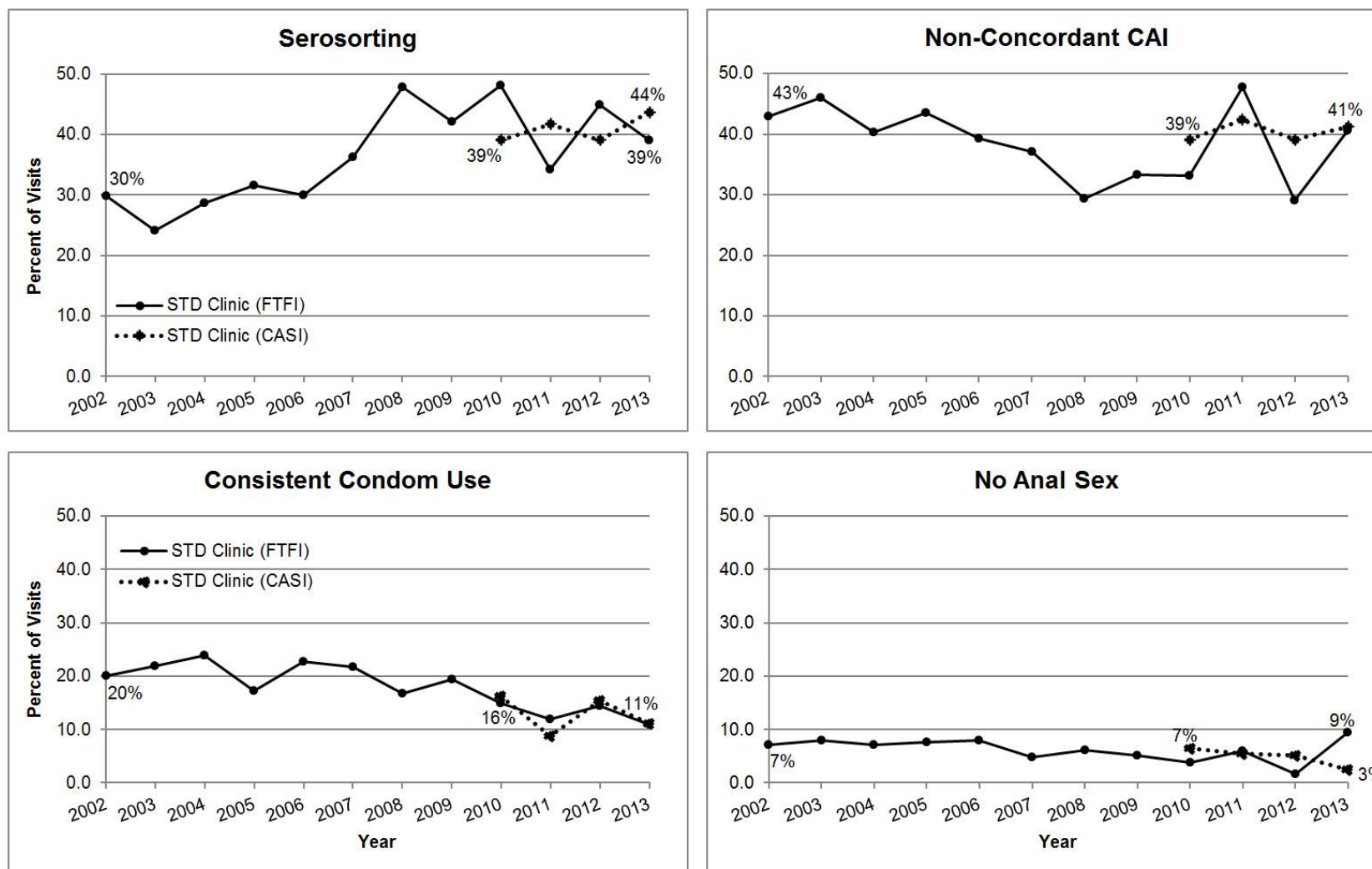


Table 1.2. Association between serosorting and testing newly positive for HIV and bacterial STIs among MSM attending the Public Health – Seattle & King County STD clinic and Gay City Health Project 2002-2013

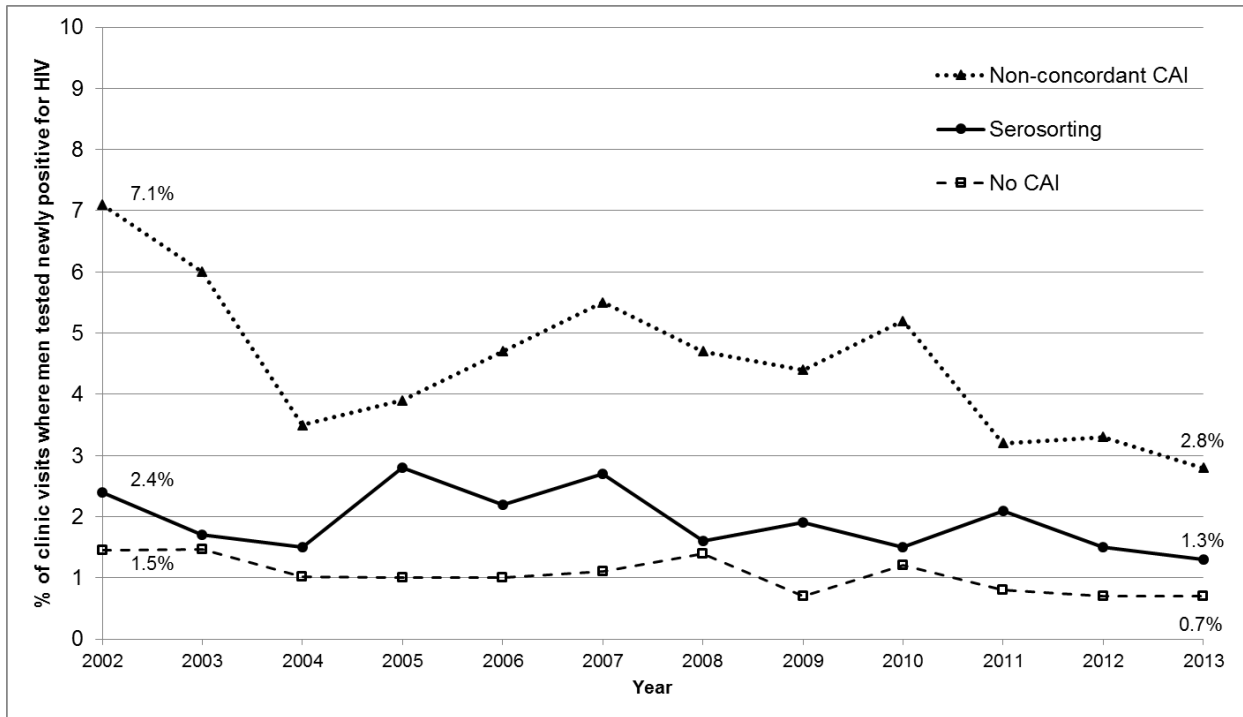
	NCCAI n/N (%)*	Serosorting n/N (%)*	No CAI n/N (%)*	aRR (95% CI)** Serosorting vs NCCAI	aRR (95% CI)** Serosorting vs no CAI
HIV-Negative MSM					
HIV	421/10,035 (4.2)	255/13,768 (1.9)	147/15,042 (1.0)	0.53 (0.45-0.62)	1.98 (1.61-2.44)
Urethral CT/GC	745/6,078 (12.3)	822/8,386 (9.8)	665/9,436 (7.1)	0.89 (0.80-0.99)	1.48 (1.33-1.65)
Rectal CT/GC	832/5,618 (14.8)	1142/7,661 (14.9)	504/5,895 (8.6)	1.02 (0.93-1.11)	1.72 (1.54-1.91)
Early syphilis	262/10,767 (2.4)	202/14,525 (1.4)	129/16,286 (0.8)	0.76 (0.62-0.92)	1.98 (1.56-2.52)
HIV-Positive MSM					
Urethral CT/GC	236/1,277 (18.5)	268/1,390 (19.3)	102/689 (14.8)	1.22 (1.02-1.45)	1.36 (1.11-1.73)
Rectal CT/GC	357/1,390 (25.7)	292/1,220 (23.9)	87/480 (18.1)	0.91 (0.80-1.05)	1.27 (1.00-1.62)
Early syphilis	148/1,717 (8.6)	143/1,642 (9.0)	53/923 (5.7)	1.02 (0.81-1.30)	1.40 (1.02-1.92)

aRR, adjusted relative risk; CI, confidence interval; NCCAI, Non-concordant condomless anal intercourse; CAI, condomless anal intercourse; CT, chlamydia; GC, gonorrhea

