Title
HIV Transmission Among Men Who Have Sex With Men: Tools, Risks, and Consequences

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Publication Date
2016

Peer reviewed|Thesis/dissertation

HIV Transmission Among Men Who Have Sex With Men: Tools, Risks, and Consequences

by

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DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

Epidemiology and Translational Sciences

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

HIV Transmission Among Men Who Have Sex With Men:

Tools, Risks, and Consequences

Yea-Hung Chen

Abstract

The focus of this dissertation is estimating the distribution of behavioral patterns prior to HIV infection—including behaviors such as serosorting and use of pre-exposure prophylaxis—among newly HIV-infected San Francisco MSM. These quantities have been surprisingly elusive, particularly for the complex behavioral patterns considered in our studies. Though officials and researchers have hypothesized—and sometimes assumed—that HIV infection primarily occurs among high-risk MSM, it is alternatively possible that infection mostly occurs among relatively low-risk MSM, since there are more low-risk MSM in San Francisco than high-risk MSM. Understanding of these quantities could help identify what groups of San Francisco MSM should be reached by HIV prevention.

The 2nd chapter of this dissertation examines per-act risks for HIV transmission, which are a crucial basis for a mathematical model we developed and used to estimate the distribution of prior behavioral patterns among newly HIV-infected San Francisco MSM. The 3rd chapter presents the model and its findings. Finally, the 4th chapter examines possible barriers to intervening on the risk group identified via the model.

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Chapter 1

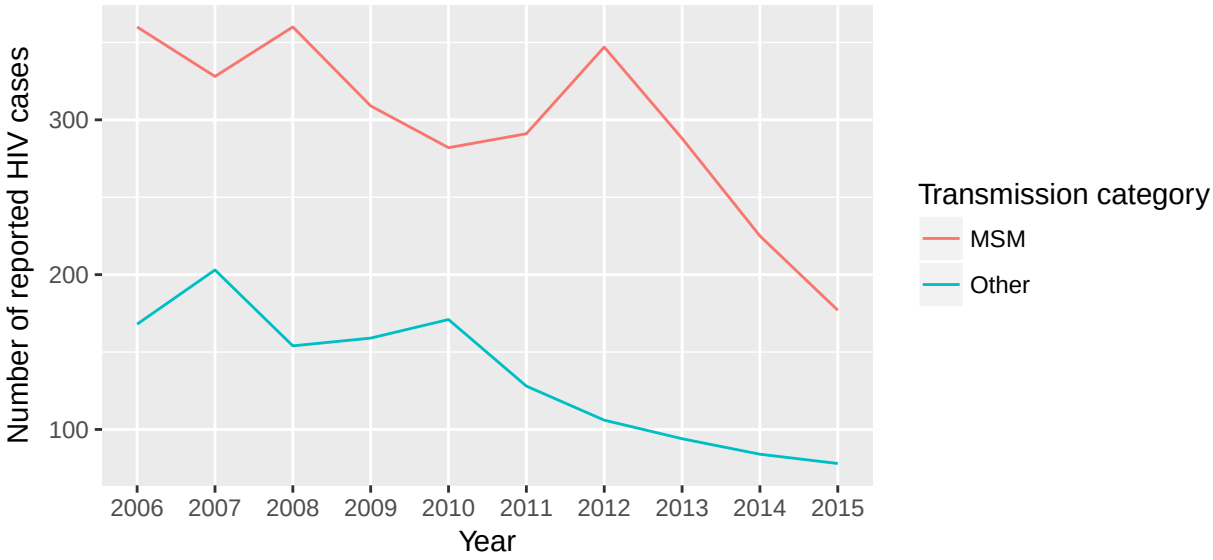
Background

1.1 HIV among San Francisco MSM

In San Francisco, a majority of human immunodeficiency virus (HIV) infections occur among men who have sex with men (MSM). Non-injecting MSM made up 69% of the 255 HIV cases newly reported in the city in 2015, while MSM who inject drugs made up an additional 10% of reported cases.[1] The 177 cases reported among non-injecting MSM in 2015 represent a low—down 51% from the number reported in 2006[1] (Figure 1.1)—and follow a dramatic city-wide decrease in the number of reported cases of acquired immune deficiency syndrome (AIDS), the third stage of HIV infection (Figure 1.2).

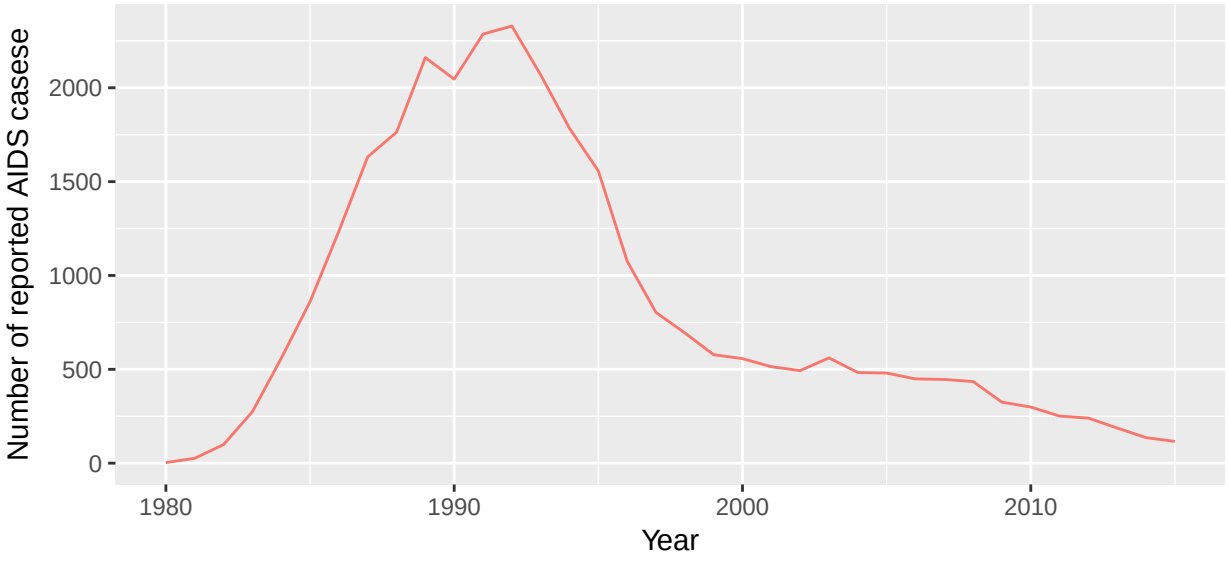
San Francisco's decades-long success in reducing HIV infections among MSM is attributable to various prevention approaches, beginning with efforts in the 1980s and 1990s encouraging behavioral strategies such as condom use.[2] The 1990s saw the rise of antiretroviral medications to treat HIV-infected individuals, which were recognized as having a possible preventative effect on onward transmission.[3] Meanwhile, new behavioral strategies emerged.

Figure 1.1: Number of reported HIV cases in San Francisco, 2006–2015, by transmission category.



Abbreviations: MSM, men who have sex with men.
Other includes MSM who inject drugs, other men, women, and transgender individuals.
The data are from the San Francisco Department of Public Health.[1]

Figure 1.2: Number of reported HIV cases in San Francisco, 1980–2015.



The data are from the San Francisco Department of Public Health.[1]

Serosorting, for example, is the practice of only having intercourse with partners perceived to be HIV-concordant.[4–6] The preventative efficacy of such behaviors is controversial.[6]

The current decade has seen San Francisco lead the way with pharmaceutical approaches to HIV prevention; indeed, the combination of strategies has been termed the "San Francisco model."[7] In 2010, the city adopted the test-and-treat approach, a form of treatment as prevention: frequent testing of those at risk for infection and immediate treatment of newly diagnosed cases to prevent onward transmission.[8] Between 2011 and 2014,[9] the city began seeing uptake among MSM of a newly available antiretroviral strategy for HIV-uninfected individuals: use of tenofovir disoproxil fumarate and emtricitabine as pre-exposure prophylaxis (PrEP).

1.2 Uncertainty

Despite continued reductions in the number of HIV cases reported among San Francisco MSM and the potential offered by the newer pharmaceutical strategies, there are uncertainties and areas of concern, particularly given reported decreases in consistent condom use among HIV-uninfected San Francisco MSM.[9] A key uncertainty is what groups of MSM—if any—should be targeted. Indeed, the Centers for Disease Control and Prevention (CDC)'s recommended indications for PrEP use among MSM include various behaviors.[10,11]

The focus of this dissertation is estimating the distribution of behavioral patterns prior to HIV infection—including behaviors such as serosorting and PrEP use—among newly HIV-infected San Francisco MSM. These quantities have been surprisingly elusive, particularly for the complex behavioral patterns considered in our studies. Though officials and researchers have hypothesized—and sometimes assumed—that HIV infection primarily occurs among

high-risk MSM, it is alternatively possible that infection mostly occurs among relatively low-risk MSM, since there are more low-risk MSM in San Francisco than high-risk MSM. Understanding of these quantities could help identify what groups of San Francisco MSM should be reached by HIV prevention.

The 2nd chapter of this dissertation examines per-act risks for HIV transmission, which are a crucial basis for a mathematical model we developed and used to estimate the distribution of prior behavioral patterns among newly HIV-infected San Francisco MSM. The 3rd chapter presents the model and its findings. Finally, the 4th chapter examines possible barriers to intervening on the risk group identified via the model.

Chapter 2

Per-act risks of HIV transmission among MSM

2.1 Introduction

Researchers have long been interested in estimating the probabilities of HIV transmission associated with single acts (occurrences) of male-male anal intercourse. Estimated per-act risks (PARs) are available for numerous types of anal intercourse, in various contexts.[12–14] The quantities are of interest for various reasons: they can inform prevention strategies,[13] encourage reduction of risk behaviors (see, for example, CDC's online *HIV Risk Reduction Tool*), and may offer insight regarding HIV epidemics. Regarding the last of these reasons, per-act risks are the basis for mathematical models for HIV infection, such as the one presented and discussed in the next chapter.

In this chapter, we present updated per-act risks of HIV transmission, using data from 4 cohorts of MSM. The motivating question is methodological: the original analysis of the 4

cohorts used a novel pooled-logistic approach,[15] instead of the simple Bernoulli approach used in numerous prior studies.[12,13,16–18] We were curious whether the original study's estimates—as well as its finding that per-act risks differ by age, race/ethnicity, and behavioral risk factors—are dependent on the estimation method.

2.2 Methods

2.2.1 Data

The analysis uses data from 4 longitudinal cohorts of high-risk HIV-uninfected MSM living in the US, all followed for HIV seroconversion at 6-month intervals. Jumpstart enrolled 2,189 MSM (from Chicago, Denver, and San Francisco) in 1993–1994 and followed them for up to 18 months. The Vaccine Preparedness Study (VPS) enrolled 3,257 MSM (from Boston, Chicago, Denver, New York Philadelphia, San Francisco, and Seattle) in 1995 and followed them for up to 18 months. The VAX004 trial randomized 5,095 MSM (from 61 sites, most in the US) to an HIV vaccine or placebo in 1998–1999 and followed them for up to 36 months. Finally, the EXPLORE trial randomized 4,295 MSM (from Boston, Chicago, Denver, New York, San Francisco, and Seattle) to an intensive behavioral intervention or standard counseling in 1999–2001, and followed them for up to 48 months. Individuals in the treatment arms of trials were not excluded from the analysis, since the treatments were not effective.

We dropped all person-visits with no reported sexual acts. This left a total of 45,419 person-visits: 4,168 from Jumpstart, 4,833 from VPS, 19,314 from VAX004, and 17,104 from EXPLORE. There were 52 person-visits with serconversions in Jumpstart, 51 in VPS, 328

in VAX004, and 199 in EXPLORE.

Retrospective recall of sexual behaviors occurred at each person-visit. The data allow for classification of each reported act of anal intercourse by 3 dimensions: condom use (yes or no), position of the respondent (receptive or insertive), and HIV status of the partner (uninfected, infected, or unknown to the respondent). This results in a total of 12 possible classification types. Additionally, the surveys assessed for acts of receptive oral intercourse with ejaculation.