*n/N = number who tested positive out of the total number tested for each behavior

**HIV models adjusted for age, race, time since last HIV test, number of male sex partners in the past 12 months, methamphetamine use, clinic location, and year of visit; STI models adjusted for age, race, number of male sex partners in the past 12 months, methamphetamine use, clinic location, and year of visit

Figure 1.3. Secular trends in HIV test positivity among HIV-negative MSM attendees of the Public Health – Seattle & King County STD clinic and Gay City Health Project 2002-2013, by reported sexual behavior (N=38,845)



CHAPTER 3. Evaluation of a computer-based recruitment system to enroll men who have sex with men (MSM) into an observational HIV behavioral risk study

ABSTRACT

Background: Enrolling large numbers of men who have sex with men (MSM) into HIV prevention research is necessary for studies with an HIV outcome, but the resources and time required for such recruitment can be prohibitive in some settings. New methods to efficiently recruit a representative sample of MSM for behavioral studies are needed.

Methods: At an STD clinic in Seattle, Washington, we used our existing routine clinical computer-assisted self-interview (CASI) that collects patient medical and sexual history to develop a computer-based method to recruit, screen and enroll MSM into a cross-sectional HIV behavioral risk study. Patients initially completed the routine clinical CASI; upon completion of the CASI, men aged ≥ 18 years who reported sex with a man in the prior 12 months were presented with a study description and electronic consent. Subjects could request to speak with study staff but did not need to do so to enroll. We obtained demographic and behavioral information and HIV/sexually transmitted infection (STI) test results from the clinic's electronic medical record to compare characteristics of enrolled versus non-enrolled MSM.

Results: From February 2013 – July 2014 (18 months), we enrolled men at 2,661 (54%) of 4,994 visits, including 1,748 unique MSM. Less than 1% of eligible MSM required personal assistance from study staff. Enrolled men were broadly representative of all MSM attending the clinic, though MSM who consented to participate were younger (mean age: 34 vs. 37; $P < 0.001$),

reported a higher number of male sex partners (11 vs. 8; $P < 0.001$) and were more likely to report methamphetamine use in the prior year (15% vs 8%; $P < 0.001$) compared to men who declined to participate. The HIV test positivity of the two groups was similar (1.9% vs. 2.0%; $P = 0.8$).

Conclusion: Using procedures built into an existing computerized clinic intake system, we successfully enrolled a large sample of MSM that may be an ideal population for an HIV prevention study.

INTRODUCTION

Though men who have sex with men (MSM) represent the group at highest risk for HIV infection in the United States (US) [1], the estimated incidence of infection among high-risk MSM enrolled in observational or interventional (control arm) studies is typically between 2-8% [6, 23, 48-50]. Given this incidence, biomedical and behavioral HIV prevention studies that use an HIV outcome require very large sample sizes to achieve adequate statistical power. Due to budget and human resource constraints, recruitment of such populations (i.e., typically over 1,500 individuals), may be challenging for studies that employ traditional in-person recruitment methods, and new approaches to quickly and efficiently recruit a large number of MSM into HIV prevention studies are needed.

For some studies, recruitment of this large sample size must be balanced with the need to obtain a representative sample of participants. Consent bias, which is a type of selection bias, occurs when individuals who consent to participate in research differ from the group who does not consent [51]. For behavioral studies, this bias may result in inaccurate results and reduce the generalizability of findings, but the degree to which consent bias is present in HIV prevention research among MSM is not well-studied.

The work described here was funded through a National Institutes of Health (NIH) R21 grant, a funding mechanism designed to support early project development or novel research methodologies or applications [52]. The funded study's primary aim was to assess the prevalence of seroadaptive behaviors and their association with testing newly HIV positive. Because new HIV diagnoses are a rare event in our STD clinic, one of the study's primary challenges – and one of grant's specific aims – was to develop and test an automated and

efficient mechanism for enrolling large numbers of MSM into a cross-sectional seroadaptive behaviors study using limited staffing. The objectives of the current analysis were to describe the proportion of MSM who agree to enroll in the study using this automated mechanism and to characterize differences between enrollees and non-enrollees. We hypothesized that 80% of eligible MSM would enroll in the study and that characteristics of participants would be representative of the entire clinic population of eligible MSM.

METHODS

Study design and population

Since 2010, the Public Health – Seattle & King County (PHSKC) STD clinic in Seattle, Washington has used a clinical computer-assisted self-interview (CASI) as part of routine care to collect patients' medical and sexual behavior history. All English-speaking patients presenting for a new problem visit are asked to complete this clinical CASI which includes information on demographics, reason for visit, symptoms, sexual behaviors (e.g., number of sex partners, condom use with sex partners stratified by HIV status), sexually transmitted infection (STI) history, drug use, and HIV testing history. The information provided in the clinical CASI is used by clinical providers to guide HIV/STI clinical evaluations, screening, care, and behavioral counseling.

Beginning on February 1, 2013, individuals who completed the clinical CASI and indicated that they were male and had ≥ 1 male sex partner in the prior 12 months were invited to enroll in a cross-sectional study of seroadaptive behaviors and HIV/STI risk. The specific recruitment procedures were as follows: at the conclusion of the clinical CASI, individuals were

presented with an informational screen on the computer that briefly described the study and asked if the individual was interested in “learning more” about the study. This screen indicated the length of time of the study questionnaire and that participants would be financially compensated for participating. Men who indicated that they would like more information were taken to an electronic informed consent module that fully described the study and provided an option to give electronic consent. If men had a question during the informed consent process, they could click a button on the computer that automatically sent a text message to a phone carried by research staff to alert staff that their presence was needed at the computers. Men who provided electronic consent were immediately directed to the questionnaire. Men were allowed to participate in the study more than once.

We made two changes after recruitment began to enhance enrollment. First, four weeks after starting enrollment, we added one sentence to the study introduction screen describing the overall goal of the study (i.e., to develop better HIV/STI prevention methods for MSM). Previously, we had only described the study procedures but not the overall goal. We also changed the text describing the length of the study questionnaire – from 10 minutes to 5 minutes – after we noted that the questionnaire did not take as long to complete as we initially anticipated. Second, six weeks after the initiation of enrollment, we increased the compensation amount from \$5.00 cash to \$10.00 cash.

Data collection and measures

As part of our clinic’s routine data storage procedures, all patient registration information (i.e., demographic data), clinical CASI data, and HIV/STI test results are linked to one another and

stored in the clinic's electronic medical record database. Using a unique code generated from the clinical CASI, we abstracted data from the electronic medical record database to link to research records for the purposes of this study. We also obtained de-identified demographic, behavioral, and test result data from men who did not consent to participate in the study. All study procedures, including use of de-identified data from non-consenting patients, were reviewed and approved by the University of Washington Institutional Review Board (IRB).

Since the overall goal of the cross-sectional study was to examine the association between select sexual behaviors and new HIV diagnoses, we were interested in understanding if men who enrolled in the study reported different sexual behaviors or had a different prevalence of newly diagnosed HIV infection than men who declined to enroll. We used data from the clinical CASI to define the following four sexual behaviors: non-concordant condomless anal intercourse (NCCA; men who reported inconsistent condom use for anal sex with HIV-discordant/unknown-status partners); serosorting (men who reported inconsistent condom use for anal sex with HIV-concordant partners only); consistent condom use (men who reported always using condoms with all partners); and no anal sex.