2.2.2 Bernoulli analysis

The Bernoulli approach uses maximum-likelihood estimation, using a Bernoulli expression for the likelihood function:

$$\left(1 - \prod_k (1-\pi_k)^{n_{jk}}\right)^{x_j} \left(\prod_k (1-\pi_k)^{n_{jk}}\right)^{1-x_j}$$

Here, j is an index for person-visit, k is an index for type of contact, π_k is per-act risk, n_{jk} is number of acts, and x_j is seroconversion status (taking a value of 1 if seroconversion occurs, and 0 otherwise). The likelihood function treats HIV infection as being probabilistically independent across sexual acts and assumes a constant PAR for each type of sexual contact. We obtained maximum-likelihood estimates using the Broyden-Fletcher-Goldfarb-Shanno algorithm, as implemented in the *maxLik* package[19] for R. We computed Wald-based 95% confidence intervals for the estimates using standard errors provided by the package.

We first estimated PARs using the pooled data and contact types used in the original analysis.[15] Then, we used stratification to estimate PARs by cohort and (separately)

by possible risk groups (age group, race/ethnicity, number of partners, injection drug use, methamphetamine and popper use, and sexually transmitted infections). These analyses allow for heterogeneity across cohorts and risk groups, although not among individuals within the aggregations. We compared the PARs across cohorts and risk groups using Wald tests, with standard errors provided by the *maxLik* package.

In various sensitivity analyses, we used other estimation algorithms, different starting values for the algorithms, different pooled cohorts, and different sets of types of sexual contact. In addition, we assessed for differences in PARs using bootstrapped CIs rather than the Wald tests. Finally, to assess potential sensitivity of the Bernoulli method to a small number of outlying values, we repeated analyses after trimming numbers of acts at 50.

2.2.3 Pooled-logistic analysis

The pooled-logistic approach was described in detail in the appendix to the study's manuscript.[15] Briefly, it involves using a pooled-logistic model for seroconversion, with adjustment for the risk groups, the number of acts, and the type of sexual contact. The model can then be used to compute two probabilities of seroconversion for each person-visit: one using observed data and one assuming no acts of the contact type of interest. In conjunction with a Bernoulli expression, these probabilities allow for computation of a PAR for each person-visit and contact type of interest. Finally, these per-act risks can be averaged to obtain overall estimates of PARs. The original analysis obtained these averages using equal weighting of person-visits. In our updated analysis, we also averaged the person-visit PARs by weighting each person-visit PAR by the person-visit's number of acts (of the type of interest).

2.3 Results

Table 2.1 shows PAR estimates by method. Three methods are represented: the Bernoulli method and both variants of the pooled-logistic approach. These analyses involve the same pooled data and types of contact used in the original analysis.[15] The Bernoulli estimates are similar to the corresponding estimates from the pooled-logistic approach with weighting by number of acts. In comparison, the original analysis—the pooled-logistic approach with equal weighting of person-visits—resulted in substantially larger estimates for the PARs via condomless receptive anal intercourse (C-RAI) with HIV-infected and unknown-status partners.

Table 2.2 shows Bernoulli PAR estimates by cohort. Statistical tests reveal differences by cohort, and notably suggest that the per-act risk via C-RAI with HIV-infected partners differs between VAX004 and EXPLORE. That finding persisted in a sensitivity analysis trimming numbers of acts at 50.

Table 2.3 shows Bernoulli estimates using pooled data from Jumpstart, VPS, and EXPLORE. This pooled analysis excludes VAX004 due to the relatively low PAR estimates associated with the cohort. Using this pooled data, the estimated PARs via C-RAI with HIV-infected and unknown-status partners are 0.64% (95% CI: 0.43–0.84%) and 0.21% (95% CI: 0.13–0.29%), respectively.

Figure 2.1 shows estimated PARs via C-RAI, stratified by various risk groups of interest, again estimated using data from Jumpstart, VPS, and EXPLORE. Statistical tests for the differences suggest no statistically significant between-group differences. These results were qualitatively unchanged when we included all 4 cohorts, or only the VPS, VAX004, and

Table 2.1: Estimates of per-act risk (and 95% confidence intervals, in parentheses), by method, using data from 3 cohorts of men who have sex with men (Vaccine Preparedness Study, 1995–1997; VAX004, 1998–2002; and EXPLORE, 1999–2005).

		Pooled-logistic	
Contact type	Bernoulli	Acts*	Equal†
HIV-infected			
C-RAI	0.26 (0.18, 0.34)	0.33 (0.22, 0.45)	0.73 (0.45, 0.98)
C+RAI	0.06 (0.03, 0.09)	0.04 (0.00, 0.08)	0.08 (0.00, 0.19)
C-IAI	0.05 (0.02, 0.08)	0.07 (0.02, 0.14)	0.22 (0.05, 0.39)
Unknown‡			
C-RAI	0.31 (0.23, 0.38)	0.30 (0.22, 0.38)	0.49 (0.32, 0.62)
C+RAI	0.11 (0.07, 0.14)	0.07 (0.02, 0.13)	0.11 (0.02, 0.20)
HIV-uninfected			
C-RAI	0.01 (0.01, 0.02)	0.01 (0.00, 0.03)	0.03 (0.00, 0.11)
C+RAI	0.09 (0.07, 0.11)	0.06 (0.03, 0.09)	0.12 (0.06, 0.18)

Abbreviations: C-RAI, condomless receptive anal intercourse; C+RAI, condom-protected receptive anal intercourse; C-IAI, condomless insertive anal intercourse.
*The pooled-logistic approach with weighting by number of acts. †The pooled-logistic approach with equal weighting of person-visits. The estimates were also reported in the original analysis.[15] ‡HIV status of partner unknown to respondent.

Table 2.2: Bernoulli estimates of per-act risks (and 95% confidence intervals, in parentheses), by cohort of men who have sex with men (Jumpstart, 1993–1995; VPS, 1995–1997; VAX004, 1998–2002; and EXPLORE, 1999–2005).

Contact type	Jumpstart	VPS	VAX004	EXPLORE
HIV-infected				
C-RAI	0.78 (0.00, 1.60)	0.95 (0.07, 1.83)	0.13 (0.06, 0.21)	0.61 (0.38, 0.84)
C+RAI	0.01 (0.00, 0.12)	0.06 (0.00, 0.22)	0.08 (0.04, 0.12)	0.00 (0.00, 0.03)
C-IAI	0.03 (0.00, 0.10)	0.14 (0.00, 0.35)	0.04 (0.01, 0.07)	0.02 (0.00, 0.06)
Unknown*				
C-RAI	0.13 (0.00, 0.31)	0.01 (0.00, 0.21)	0.34 (0.21, 0.48)	0.26 (0.16, 0.37)
C+RAI	0.16 (0.08, 0.25)	0.14 (0.04, 0.24)	0.14 (0.09, 0.20)	0.09 (0.04, 0.13)
C-IAI	0.04 (0.00, 0.11)	0.02 (0.00, 0.15)	0.06 (0.00, 0.12)	0.05 (0.00, 0.10)
Other†	0.01 (0.00, 0.01)	0.02 (0.01, 0.03)	0.03 (0.03, 0.04)	0.02 (0.01, 0.02)

Abbreviations: VPS, Vaccine Preparedness Study; C-RAI, condomless receptive anal intercourse; C+RAI, condom-protected receptive anal intercourse; C-IAI, condomless insertive anal intercourse.
*HIV status of partner unknown to respondent. †Other: condom-protected insertive anal intercourse with HIV-infected and unknown-status partners, acts with HIV-uninfected partners, and receptive oral intercourse with ejaculation.

EXPLORE cohorts, or when we used bootstrapping to assess differences (results not shown).

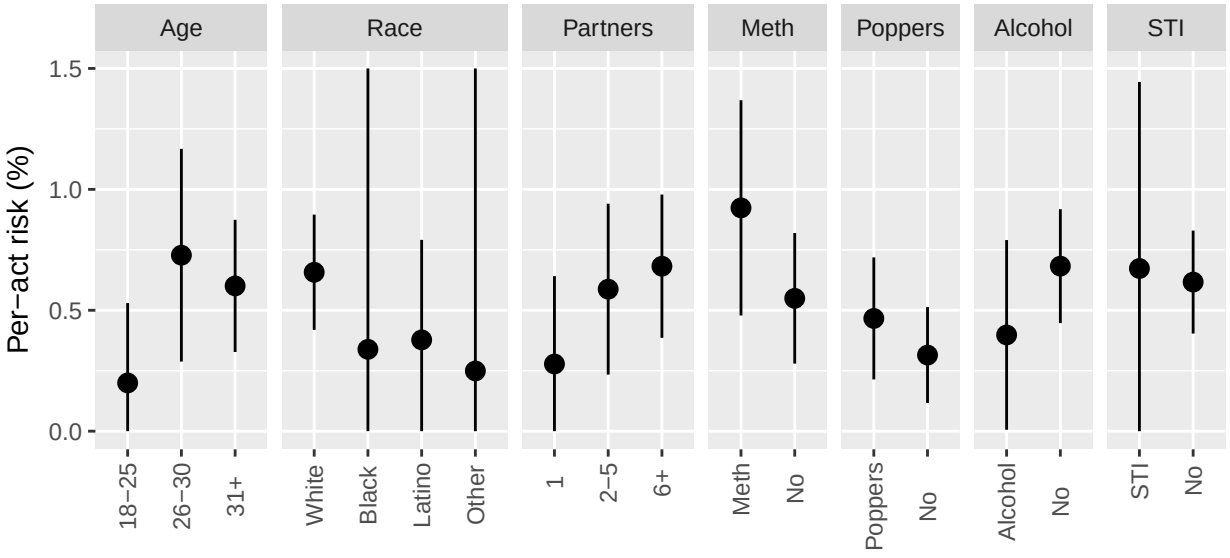
2.4 Discussion

This reanalysis of data from 4 cohorts of MSM provides insight regarding methods for estimating per-act risks, suggesting that the traditional Bernoulli method is similar to the pooled-logistic approach with weighting by acts. Meanwhile, the reanalysis uncovers previously unnoticed differences by cohort. We hypothesize that the relatively low PAR estimates obtained using data from VAX004 are attributable to over-reporting of numbers of acts in the cohort or large representation in the cohort of individuals with low susceptibility for HIV infection, or both. Finally, we hypothesize that the failure of the Bernoulli method to confirm previously reported differences across risk groups is attributable to the methods of comparison.

A major limitation of the study is the self-reported nature of the data. We acknowledge, for example, that infection statuses of sexual partners and numbers of sexual acts were almost certainly reported with error, possibly even differentially across groups of interest. However, sensitivity analysis (not shown) with trimming of numbers of acts resulted in no substantial changes in any of our findings. An additional weakness of the study is the failure of the data to provide information on HIV treatment or viral suppression among HIV-infected sexual partners. We believe this to be a relatively minor concern, as viral suppression was unlikely to have been very common during our data's early era of antiretroviral medication.

Despite these limitations, we believe that our study provides valuable insight to possible connections between two methods for estimating per-act risks: the pooled-logistic approach with weighting by acts (a method, to the best of our knowledge, never reported elsewhere)

Figure 2.1: Bernoulli estimates of per-act risks via condomless receptive anal intercourse, stratified by risk group, using data from 3 cohorts of men who have sex with men (Jumpstart, 1993-1995; Vaccine Preparedness Study, 1995–1997; and EXPLORE, 1999–2005).



Abbreviations: STI, sexually transmitted infection.
The y axis is truncated at 1.5%.

and the traditional Bernoulli approach. We recommend further research regarding this relationship as well as the hypothesized issues relating to the statistical comparisons. We hypothesize that the two estimation methods provide similar point estimates but that traditional tools for comparison of estimates from the Bernoulli method—the Wald method and bootstrapping—have undesirable statistical properties.

Table 2.3: Bernoulli estimates of per-act risks (and 95% confidence intervals, in parentheses), using pooled data from 3 cohorts of men who have sex with men (Jumpstart, 1993–1995; Vaccine Preparedness Study, 1995–1997; and EXPLORE, 1999–2005).

Contact type	PAR (95% CI)
HIV-infected	
C-RAI	0.63 (0.43, 0.84)
C+RAI	0.00 (0.00, 0.04)
C-IAI	0.04 (0.00, 0.07)
Unknown*	
C-RAI	0.21 (0.13, 0.29)
C+RAI	0.11 (0.07, 0.15)
C-IAI	0.05 (0.01, 0.08)
Other†	0.01 (0.01, 0.02)

Abbreviations: PAR, per-act risk; CI, confidence interval; C-RAI, condomless receptive anal intercourse; C+RAI, condom-protected receptive anal intercourse; C-IAI, condomless insertive anal intercourse.
*HIV status of partner unknown to respondent. †Other: condom-protected insertive anal intercourse with HIV-infected and unknown-status partners, acts with HIV-uninfected partners, and receptive oral intercourse with ejaculation.