HIV and STI testing was performed per routine clinical care. HIV testing was recommended for MSM who had not previously tested HIV positive. The clinic's protocol is to offer both rapid and laboratory testing to all MSM. Staff perform rapid tests using the INSTI test on whole blood (bioLytical Laboratories, British Columbia). Our laboratory tests for HIV using a third-generation EIA (Genetic Systems HIV1/2 Plus O EIA, Biorad Laboratories, Redmond, WA); MSM with a negative HIV EIA are tested using pooled HIV RNA testing [41-44]. Urethral specimens (swab or urine) were obtained from MSM with signs/symptoms of urethritis or who

reported exposure to a partner with gonorrhea or chlamydia. Rectal specimens were obtained from MSM who reported receptive anal sex in the prior year. Urethral and rectal specimens were tested for gonorrhea and chlamydia using nucleic acid amplification testing (NAAT; APTIMA Combo 2, GenProbe Diagnostics, San Diego, CA). All MSM who agreed to have a blood sample obtained were tested for syphilis using the rapid plasma regain (RPR) test. A single, experienced disease investigational specialist (DIS) reviews all cases of syphilis in King County and assigns a stage based on laboratory and clinical findings. We defined early syphilis as primary, secondary, or early latent infection.

Statistical methods

We report the proportion of men who consented to participate in the study and compare differences in demographic characteristics, sexual behaviors, and HIV, rectal and urethral gonorrhea/chlamydia and early syphilis test positivity of enrolled men versus those who did not enroll. The latter analysis was limited to men's first approach to participate in the study and only included men who were approached about participation at the \$10 compensation amount. We used t-tests for continuous variables and chi-square tests for categorical variables to test for statistically significant differences in characteristics between the two groups. Two-sided statistical tests were performed at a significance level (α) of 0.05.

RESULTS

From February 1, 2013 to July 31, 2014, men were approached about participation at 4,944 clinic visits; of these, MSM agreed to "learn more" more about the study at 2,897 (58.6%) visits

and provided informed consent at 91.9% (2,661 of 2,897) of these visits. Thus in total, we enrolled men at 54% (2,661 of 4,944) of visits, which includes 1,488 unique HIV-negative MSM and 260 unique HIV-positive MSM. At less than 1% of visits (25 of 2,897), men who viewed the consent screen asked to speak to research staff. In the first four weeks of recruitment we enrolled men at 95 (38.2%) of 154 visits. Enrollment increased to 47.0% (55 of 117 visits) after we modified the study introductory screen, and to 54.9% (2,511 of 4,578 visits) after we increased the compensation from \$5 to \$10.

Fifty-two percent (1,599 of 3,106) of unique men agreed to enroll in the study the first time they were approached about participation. Of the 995 men who were approached about participation twice, 54.5% consented to enroll at the second approach, including 426 (78.5%) of 512 who had enrolled at the first approach and 117 (24.2%) of 483 who declined to enroll at the first approach. Among men who were only approached about participation once (N=2,111), 52% agreed to enroll, while 66% (661 of 995) of those who were approached about participation at least twice agreed to enroll.

At 4,578 visits with a compensation amount of \$10, 2,744 unique MSM were approached for the first time about participating; 1,452 (52.9%) of these men enrolled in the study (Table 2.1). Enrolled men were significantly younger than men who did not enroll but the racial/ethnic distribution of enrollees and non-enrollees was similar. Men who enrolled reported a higher number of male sex partners, were more likely to report NCCAII, and were more likely to report methamphetamine use in the prior 12 months compared to men who did not enroll. Enrolled men were more likely to report HIV/STI testing as the reason for their clinic

visit, but the proportion of enrolled men who had an HIV test in the prior 12 months was comparable to men who declined to enroll.

There were no statistically significant differences in the HIV/STI test positivity between enrollee and non-enrollees. The proportion of enrollees who tested newly positive for HIV was 1.9%, compared to 2.0% among men who did not enroll (Table 2.2). Urethral chlamydia and gonorrhea test positivity was slightly higher among enrollees compared to non-enrollees, while rectal chlamydia and gonorrhea test positivity was slightly lower. Early syphilis diagnosis did not differ between the two groups.

DISCUSSION

Using recruitment and consent procedures built into a CASI that is routinely used to collect non-research clinical and sexual history data, we enrolled 1,748 MSM STD clinic patients into a cross-sectional sexual behavior study (at 54% of eligible visits) in 18 months of recruitment. Outside of the initial development, programming and monitoring of incoming data, these enrollment procedures required no full-time staff and <1% of MSM required assistance from study staff. Our enrolled population was somewhat younger and reported higher-risk behaviors compared to men who declined to enroll in the study, but had almost identical levels of HIV and STI test positivity. These findings suggest that using automated processes to enroll a large, relatively young and high-risk sample of MSM into cross-sectional HIV prevention research is feasible and highly efficient.

The overall proportion of men who enrolled in the study (54%) was lower than our initial hypothesis of 80%, but is comparable to or higher than that of other observational studies of

MSM in the US. In the 2011 National HIV Behavioral Surveillance (NHBS) survey of MSM, 39,792 persons were approached and 9,828 (25%) provided consent and completed an interview [53]. A 2007-2008 San Francisco study of seroadaptive behaviors enrolled 1,305 MSM (51%) of 2,558 approached [54] while a 2010-2012 Atlanta study enrolled 1,543 MSM (8%) of 19,931 approached [55]. Compared to studies that have recruited patients from STD clinics, our overall enrollment was lower than other cross-sectional studies, which have enrolled 78-86% of approached patients [56-59], but higher than Project AWARE, a randomized, controlled trial conducted in 9 US STD clinics that enrolled 34% (5,028 of 14,948) of approached patients [49]. Notably, the burden of participation in this study was low, and it is unclear how enrollment would differ for studies with a greater time commitment.

Although the proportion of men that we enrolled fell below our expectations, the absolute number of men we enrolled – 1,748 unique MSM including 1,488 HIV-negative MSM – is notable. We were able to enroll this large number of individuals quickly (in 18 months), at relatively low cost (i.e., using an NIH R21 funding mechanism) and with minimal human resources. Given the large number of persons required to obtain a sufficient sample size for an HIV outcome, it is almost unimaginable that studies using traditional in-person recruitment methods could recruit such a large sample size in this time frame and with comparable resources. Most published studies that have enrolled a number of HIV-negative MSM comparable to ours have had study budgets of over \$1million, highlighting the difficulties investigators face in recruiting an adequate number of subjects quickly and at low cost.

We noted several differences between enrolled men and those who declined to enroll. Enrolled men were significantly younger and more likely to report high-risk sexual behaviors

and methamphetamine use than men who did not enroll. However, these characteristics are risk factors for HIV infection [4, 60, 61] and thus we were encouraged that our enrolled population actually represents the key population to target for HIV prevention interventions. We also found that enrollees were more likely to report attending the clinic for HIV/STI testing compared to non-enrollees. It is possible that enrolled men were more frequent testers than non-enrolled men – though the proportion who reported an HIV test in the prior 12 months was similar – or that these men were presenting to the clinic after a high-risk sexual exposure. Of note, the racial/ethnic distribution of enrolled participants was similar to non-enrolled men and the proportion of black MSM who agreed to enroll (118 of 215; 55%) was approximately the same as the overall population. This is reassuring, given that black MSM represent the group with the highest HIV incidence [62] yet have been systematically under-enrolled in HIV prevention studies [63, 64].

Despite differences in characteristics between enrolled and non-enrolled MSM, the HIV and STI test positivity between the two groups was similar. This finding has important implications for consent bias. There are two conditions necessary for consent bias to be problematic: consent status must be associated with (1) the exposure of interest and (2) the outcome of interest [65]. In the case of our cross-sectional study, which seeks to examine the association between seroadaptive behaviors (exposure) and testing newly positive for HIV (outcome), our data suggest that the risk of consent bias for a study with this exposure and outcome is likely minimized – we observed significant differences between enrollees and non-enrollees with regard to sexual behaviors but the HIV test positivity of the two groups was approximately equal. Though the importance of consent bias is somewhat debatable [66-68],

our findings are reassuring to researchers in clinical settings where broader issues of selection bias are already of concern.

There are several methodological considerations from our study that may be useful to other researchers and thus merit discussion. First, we noted incremental improvements in enrollment with modifications to our study screen (from 38% to 47%) and with an increase in compensation amount (from 47% to 55%). Though the basis for this latter increase is clear, the reason for the former increase is less so. This higher enrollment proportion that accompanied the change in study screen may be due to the addition of a phrase which appealed to men's altruistic approach to research [69] or to the modification of text describing the time required to complete the study questionnaire. Second, we found that 24% of men who declined to participate in the study the first time they were approached subsequently agreed to participate at the second approach, and that 66% of men who were approached more than once agreed to enroll in the study, compared to 50% among those who were only approached once. Although many research studies actively avoid approaching the same individual multiple times, our findings suggest that, at least for cross-sectional studies, there may be transient circumstances for potential participants (i.e., time constraints on a given day) which do not permanently preclude them from participating in a study.

Strengths of our study include our novel recruitment strategy and ability to examine exposure and outcome data on enrolled and non-enrolled MSM. This allowed us, for the first time to our knowledge, to examine factors associated with research participation among a clinic-based population of MSM. There are also several key limitations. First, our recruitment success built upon an existing clinical CASI system that took substantial resources to implement.

It is unclear if other settings, which may require additional time or resources to initiate this computerized system, would enroll the same number of individuals at a comparable cost. On the other hand, our findings should be an additional impetus for creating such electronic systems in clinics that have a research mission; prior studies suggest that self-interviews increase data completeness and can be used to prompt improved clinical care [70-76]. Second, as mentioned above, these men provided consent for a single-visit, cross-sectional study where all research procedures were completed on the computer. How the proportion of men enrolled in the study would have differed if follow-up visits or additional research procedures were required is not known, and IRB considerations would also likely vary for studies that included greater risks. Third, this study was conducted among MSM at a single STD clinic in Seattle. It is unclear if non-MSM, non-clinical populations would enroll at a comparable proportion to our study.

In conclusion, we demonstrated the feasibility of integrating a study into an existing, high volume HIV testing infrastructure to offer a feasible, efficient, and relatively low-cost approach to evaluating HIV outcomes. Our enrolled population was relatively young and reported higher-risk behaviors than men who declined to enroll, further supporting the use of this mechanism for recruitment for HIV prevention studies with an HIV outcome. With recent advances in the development of new biomedical methods to prevent HIV, this research strategy may also provide an ideal mechanism for recruiting participants into HIV prevention intervention studies or at minimum, screening individuals to identify those who are eligible. We are only aware of one other STD clinic (the Melbourne STD clinic) that routinely uses CASI to collect patients' sexual history data as part of clinical care. However, our demonstrated

success with this computer-based approach may encourage other research-focused STD and non-STD clinics to adopt similar systems.

TABLES AND FIGURES

Table 2.1. Demographic, clinical, and behavioral characteristics of PHSKC STD clinic male patients eligible to participate in a research study 2013-2014, by enrollment status (N=2,744)

Characteristic	Total (N = 2,744)	Enrolled (N = 1,452)	Did not enroll (N = 1,292)	P- value
	N (%)	N (%)	N (%)	
Age, mean \pm SD	35 \pm 11	34 \pm 11	37 \pm 11	<0.001
Age				
18-34 years	1552 (56.6)	920 (63.4)	632 (48.9)	<0.001
\geq 35 years	1192 (43.4)	532 (36.6)	660 (51.1)	
Race/ethnicity				
White, NH	1,810 (66.2)	975 (67.4)	835 (64.8)	0.21
Black, NH	215 (7.9)	118 (8.2)	97 (7.5)	
Asian, Pacific Islander or Hawaiian, NH	211 (7.7)	96 (6.6)	115 (8.9)	
Native American or Alaskan Native, NH	28 (1.0)	17 (1.2)	11 (1.0)	
Other, NH	156 (5.7)	82 (5.7)	74 (5.8)	
Hispanic	315 (11.5)	159 (11.0)	156 (12.1)	
HIV Status				
Negative	2,321 (84.6)	1,239 (85.3)	1,082 (83.8)	0.34
Positive	423 (15.4)	213 (14.7)	210 (16.3)	
Had HIV test in past 12 months	1,528 (65.8)	828 (66.5)	700 (65.0)	0.46
Reason for clinic visit*				
Symptoms	930 (33.9)	496 (34.2)	434 (33.6)	0.75
HIV/STI testing	1,914 (69.8)	1,060 (73.0)	854 (66.1)	<0.001
Tested positive for HIV/STI**	220 (8.0)	124 (8.5)	96 (7.4)	0.29
Follow-up on previous visit***	480 (17.5)	252 (17.4)	228 (17.7)	0.84
Health department request	284 (10.4)	148 (10.2)	136 (10.5)	0.78
Referral	149 (5.4)	77 (5.3)	72 (5.6)	0.76
Other	351 (12.8)	200 (13.8)	151 (11.7)	0.10
Contact to partner with symptoms or diagnosed HIV/STI	1,088 (39.7)	566 (39.0)	522 (40.4)	0.45
Always discloses HIV status to partner	1,917 (73.6)	1,020 (73.2)	897 (74.0)	0.27
Methamphetamine use, past 12 months	321 (11.7)	221 (15.2)	100 (7.7)	<0.001
Number of MSP, past 12 months, mean \pm SD	9.4 \pm 20.4	10.5 \pm 5.2	8.3 \pm 13.1	0.03
Sexual behaviors: HIV Negative MSM				
NCCAI	652 (30.4)	375 (32.3)	277 (28.1)	<0.001
Serosorter	796 (37.1)	457 (39.4)	339 (34.4)	
Always uses condoms	464 (21.6)	227 (20.0)	237 (24.0)	
No anal sex	236 (11.0)	102 (8.8)	134 (13.6)	
Sexual behaviors: HIV Positive MSM				
NCCAI	164 (42.4)	93 (48.2)	71 (36.6)	0.04
Serosorter	161 (41.6)	78 (40.4)	83 (42.8)	
Always uses condoms	50 (12.9)	18 (9.3)	32 (16.5)	
No anal sex	12 (3.1)	4 (2.1)	8 (4.1)	

Abbreviations: NH, non-Hispanic; NCCAI, non-concordant condomless anal intercourse; MSP, male sex partner; SD, standard deviation

*Not mutually exclusive

**Previously tested positive for STI and need treatment or previously tested positive for HIV

***HIV follow-up visit or follow-up testing after treatment for STI

Table 2.2. Number and proportion of PHSKC STD clinic male patients testing newly positive for HIV/STIs 2013-2014, by enrollment status

HIV/STI test	Enrolled		Did not enroll		P-Value
	n/N*	%	n/N*	%	
HIV	19/1,015	1.9	17/832	2.0	0.79
Urethral chlamydia	55/702	7.8	48/688	7.0	0.54
Urethral gonorrhea	69/713	9.7	51/688	7.4	0.13
Early syphilis**	50/1,231	4.1	45/1,055	4.3	0.81
Rectal chlamydia	129/871	14.8	116/727	16.0	0.53
Rectal gonorrhea	114/884	12.9	102/737	13.8	0.58

*Number who tested positive (n) /Number tested (N)

**Primary, secondary or early latent

CHAPTER 4. The operationalization of seroadaptive behaviors among men who have sex with men (MSM): a comparison of reported sexual behaviors and purposely adopted behaviors

ABSTRACT

Background: Most studies define seroadaptive behaviors based on men's self-reported sexual behavior history, regardless of whether those behaviors reflect purposely adopted risk mitigation strategies. This may not accurately characterize the risks and/or benefits associated with the behaviors.