Chapter 3

Prior behavioral patterns among newly HIV-infected MSM

3.1 Introduction

As indicated in the last chapter, per-act risks are a crucial basis for mathematical models of infection. This chapter presents such a model. The research objective is to estimate the distribution of behavioral patterns prior to HIV infection among San Francisco MSM newly infected with HIV in 2014. A key feature of our study is that it uses a mutually exclusive classification of behavioral patterns that includes modern behaviors such as serosorting and PrEP use.

The quantities of interest have been elusive. Though numerous prior studies have estimated risks,[13,15] relative risks,[20] or odds ratios[21,22] of HIV infection associated with behaviors, we are not aware of any study that has estimated our quantities of interest, and certainly not for the same population and time period. One study estimated population-attributable

fractions,[23] but this measure is the proportion of additional infections attributable to the exposure, not the percent of newly infected individuals who had the exposure. Additionally, this study did not examine modern behaviors such as serosorting.

The scarcity of information on the quantities of interest is not due to lack of interest. Officials and researchers have hypothesized—and sometimes assumed—that HIV infection primarily occurs among high-risk MSM. However, it is in fact alternatively possible that infection mostly occurs among relatively low-risk MSM, since there are more low-risk MSM in San Francisco than high-risk MSM. Clarification of this uncertainty could help inform targeted prevention efforts among San Francisco MSM.

In this chapter, we present a novel modeling approach to estimate the distribution of prior behavioral patterns among San Francisco MSM newly infected with HIV in 2014, a year in which roughly 10% of HIV-uninfected San Francisco MSM accessed PrEP.[9] As a secondary aim, we estimated the probabilities of infection associated with these groups.

3.2 Methods

Though the research question is fairly simple, it can not be directly answered via data. Surveys of newly HIV-infected individuals are challenging and a longitudinal study would require a large population since the incidence rate in the population is low.[24] Thus, to address the research question, we used a data-informed modeling approach.

3.2.1 Data

Table 3.1 summarizes the model's data sources.

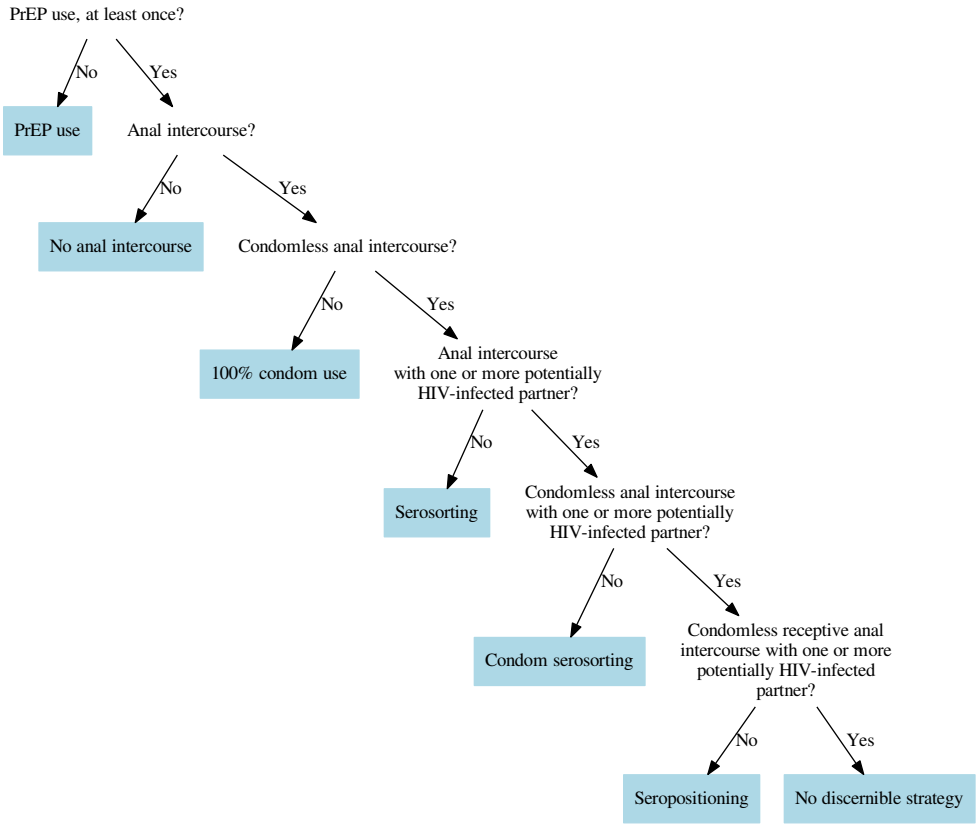
We primarily relied on data from San Francisco's third (MSM3) and fourth (MSM4) im-

plementations of the CDC's National HIV Behavioral Surveillance for MSM (NHBS MSM). Recruitment occurred via time-location sampling, and captured diverse samples of MSM, believed to be generalizable to adult MSM who visit venues included in the sampling frame; these include bars or dance clubs, parks and street locations, cafes and restaurants, and social organizations.[25] Sampling for MSM3 and MSM4 took place in 2011 and 2014, respectively. We only used data from MSM who reported being HIV-uninfected, under the rationale that perceived status—not true infection status—is what informs behavior; this left 353 individuals from MSM3 and 279 individuals from MSM4.

The surveys collected detailed behavioral information from each respondent on up to five recent sexual partnerships. These responses allowed for measurement of the 7 mutually exclusive behavioral patterns considered in the study (Figure 3.1): accessing PrEP at least once, no anal intercourse, 100% condom use (not having condomless anal intercourse), serosorting (not having anal intercourse with potentially HIV-infected partners), condom serosorting (not having condomless anal intercourse with potentially HIV-infected partners), seropositioning (not having receptive anal intercourse with potentially HIV-infected partners), and no discernible strategy (describing individuals with none of the other behavioral patterns). Serosorting and seropositioning are often termed seroadaptive behaviors.[6,29] The names of these categorizations are consistent with prior literature[6,9,29]; our use does not imply that the patterns always result from intent. The survey did not assess for frequency or persistence of PrEP use.