Methods: Among MSM attending an STD clinic in Seattle, Washington 2013-2015, we used two methods to measure seroadaptive behaviors: (1) a 12-month sexual behavior history reported in a routine clinical computer-assisted self-interview (CASI) (behavioral definition); and (2) a research CASI which asked if men purposely adopted risk reduction behaviors in the past 12 months based on partners' perceived HIV status (purposely-adopted definition). We compared the prevalence and agreement of the two measures for four seroadaptive behaviors, stratified by respondent HIV status: pure serosorting (only partners of concordant HIV status), condom serosorting (condom use with discordant/unknown-status partners but not with concordant partners), seropositioning (HIV-negative partner in insertive anal sex role and HIV-positive partner in receptive role), and condom seropositioning (condom use by HIV-negative partner for receptive but not insertive anal sex with discordant/unknown-status partners) .

Results: We enrolled MSM at 3,556 (55%) of 6,514 visits; 3,410 visits had complete data for both CASI's. Using the behavior definition, pure serosorting was reported at 43% of visits by HIV-negative MSM and 31% of visits by HIV-positive MSM. For the purposely-adopted definition the comparable proportions were 47% and 37%, respectively. At approximately 70% of visits where MSM were classified as pure serosorters by the behavior definition, men also reported purposely adopting that behavior ($\kappa=0.40$; moderate agreement). The prevalence of other behaviors was low overall (<15%) and the agreement between the two measures was only slight to fair ($\kappa: 0.11-0.35$).

Conclusion: Pure serosorting is overwhelmingly the most common seroadaptive behavior in our clinic but yielded only moderate agreement between the two measures. Using men's sexual behavior history likely includes men who did not purposely adopt these behaviors. This misclassification may alter the estimated effect of seroadaptive behaviors on HIV risk.

INTRODUCTION

Seroadaptive behaviors, such as serosorting (i.e., choosing partners based on a partner's perceived HIV status) and seropositioning (i.e., choosing an insertive or receptive anal sex role based on a partner's perceived HIV status) are common among men who have sex with men (MSM) [23-28, 37]. Serosorting and other seroadaptive behaviors are associated with a lower risk of HIV than condomless anal intercourse (CAI) with an HIV-positive/unknown-status partner but a higher risk of HIV than consistent condom use [23, 28, 34, 35].

Though seroadaptive behaviors have been recognized since the 1990s, how these behaviors should be defined is still a topic of debate. The Centers for Disease Control and Prevention (CDC) defines serosorting as "choosing a sexual partner known to be of the same HIV serostatus, often to engage in unprotected sex, in order to reduce the risk of acquiring or transmitting HIV" [77]. However, nearly all studies, including those from which HIV risk estimates were obtained, have defined seroadaptive behaviors based only on a man's reported sexual behavior history. This definition, henceforth referred to as a "behavioral definition" or "behavioral measure" classifies an individual as engaging in seroadaptive behaviors without regard to whether or not the behaviors reflected a purposive decision to reduce his or his partner's risk of acquiring HIV. As an alternative measure, some studies have employed a definition that explicitly asks men if they purposely adopted behaviors based on their partner's HIV status (henceforth referred to as a "purposely-adopted definition" or "purposely-adopted measure"). Though this latter definition is more closely aligned with that of CDC, the behaviors that men report purposely adopting to reduce the risk of HIV transmission or acquisition do not necessarily align with their reported sexual behavior history [22, 78]. Thus it is unclear if

measuring purposely adopted behaviors will provide a better estimate of HIV risk or be more useful for behavioral counseling compared to only measuring the behaviors themselves.

Only a few studies have used a combination of behavior and purposely-adopted definitions of seroadaptive behaviors in the same population [22, 78-80]. A longitudinal study of San Francisco MSM found that few seroadaptive behaviors were the result of intentional HIV risk-reduction strategies [79], and an Internet-based study noted that 20-35% of seroconcordant partnerships were not purposive [80]. While these studies suggest that the two definitions of seroadaptive behaviors are distinct, neither directly compared the two definitions as independent measures of seroadaptive behaviors. Thus, the extent to which these two measures provide different estimates of the prevalence and risks/benefits associated with seroadaptive behaviors remains uncertain.

The objective of this study was to use two separate surveys in the same patient population – one that collected sexual behavior history and one that collected information on purposely-adopted seroadaptive behaviors – to compare the prevalence and agreement of two measures of seroadaptive behaviors (behavior definition vs. purposely-adopted definition).

METHODS

Study design and population

This was a cross-sectional study of MSM attending the Public Health – Seattle & King County (PHSKC) STD clinic. Detailed recruitment and enrollment procedures are described in Chapter 3. Briefly, all patients presenting to the PHSKC STD clinic for a new problem visit are asked to complete a clinical computer-assisted self-interview (clinical CASI) which includes information

on demographics, sexual behaviors, drug use, and HIV testing history. Men who reported in the clinical CASI that they had ≥ 1 male sex partner in the prior 12 months were eligible to enroll in the study. Immediately after completion of the clinical CASI, participants completed a 5-minute research CASI which queried men on their purposely-adopted seroadaptive behaviors in the prior 12 months, as described below. Data from the clinical CASI and research CASI were subsequently linked. During the first 6 weeks of the study, participants were paid \$5 for their participation, but this increased to \$10 thereafter. Men were allowed to participate in the study more than once.

Data collection and measures

Data from the clinical CASI were used to construct the behavioral definition of seroadaptive behaviors. The sexual behavior information collected in the clinical CASI included sexual role (insertive or receptive) stratified by partner HIV status (i.e., HIV-positive, HIV-negative and unknown status), and condom use with partners stratified by sexual role and HIV status of partners. For example, *“Have you topped anyone who was HIV-positive in the last 12 months?”* and (for men who indicate “yes”) *“In the last 12 months how often have you used condoms when topping HIV-positive partners?”* Information about sexual role with partners was collected as yes/no, while condom use information was collected as always/usually/sometimes/never [28, 36].

Data from the research CASI was used to construct the purposely-adopted definition of seroadaptive behaviors. To develop the research CASI, research staff conducted four rounds of cognitive interviews with 16 MSM PHSKC STD clinic patients. During the interviews, staff probed

respondents about their comprehension of each question, including their ability to recall the requested information and their cognitive process to arrive at their response. We incorporated modifications to the CASI instrument after each interview round, and used the revised CASI in the subsequent interview round. The research CASI asked men if their decision to form partnerships, use condoms, or adopt a sexual role was based on the HIV status of their partner. The preamble to the survey indicated that questions referred to behaviors adopted by the respondent to reduce his risk of acquiring or transmitting HIV. All questions were stratified by partnership type (main versus casual) and partner HIV status. Examples of these questions for HIV-negative respondents include: *“In the past 12 months, did you ever top an HIV-positive casual partner instead of bottom him **because** he was HIV-positive?”* or *“In the past 12 months, did you ever decide **not** to use condoms with an HIV-negative casual partner **because** he was HIV-negative?”* In the research CASI, men were initially asked about ever engaging in behaviors (yes/no) and for men who indicated “yes”, they were asked about the frequency of engaging in each behavior (always/usually/sometimes/never). In both CASI’s, all questions were asked about behaviors in aggregate in the prior 12 months and did not query men on behaviors with specific partners. Respondent HIV status was self-reported. Men who reported that they did not know their HIV status were considered to be HIV-negative for the purposes of this analysis.

We compared clinical and research CASI responses for four seroadaptive behaviors, defined in Table 3.1. Because the clinical CASI data did not ask men about behaviors separately for main and casual partners, we collapsed partnership type data from the research CASI to more accurately map to the clinical CASI data. We categorized all behaviors into binary categories, “always” versus “not always”. In the clinical CASI, the information to construct the

definitions for pure serosorting and seropositioning were only available as binary (yes/no) categories; however the definitions of these behaviors allowed us to create “always” versus “not always” categories. For example, men who reported only having HIV-concordant partners and no discordant/unknown-status partners were considered to “always” engage in serosorting. In the research CASI, frequency data were available for these two behaviors, so we combined the categories “usually”, “sometimes” or “never” to create a “not always” category. For condom serosorting and condom seropositioning, frequency data were available from both the research and clinical CASI to create “always” versus “not always” (i.e., usually/sometimes/never) categories.

Statistical methods

The unit of analysis was the clinic visit and the study sample was limited to visits where men completed both the clinical and research CASI’s. We describe the baseline characteristics of the total analytic sample (Table 3.2) and present the prevalence of seroadaptive behaviors as reported in the clinical CASI (behavior definition) and research CASI (purposely-adopted definition), stratified by the HIV status of the respondent (Table 3.3). We used Cohen’s kappa statistic to measure agreement between the clinical and research CASI and classified the magnitude of agreement as slight (0.0-0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61-0.80) and almost perfect (0.81-1.00) [81]. We used two approaches to describe the agreement between the behavioral definition and purposely-adopted definition. First, we examined the proportion of visits where men reported purposely adopting a behavior (per the research CASI), among visits where men were classified as engaging in that behavior per their

sexual history (per the clinical CASI) (Table 3.3, Column D). Second, we examined the proportion of visits where men were classified as engaging in a behavior per their sexual history (per the clinical CASI), among visits where men reported purposely adopting the behavior (per the research CASI) (Table 3.3, Column E). The first comparison can be considered as the group of men who purposely adopted their reported behaviors and the second group is men who completed or “executed” their purposive behaviors. These two approaches are analogous to a sensitivity/specificity and positive predictive value/negative predictive value, respectively, when a gold-standard measure is available. All study procedures were reviewed and approved by the University of Washington Institutional Review Board.

RESULTS

From February 2013 to March 2015, we enrolled MSM at 3,556 (55%) of 6,514 visits, including 1,851 unique HIV-negative MSM and 327 unique HIV-positive MSM. Ninety-six percent of visits (3,410 of 3,556) had complete behavioral data from the clinical and research CASI and are included in this analysis. Slightly more than one-half of visits were made by participants who were ≥ 30 years old, two-thirds of visits were by white, non-Hispanic MSM, and at $>96\%$ of visits men reported ever disclosing their HIV status or asking their partner’s HIV status in the prior year (Table 3.2). The proportion of visits where HIV-negative and HIV-positive men reported having an HIV-discordant or unknown-status partner in the prior year was 48% and 65%, respectively.

The prevalence and agreement of seroadaptive behaviors by method of definition is presented in Table 3.3. Pure serosorting was overwhelmingly the most commonly reported

behavior at visits by both HIV-negative and HIV-positive respondents. The agreement of the two measures was highest for pure serosorting (moderate agreement) and condom serosorting (fair agreement) and lowest for seropositioning (slight agreement) and condom seropositioning (slight agreement).

Among HIV-negative respondent-visits, 42.8% were classified as pure serosorting using the behavioral definition and 47.4% using the purposely-adopted definition (Table 3.3). Over seventy percent (71.5%; 890 of 1,245) of visits where men's sexual behavior history indicated that they engaged in pure serosorting also indicated that they purposely adopted that behavior, while 64.5% (890 of 1,379) of visits where men reported purposely adopting pure serosorting also reported that behavior in their sexual behavior history. The proportion of visits where HIV-negative men reported always seropositioning with discordant/unknown-status partners or always condom seropositioning with discordant/unknown-status partners was low overall. Only 11.9% and 20.0% of visits, respectively, where men were classified as engaging in these behaviors per the behavior definition were also visits where men reported purposely adopting that behavior. The proportion of visits where men reported "completing" their purposely adopted behavior was lowest for condom serosorting (22.9%) and condom seropositioning (29.0%). Using as a denominator visits where HIV-negative men reported having HIV-positive or unknown-status partners, the proportion who reported seroadaptive behaviors via the behavioral or purposely-adopted definition was 13% and 23%, respectively, for condom serosorting, 16% and 4% for seropositioning, and 17% and 12% for condom seropositioning.

Slightly less than one-third (31.1%) of HIV-positive respondent-visits were behaviorally classified as pure serosorting; men reported purposely adopting pure serosorting at 68.6% of

these visits. Similar to HIV-negative respondent-visits, a low proportion of HIV-positive respondent-visits that were classified as seropositioning or condom seropositioning per the behavioral definition were also visits where men reported purposely adopting these behaviors (14.3% and 13.5%, respectively). Modifying the denominator to include only visits where HIV-positive MSM reported having HIV-negative or unknown-status partners increased the proportion of these behaviors for both the behavioral and purposely-adopted definition for condom serosorting (12% and 19%, respectively), seropositioning (16% and 6%) and condom seropositioning (17% and 9%).

DISCUSSION

In this clinic-based population of MSM, we found that pure serosorting was the most commonly reported seroadaptive behavior, regardless of whether a behavioral definition or purposely-adopted definition was used. Overall, the prevalence of seroadaptive behaviors differed only slightly depending on the definition, but the agreement between the two measures was suboptimal and the concordance varied widely depending on the behavior. These findings suggest that the two definitions of seroadaptive behaviors are distinct and thus measuring these behaviors via men's sexual behavior history likely includes men who did not adopt the behaviors as explicit risk-reducing strategies.

The prevalence of pure serosorting that we observed using either definition is somewhat higher than previous estimates. Studies in North America that have employed a behavioral definition of pure serosorting have found that 8-31% of HIV-negative MSM and 12-21% of HIV-positive MSM engage in pure serosorting [23, 27, 79], while we noted a prevalence

of 43% and 31%, respectively. The proportion of purposely-adopted pure serosorting in our study population (47% of visits by HIV-negative men and 37% visits by HIV-positive men), is slightly higher than two Swiss studies where 38-42% of men reported purposely-adopting pure serosorting [22, 78]. There are several explanations for these somewhat disparate findings between our study and previously reported findings. First, the aforementioned studies were conducted in several different MSM populations in Europe and North America and span nearly two decades (1995-2011; with the oldest study reporting the lowest prevalence). This difference in prevalence may reflect differences in behaviors across populations and time. The latter is supported by our findings in Chapter 2, which demonstrated a substantial increase in serosorting in the past 12 years. Second, our definitions of pure serosorting differed slightly from those of previous studies. Our behavioral definition did not require MSM to report CAI with seroconcordant partners, a stipulation of previous studies that would undoubtedly lower the prevalence of the behavior. Our purposely-adopted definition was also more inclusive in that we specifically asked men if they avoided serodiscordant or unknown-status partners. Employing this definition permitted us to assess how often men choose *not* to have partners based on the partner's HIV status, instead of only examining how often men choose to have partners based on the partner's HIV status. Despite differences in the prevalence of pure serosorting between our study and others, we found that the prevalence of the other seroadaptive behaviors was largely similar to studies that have employed behavioral [23, 27, 79] or purposely-adopted [78] definitions.

In our study population, pure serosorting was not only the most commonly reported behavior, but also had the largest degree of overlap between the two definitions. We found

that 72% of HIV-negative and 69% of HIV-positive respondents who were classified as pure serosorters based on their behavior reported purposely adopting that behavior. This is similar to a partnership-level, Internet-based study of MSM [80], where the proportion of HIV-negative seroconcordant and HIV-positive seroconcordant partnerships that were purposely adopted (i.e., purposely adopted pure serosorting) was 80% and 48%, respectively. In a longitudinal study of San Francisco MSM [79], the seroadaptive strategy most adhered-to among HIV-negative MSM was pure serosorting (38% who intended to only have sex with men of concordant HIV status also reported that behavior at 12 months). Taken together, these studies suggest that, relative to other seroadaptive behaviors, pure serosorting is a common, purposely-adopted strategy that men are able to consistently execute.