Additional questions in the survey—involving demographics, sexual behaviors, and sexual infection—permitted measurement of indication for PrEP use (ie, possible eligibility for PrEP use), as defined via two methods proposed by the CDC: an assessment tool and a risk

Figure 3.1: Classification scheme for behavioral patterns among HIV-uninfected men who have sex with men. The scheme is an adaptation of previously defined grouping systems.[6,29]



index.[10,11]

Several additional estimates supplemented the primary data. We used estimates of prevalences of durable viral suppression (viral load less than 200 copies/ml, consistently across time) from the MSM subset of the CDC's 2014 implementation of the Medical Monitoring Project.[26] We used 3 prevalence estimates (Alison Hughes, email communication, 2016): one for all main partnerships (68.4%), one for casual partnerships involving condomless receptive anal intercourse (63.2%), and one for casual partnerships not involving condomless receptive anal intercourse (84.4%).

To capture the effect of accessing PrEP at least once, we used estimates of PrEP efficacy obtained from two large clinical trials among MSM: 43.9% and 86.7%.[27,28] For the main component of our analysis, we used the midpoint between the two efficacy estimates, 65.3%. We believe this value to be consistent with what might be expected with moderate-to-high levels of PrEP persistence. For comparison, the iPrEx trial estimates that if the medication is used on at least 90% of days, efficacy is 73%, slightly higher than our midpoint of 65.3%. Moreover, 7% of individuals in our sample who accessed PrEP did not report receiving it from a provider, implying low persistence for at least 7% of the group.

We used estimates for per-act risks of HIV infection reported in a recent meta-analysis.[14] Our model allows for transmission via 4 types of sexual contact with HIV-infected, virally nonsuppressed partners: condomless receptive anal intercourse (per-act risk of 1.38%), condom-protected receptive anal intercourse (0.28%), condomless insertive anal intercourse (0.11%), and condom-protected insertive anal intercourse (0.02%). Finally, we used an estimated population size, 44,161, from a recent modeling study (Alison Hughes, email communication, 2016).

3.2.2 Model

We simulated a population of 44,161 HIV-uninfected MSM, randomly jointly assigning a behavioral pattern (Figure 3.1) and indications for PrEP use to each individual, using estimates from MSM4. Essentially, we simply resampled individuals from MSM4 with replacement.

We then randomly assigned a categorized number of sexual partners (0, 1, 2, 3, 4, 5, or more than 5) to each individual conditionally on behavioral group, using multinomial distributions and group-specific probability estimates from MSM3 and MSM4. If an individual had 6 or more sexual partners, we randomly assigned the number of partners by randomly generating from a standard uniform distribution and applying the random value to a linear-spline fit of the MSM3- and MSM4-based cumulative distribution function for the individual's behavioral group (each fit is simply a straight line through the observed distribution points).

We randomly assigned partnership data from MSM3 and MSM4, by partnership, to each simulated individual, conditionally on behavioral group and number of partners. In other words, for each simulated partnership for each simulated individual, we randomly sampled a partnership from the pool of partnerships reported by survey respondents with the same behavioral group and categorized number of partners as the simulated individual.

If a simulated individual had more than 5 sexual partners, we randomly sampled additional partnerships from the set of casual partners reported by respondents of the same behavioral group as the individual of interest. The sampling process takes advantage of the pool of reported partnerships, rather than assuming mixing patterns for partnership formation.

Because MSM3 and MSM4 assessed HIV statuses of sexual partners via respondent report, misclassificaton was possible. We assumed that partners reported as being infected were in fact infected. However, for each partner reported as being uninfected, we randomly imputed HIV infection using a Bernoulli distribution and a probability equal to the MSM4-estimated prevalence of unrecognized infection among self-reported HIV-uninfected MSM. Similarly, for each partner reported as having an unknown HIV status, we randomly imputed HIV infection using a Bernoulli distribution and a probability equal to the MSM4-estimated prevalence of HIV.

As MSM3 and MSM4 did not elicit information regarding antiretroviral use among HIV-infected sexual partners, we randomly assigned durable viral suppression using Bernoulli distributions with probability estimates from the Medical Monitoring Project. As explained in the Data subsection, we used 3 prevalence estimates (for each of 3 probability distributions), defined by partnership type (main or casual) and the occurrence of condomless receptive anal intercourse. We did not allow partners with unrecognized infection—ie, partners reported as being uninfected who were in fact infected—to be virally suppressed.

We allowed for error in the reporting of numbers of sexual acts. Specifically, if the number of reported acts exceeded 10, we randomly assigned the number of acts using a normal distribution with a mean equal to the self-reported count and a standard deviation equal to 10% of the mean.

We computed each simulated individual's probability of infection using per-act risks of infection and the number of sexual acts with HIV-infected partners who were not durably virally suppressed. As explained in the Data subsection, we allowed for HIV infection via 4 types of sexual contact with virally nonsuppressed HIV-infected partners: condomless recep-

tive anal intercourse, condom-protected receptive anal intercourse, condomless insertive anal intercourse, and condom-protected insertive anal intercourse. We assumed that per-act risks of infection are equal to 0 via sex with HIV-uninfected partners or virally suppressed HIV-infected partners. We accounted for PrEP efficacy among individuals who accessed PrEP by multiplying the probability of infection by 1 minus the efficacy. Finally, we randomly assigned each individual's infection status using a Bernoulli distribution and the individual's calculated probability of infection.

In our primary set of analysis, we used constant values for the probability distributions' parameters, using estimates from the aforementioned data sources. We repeated the modeling exercise 1,000 times, and report the means of output values across replications. We conducted all analysis in R.

In our uncertainty analysis, described in the following subsection, we allowed the probability distributions' parameters to vary across simulation runs.

3.2.3 Uncertainty analysis

For our uncertainty analysis, we used Latin hypercube sampling[30] to allow values of some of the probability distributions' parameters to vary across simulation runs. Computational demands limited the number of parameters we were able to include in the analysis. In reducing the possible list, we prioritized parameters that were likely to impact HIV transmission, based on current scientific understanding. Additionally, we favored parameters that have estimates that originate from relatively small samples or are not within 0.01 of 0 or 1 on a probability scale.

Ultimately, we selected 6 distributional parameters (Table 3.2): (1) the prevalence of

no discernible strategy among MSM who accessed PrEP at least once, (2) the prevalence of HIV among unknown-status partners, (3) the prevalence of recognized infection among HIV-infected MSM, (4) the prevalence of viral suppression among HIV-infected partners with whom condomless receptive anal intercourse (C-RAI) occurred, (5) the per-act risk of HIV infection via C-RAI with an HIV-infected person who is not virally suppressed, and (6) PrEP efficacy.

We used a triangular distribution for each of the 6 parameters (Table 3.2). In most cases, we allowed the mode to be the point estimate for the parameter and the distributional limits to be the 95% confidence intervals. In the case of PrEP efficacy, we allowed the mode to be the midpoint between two published estimates[27,28] and the limits to be the two point estimates.

We used 75 parameter combinations, with 50 replications per parameter combination. We computed the 2.5th and 97.5th percentiles of the means of the replications, which we report as the 95% uncertainty intervals accompanying the point estimates from the primary analysis. Additionally, we computed partial rank correlation coefficients between the parameters and output values. We conducted all analysis in R.

3.3 Results

The modeling exercise suggests that the incidence rate of HIV infection among San Francisco MSM in 2014 was 0.6 (95% interval from uncertainty analysis: 0.5–0.7) per 100 person-years. With rounding, this matches a previously published estimate for the same population and year.[24] Assuming a population size of 44,161 HIV-uninfected MSM, our study suggests 255 non-injecting MSM were infected in 2014. In comparison, the number of cases reported in

Table 3.1: Model variables and parameters, and corresponding data sources.

Variable or parameter	Source
Behaviors	MSM4[25]
Number of partners	MSM4 and MSM3[25]
Partnership characteristics	
Number of acts	MSM4 and MSM3
Reported HIV discordance*	MSM4 and MSM3
True HIV discordance†	MSM4
Viral suppression	Medical Monitoring Project[26]
Number of transmissible acts‡	By definition, from above
Per-act risks	Meta-analysis[14]
PrEP efficacy	iPrEx[27] and PROUD[28]

*HIV status of sexual partner, reported by the survey respondent. †True HIV status of sexual partner, assigned according to estimates. ‡Number of acts with HIV-infected partners who are not virally suppressed.

Table 3.2: Parameters for the triangular distributions used in the uncertainty analysis.

Distributional parameter	Lower	Upper	Mode
No discernible strategy, given PrEP*	0.062	0.366	0.214
HIV prevalence of unknown partners†	0.221	0.311	0.266
Recognized infection‡	0.937	1.000	0.970
Viral suppression of C-RAI partners§	0.415	0.848	0.632
Per-act risk via C-RAI¶	0.010	0.019	0.014
PrEP efficacy	0.439	0.867	0.653

*The prevalence of no discernible strategy among MSM who accessed PrEP. †The prevalence of HIV among unknown-status partners. ‡The prevalence of recognized infection among HIV-infected MSM. §The prevalence of viral suppression among HIV-infected partners with whom condomless receptive anal intercourse (C-RAI) occurred. ¶The probability of HIV infection via C-RAI with an HIV-infected partner who is not virally suppressed.

2014 among non-injecting San Francisco MSM was 225.[31]

Table 3.3 summarizes the percent of newly infected MSM belonging to various behavioral or PrEP-related groups. It also shows the distribution of the groups among all HIV-uninfected San Francisco MSM in 2014, estimated from MSM4. On average, the modeling exercise suggests that 76.4% (95% interval: 72.6–80.0%) of newly infected San Francisco MSM in 2014 were individuals with no discernible strategy prior to infection. An estimated 7.4% (95% interval: 6.3–8.0%) of newly infected MSM in 2014 were serosorters prior to infection while an estimated 8.0% (95% interval: 3.8–12.7%) were individuals who accessed PrEP at least once prior to infection.

Table 3.4 presents the probability of infection for various behavioral groups. The modeling exercise suggests that MSM with no discernible strategy had a 2.9% (95% interval: 2.5–3.5%) probability of becoming infected HIV over a 6-month period in 2014. Serosorters had a 0.1% (95% interval: 0.0–0.1%) probability of infection while individuals who accessed PrEP at least once had a 0.2% (95% interval: 0.1–0.4%) probability of infection.

3.4 Discussion

Our study suggests that newly infected San Francisco MSM are overwhelmingly individuals with no discernible risk-reduction strategy prior to infection. This finding suggests that HIV prevention in San Francisco must reach HIV-uninfected MSM with this behavioral pattern. Possible interventions for this risk group, which made up an estimated 8% of HIV-uninfected San Francisco MSM in 2014, include PrEP or seroadaptive behaviors such as serosorting. Indeed, our study suggests that if all HIV-uninfected MSM with no discernible strategy had been on PrEP in 2014 we would have seen a 70% lower number of infections among MSM in

Table 3.3: Distribution of behavioral patterns among HIV-uninfected men who have sex with men and distribution of prior behavioral patterns among newly HIV-infected men who have sex with men. San Francisco, 2014.

	Distribution among HIV-uninfected MSM, percent scale*	Distribution among newly HIV-infected MSM, percent scale (95% interval)†
PrEP, at least once	9.7	8.0 (3.8, 12.7)
No anal intercourse	21.5	0.0‡
100% condom use	16.5	2.2 (1.7, 2.6)
Serosorting	34.8	7.4 (6.3, 8.0)
Condom serosorting	4.7	3.8 (3.1, 4.4)
Seropositioning	5.4	2.3 (1.7, 2.7)
No discernible strategy	7.5	76.4 (72.6, 80.0)
PrEP indication, assessment	65.9	97.1 (96.7, 97.5)
PrEP indication, risk index	50.9	98.3 (98.1, 98.8)

*The point estimates are from a 2014 sample of San Francisco MSM. †The point estimates are the means of replications of the simulation exercise. The intervals are the 2.5th and 97.th percentiles of means of replications in the uncertainty analysis. ‡Assumed to be 0.

Table 3.4: Probabilities of HIV infection among San Francisco men who have sex with men, over a 6-month period in 2014.