Though the agreement between the two definitions was highest for pure serosorting, agreement across the other behaviors was poor overall and varied widely by behavior. The proportion of men who purposely adopted the sexual behavior they reported ranged from less than 15% for seropositioning to approximately 70% for pure serosorting, and the proportion of men who consistently adhered to their seroadaptive strategy ranged from 23-65%. The reasons for this wide range is unclear, but suggest a somewhat hierarchical classification of purposely adopted behaviors, with pure serosorting and condom serosorting reflecting behaviors that are most often adopted as conscious risk-reducing strategies whereas seropositioning and condom seropositioning are much less so. Findings from the aforementioned San Francisco study [79] support this interpretation for HIV-negative MSM – the adherence to seroadaptive strategies other than pure serosorting in that study was <10% – but not necessarily for HIV-positive MSM, where the most adhered to strategy in that population was seropositioning. Nonetheless, it is

possible that in our study population partnership formation or condom use is more often based on partner HIV status while adopting an insertive or receptive role is more likely to be influenced by partner-level factors other than HIV status [82-84] (i.e., preference for sexual role).

Though our study confirms that the two measures of seroadaptive behaviors are partially distinct from one another, the question remains – which measure of seroadaptive behaviors should be employed? From a clinical or HIV prevention perspective, the ultimate goal of measuring these behaviors is to better understand an individual’s risk of acquiring or transmitting HIV. To the extent that past sexual behaviors align with future behaviors, using a sexual behavior history to measure seroadaptive behaviors may be preferred. However, previous studies that have measured seroadaptive behaviors longitudinally have found that, depending on the behavior, only 1-47% of men who report seroadaptive behaviors at baseline will report engaging in that same behavior at 1-year follow-up [79]. That said, in many clinical settings, patients’ sexual behavior history is already collected as part of routine clinical care. This information can be (and has been [28, 36]) used to construct behavioral definitions of seroadaptive behaviors, which has been invaluable to our understanding of the association of these behaviors with HIV and STI risk. On the other hand, it is possible that reported strategies may be better predictors of future HIV acquisition and thus might be more useful than the behavioral definition to identify individuals at high risk for HIV. Using a purposely-adopted definition may also be more appropriate to develop messaging that promotes these behaviors as harm-reduction strategies, insofar as the behavioral definition (which includes men who did not purposely adopt a behavior) may mis-estimate the true prevention efficacy of seroadaptive

behaviors. However, there are no studies, to our knowledge, that have longitudinally measured purposely-adopted seroadaptive strategies over time; these types of studies are needed to determine the HIV incidence associated with these behaviors. Ultimately, it is likely that a combination of the two methods (i.e., purposely adopted behaviors that were successfully executed) may be the most sensitive measure, and settings where both measures can be used should be encouraged to do so.

This study has a number of strengths. We used two independent CASI's to capture behavioral and purposely-adopted definitions of seroadaptive behaviors, which allowed us to directly compare the two measures in the same population. Our definition of pure serosorting included partnership avoidance, a potential key seroadaptive strategy that has historically not been captured. Our research CASI was the result of considerable formative work to develop a series of seroadaptive strategy questions that could be consistently understood by our study population. There are also several limitations that merit discussion. First, although our data are helpful to describe the agreement between the two definitions of seroadaptive behaviors, the absence of a gold standard prohibits an assessment of the validity of the measures. However, ongoing work in our group includes determining which measure of seroadaptive behaviors is more strongly associated with testing newly positive for HIV/STI, a proxy indicator of the superiority of one measure over another. Second, to the extent that individuals' responses vary from one questionnaire to the next even with identical questions, our use of two independent CASI's, though also a strength of this study, may have made the comparison of some behaviors unclear (i.e., the prevalence of purposely-adopted condom serosorting was lower than behaviorally-defined condom serosorting). Third, we collected aggregate data on types of

partners as opposed to egocentric sexual network data (where men are asked specific questions about each sexual partner they have had in a specific time), an approach used in many prior studies. This does not allow us to understand how seroadaptive strategies may differ by partner. However, egocentric network data only collects information on partnerships that occur, thereby ignoring decisions not to form partnerships (i.e., partnership avoidance), an important seroadaptive strategy that was incorporated into our research CASI definition of pure serosorting. Also, insofar as our goal is to develop questions that can be used in clinical practice, aggregate data is simpler and likely much easier to incorporate into clinical or prevention counseling routines. Fourth, we categorized behaviors as “always” versus “not always” to fit the behavioral definitions of seroadaptive behaviors; this strict definition may have affected the agreement of the two measures. Fifth, data on primary and casual partners from the research CASI was collapsed in order to align more closely with the clinical CASI data. Given that seroadaptive strategies may differ by partnership type [85], it is unclear how this may have affected the agreement between the two measures. Sixth, data on sexual behavior are subject to recall bias since participants were asked about their sexual behaviors in the past 12 months. However, the same recall period was used for both CASI’s so although this may have affected the prevalence estimates, it likely did not affect the agreement. Seventh, the kappa statistic is sensitive to the prevalence of behaviors and may be artificially low for less commonly reported behaviors. Some behaviors were quite uncommon in our study population, perhaps influencing the kappa values we report. Finally, this was a clinic-based, frequently HIV-tested population of MSM where HIV status disclosure was high. How the two methods of measurement would compare in other settings is unclear.

In summary, we found that the two measures of seroadaptive behaviors – a behavioral definition and purposely-adopted definition – are distinct from one another, a distinction that may have important public health implications. The complexities in measuring seroadaptive behaviors have made it difficult to craft clear and simple public health messages about the practice, and as a result, we do not know which behaviors, if any, should be promoted and to whom. Behavioral definitions of serosorting, though useful, may not accurately measure seroadaptive behaviors as active risk-reduction strategies, and thus using this definition to inform the development of harm-reduction messaging is questionable. Ultimately, the preferred measure is likely one that better predicts an individual’s risk of acquiring HIV. To that end, future prospective studies are needed to be able to collectively define a standard method to measure seroadaptive behaviors so that the prevalence and impact of these behaviors can be appropriately identified.

TABLES AND FIGURES

Table 3.1. Definitions of four seroadaptive behaviors used in a cross-sectional seroadaptive behaviors study among PHSKC STD clinic MSM 2013-2015, by method of defining behavior

Behavior	Clinical CASI: Behavioral Definition	Research CASI: Purposely-Adopted Definition
Pure serosorting	Only partners of concordant HIV status	Choice to have HIV-concordant partners and avoid HIV-discordant/unknown-status partners was based on partner HIV status
Condom serosorting	Condoms with HIV-discordant/unknown-status partners but not with concordant partners	Choice to use condoms with HIV-discordant/unknown status partners and not HIV-concordant partners was based on partner's HIV status
Seropositioning	<u>HIV-negative MSM</u> : Insertive role with HIV-positive/unknown-status partner but receptive role with HIV-negative partners	<u>HIV-negative MSM</u> : Choice to adopt insertive role with HIV-positive/unknown partners and receptive role with HIV-negative partners was based on partner's HIV status
	<u>HIV-positive MSM</u> : Receptive role with HIV-negative/unknown-status partner but insertive role with HIV-positive partners	<u>HIV-positive MSM</u> : Choice to adopt receptive role with HIV-negative/unknown-status partners and insertive role with HIV-positive partners was based on partner's HIV status
Condom seropositioning	<u>HIV-negative MSM</u> : Condoms for receptive but not insertive anal sex with HIV-positive/unknown-status partners	<u>HIV-negative MSM</u> : Choice to use condoms for receptive but not insertive anal sex with HIV-positive/unknown-status partners was based on partner's HIV status
	<u>HIV-positive MSM</u> : Condoms for insertive but not receptive anal sex with HIV-negative/unknown-status partners	<u>HIV-positive MSM</u> : Choice to use condoms for insertive but not receptive anal sex with HIV-negative/unknown-status partners was based on partner's HIV status

Table 3.2. Demographic and behavioral characteristics of visits by PHSKC STD clinic MSM participants in a cross-sectional seroadaptive behaviors study 2013-2015, by HIV status (N=3,410)*

Characteristic	Total (N = 3,410) N (%)	HIV-negative (N = 2,909) N (%)	HIV-positive (N = 501) N (%)
Age			
18-29	1,534 (45.0)	1,431 (49.2)	103 (20.6)
30-39	958 (28.1)	780 (26.8)	178 (35.5)
≥ 40	916 (26.9)	696 (23.9)	220 (43.9)
Race/ethnicity			
White, NH	2,234 (65.8)	1,875 (64.7)	359 (71.8)
Black, NH	276 (8.1)	222 (7.7)	54 (10.8)
Asian, Pacific Islander or Hawaiian, NH	250 (7.4)	246 (8.5)	4 (0.8)
Native American/Alaskan Native, NH	39 (1.2)	28 (1.0)	11 (2.2)
Other, NH	208 (6.1)	183 (6.3)	25 (5.0)
Hispanic	390 (11.5)	343 (11.8)	47 (9.4)
Had HIV test, past 12 months	2,303 (74.9)	2,183 (81.7)	120 (29.6)
Discloses HIV status to partner	3,284 (96.4)	2,793 (96.1)	491 (98.2)
Asks partner to disclose his HIV status	3,271 (96.0)	2801 (96.4)	470 (94.0)
Methamphetamine use, past 12 months	514 (15.1)	315 (10.8)	199 (39.7)
Number of MSP past 12 months, median (IQR)	6 (3-12)	6 (3-11)	6 (3-12)
Had HIV-discordant/unknown-status partner, past 12 months	1,735 (50.9)	1,410 (48.5)	325 (64.9)

Abbreviations: IQR, interquartile range; MSP, male sex partner; NH, non-Hispanic

*Column numbers may not sum to total due to missing values; proportions are calculated from a denominator that does not include missing data

Table 3.3. Prevalence and agreement of seroadaptive behaviors in the prior 12 months using two definitions, reported by PHSKC STD clinic MSM study participants at 3,410 study visits 2013-2015*†‡

	Prevalence		Agreement			Kappa
	Clinical CASI: Behavioral definition	Research CASI: Purposely- adopted definition	Concordance	Purposely adopted reported behaviors	Engaged in purposely reported behaviors	
	(A)	(B)				
	N (%)	N (%)	N	(%)	(%)	
HIV-negative respondent						
Pure serosorting (N=2,909)	1,245 (42.8)	1,379 (47.4)	890	71.5	64.5	0.42
Condom serosorting (N=2,710)	169 (6.2)	302 (11.1)	69	40.8	22.9	0.23
Seropositioning (N=2,704)	211 (7.8)	57 (2.1)	25	11.9	43.9	0.16
Condom seropositioning (N=2,705)	225 (8.3)	155 (5.7)	45	20.0	29.0	0.18
HIV-positive respondent						
Pure serosorting (N=501)	156 (31.1)	187 (37.3)	107	68.6	57.2	0.43
Condom serosorting (N=462)	38 (8.2)	58 (12.6)	20	52.6	34.5	0.35
Seropositioning (N=459)	49 (10.7)	18 (3.9)	7	14.3	38.9	0.16
Condom seropositioning (N=460)	52 (11.3)	26 (5.7)	7	13.5	26.9	0.11

*Column C = Number of respondents who report “Yes” on both CASI’s

Column D = Among those who reported behavior in sexual history (clinical CASI), the proportion who also reported purposely adopting behavior (research CASI) (i.e., Column C/Column A)

Column E = Among those who reported purposely adopting behavior (research CASI), the proportion who also reported behavior in sexual history (clinical CASI) (i.e., Column C/Column B)

†For all behaviors, numbers are presented for those who reported “always” engaging in behavior

‡Sample sizes for each behavior vary owing to different amounts of missing data for each behavior

CHAPTER 5. Conclusion

In this dissertation, we conducted three analyses from two studies of Seattle MSM. In a retrospective review of medical records from the PHSKC STD clinic and GCHP 2002-2013, we identified changes in sexual behavior – an increase in serosorting and decrease in NCCAI – that signify a shift toward safer behaviors. This change paralleled a decline in the HIV test positivity for all MSM. For our ongoing cross-sectional study of seroadaptive behaviors among PHSKC STD clinic patients, we capitalized on the clinic’s existing computerized patient intake system to develop a method to recruit men into the study. Using this approach, we enrolled MSM at over one-half of eligible clinic visits. Among our enrolled study population, we found that the two measures of seroadaptive behaviors (behavioral versus purposely-adopted) were distinct, and that behavioral definitions likely include men who did not adopt behaviors as explicit risk-reduction strategies.

Findings from these studies have several important implications. First, the pervasiveness of these behaviors indicate that sexual behavior recommendations should match the realities of what MSM are willing and able to do to prevent HIV. Consistent condom use should continue to be promoted as the best strategy, but the individual needs of MSM should be addressed in order to create a personalized road map to safer sex practices. Second, our novel recruitment strategy holds promise for future cross-sectional studies to enroll large numbers of study participants at low cost. This mechanism may also be ideal to screen patients and/or to conduct the initial approach with patients (i.e., to describe the study and ask if the individual may be interested) for randomized controlled trials or observational cohort studies. Finally, findings

from our cross-sectional seroadaptive behaviors study demonstrate the complexities in measuring these behaviors but motivates the initiation of longitudinal studies of MSM to better understand which measure better predicts HIV acquisition risk.

Our studies also highlight several gaps in seroadaptive behaviors research that may inform future studies. First, though our data are helpful to describe the prevalence of seroadaptive behaviors, we did not capture the motivations or perceived benefits and barriers to adopting these behaviors. Future research should incorporate qualitative studies with MSM to elucidate these factors, an approach which may identify novel seroadaptive behavior strategies and inform the development of messaging to promote select behaviors. Second, our study population was limited to MSM in Seattle. There is a paucity of seroadaptive behaviors research from the Southern and Southeastern US, areas with some of the highest HIV rates in the US [1]. Third, there is a need for enhanced behavioral surveillance in the US to monitor changes in sexual behavior among MSM. Our trends analysis (Chapter 2) underscores the benefit of capturing these data to help explain changes in population-level HIV and STI rates, but the PHSKC STD clinic is the only STD clinic in the US, to our knowledge, that has systematically monitored these behaviors for over a decade. Although CDC's National HIV Behavioral Surveillance System (NHBS) [86] collects data on behavioral serosorting [27, 87, 88], it does not collect national data on purposely-adopted seroadaptive behaviors and NHBS's method of data collection may over-estimate behaviors with main partners. Fourth, as the number of HIV-infected MSM on antiretroviral therapy increases and the number of HIV-uninfected MSM on pre-exposure prophylaxis (PrEP) grows, it is critical to keep a pulse on how behaviors are evolving. For example, it is unclear if former HIV-negative serosorters who are

now taking PrEP will have CAI with an HIV-positive partner. As noted above, enhanced behavioral surveillance can allow us to understand what behaviors these newer ones (i.e., behaviors while on PrEP) are replacing. But it is also necessary to understand the HIV and STI risk of these novel behaviors. To that end, studies and sentinel surveillance sites should measure newer strategies in order to create an evidence base from which to develop recommendations about these behaviors. Finally, there is a need for longitudinal studies to measure purposely-adopted seroadaptive behaviors among MSM. This type of study will allow us to understand which strategies are adopted and consistently used, with which partners they are used, and what is the HIV incidence associated with each strategy. Only with comprehensive and prospective measurement of these strategies will we be able to fully recognize the risks and/or benefits of these behaviors.

In conclusion, seroadaptive behaviors are common, complex, and evolving. For some men, these behaviors represent strategies that they can use to prevent themselves or their partners from acquiring HIV, but clear and concise messages about the behaviors are absent. As we enter an era of implementing new biomedical prevention strategies, comprehensive monitoring of these behaviors is critical to identify how the population's behaviors are changing and the potential impact on HIV and STI rates.

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