	Probability of infection, percent scale (95% interval)*
PrEP, at least once	0.2 (0.1, 0.4)
No anal intercourse	0.0†
100% condom use	0.0 (0.0, 0.0)
Serosorting	0.1 (0.0, 0.1)
Condom serosorting	0.2 (0.2, 0.3)
Seropositioning	0.1 (0.1, 0.1)
No discernible strategy	2.9 (2.5, 3.5)
PrEP indication, assessment	0.5 (0.4, 0.5)
PrEP indication, risk index	0.6 (0.5, 0.7)

*The point estimates are the means of replications of the simulation exercise. The intervals are the 2.5th and 97.th percentiles of means of replications in the uncertainty analysis. †Assumed to be 0.

San Francisco. Similarly, if all no-discernible-strategy MSM had been serosorters, we would have seen a 75% lower number of infections.

Our research not only finds that most newly infected MSM are individuals who had no discernible strategy prior to infection, but also that the risk associated with the behavioral pattern is quite high: 3% over 6 months. This provides further support for the notion that HIV prevention in San Francisco should reach no-discernible-strategy MSM: such a strategy would identify potential seroconverters with relative efficiency. No other pattern in our analysis— including either of the CDC's suggested indications for PrEP use—appears as predictive of infection. Indeed, we suggest that no discernible strategy might be used as a possible primary indication for PrEP use, particularly if relatively high positive predictive value is desired.

Our results also provide insight on seroadaptive behaviors such as sersorting. Though more than one third of HIV-uninfected San Francisco MSM in 2014 were serosorters, only 7% of San Francisco MSM newly infected with HIV in 2014 were serosorters prior to infection. In congruence with some prior studies,[32] our study suggests that though serosorting is indeed risky, the risk of infection associated with the pattern is relatively low.

Meanwhile, we estimate that 8% of San Francisco MSM newly infected with HIV in 2014 used PrEP at least once in the year preceding infection. This estimate is consistent with a recent study that found that 9% of newly infected MSM at a clinic in Rhode Island had accessed PrEP.[33] Additionally, our study suggests that individuals who accessed PrEP had a 0.2% probability for HIV infection over a 6-month period in 2014, or approximately a 0.5% chance over one year by mathematically extrapolating over time. This estimate is congruent with findings from randomized controlled trials of PrEP in MSM populations: the PROUD

trial suggests a 1.2% risk over one year[28] while the cumulative probability of infection in the first year of follow-up of the iPrEx trial appears to be roughly 2%.[27] Encouragingly, there were no infections in a cohort of PrEP-initiating MSM at Kaiser Permanente Medical Center in San Francisco, but the upper bound of the study's one-year risk estimate was 1%,[34] above our estimate of 0.5%.

Assuming a population size of 44,161 HIV-uninfected MSM, our study suggests that 38 HIV infections were prevented among San Francisco MSM in 2014 due to PrEP efficacy. Two findings (results not shown) from our uncertainty analysis suggest that further work could further PrEP's impact, as measured by the proportion of newly infected individuals who had accessed PrEP and the risk of infection associated the PrEP group. First, partial rank correlation coefficients in the uncertainty analysis reveal that increases in efficacy result in increases in PrEP's impact. As we view changes in efficacy as reflecting changes in average levels of medication persistence, this finding highlights the importance of PrEP persistence. Second, the partial rank correlation coefficients reveal that reducing the prevalence of no discernible strategy in the PrEP group also increases PrEP's impact. Together, the two findings thus underscore the importance of two key components of the CDC guidelines for PrEP use: persisting with PrEP and accompanying PrEP use with reductions in risk behaviors.[10] No other factor considered in the uncertainty analysis has as large of an impact on the PrEP findings.

Models require simplification of real-world processes; we welcome curiosity regarding our model's own simplifications. One possible target of scrutiny is our assumption of constant per-act risks. Indeed, several studies have suggested that per-act risks of infection vary across individuals.[12,15,35] In an additional sensitivity analysis (results not shown), we allowed the

per-act risks to vary from individual to individual by adding normally distributed random errors, with standard distributions equal to the approximate standard errors reported in the recent meta-analysis.[14] This sensitivity analysis reveals no meaningful impact of the assumption of constant per-act risks on any of the study's findings. Another possible focus of curiosity is our assumption of no risk of infection via sex with virally suppressed partners. This assumption is not technically supported: the meta-analysis suggests, for example, that the risk of infection via one act of C-RAI with a virally suppressed partner is 0.06%.[14] This represents relatively low risk: it is one 23rd of the review's estimated risk via C-RAI with a non-suppressed partner. Nevertheless, we did perform sensitivity analysis allowing for risk via sex with virally suppressed partners. This analysis resulted in no meaningful change in any of the findings (results not shown).

Our uncertainty analysis—presented throughout the Results via the 95% intervals—addressed numerous other possible areas of scrutiny, including assumptions regarding sexual behavior among individuals who accessed PrEP, per-act risks, viral suppression (we acknowledge that our estimates come from data of individuals in care, for example), and PrEP efficacy. The analysis consistently shows that our results are fairly robust to our assumptions. Thus, despite the unavoidable simplifications involved in our approach, we are confident that our results are robust. These results have important implications for HIV prevention among MSM, clearly suggesting that prevention efforts in San Francisco must reach HIV-uninfected MSM with no discernible strategy. These individuals should be encouraged to adopt harm-reduction behaviors such as PrEP use, condom use, or serosorting, all of which carry lower risks of infection than no discernible strategy. Indeed, the relatively high risk associated with no discernible strategy makes the behavioral pattern a possible indication for

PrEP use. Finally, our uncertainty analysis is congruent with CDC recommendations[10,11] in finding that the impact of PrEP uptake can be maximized by increasing PrEP persistence and decreasing sexual risk behaviors among PrEP users. We recommend further research regarding possible barriers to PrEP persistence or risk reduction among HIV-uninfected MSM with no discernible strategy.

Chapter 4

Frequencies of possible predictors of PrEP initiation or persistence among MSM with no discernible strategy

4.1 Introduction

The findings presented in the last chapter clearly suggest that HIV prevention in San Francisco must reach HIV-uninfected MSM with no discernible harm-reduction strategy. An estimated 76% of newly infected San Francisco MSM in 2014 had no discernible strategy prior to infection, a strikingly large proportion given that no-discernible-strategy MSM made up only 8% of the HIV-uninfected population. We estimate the risk of HIV infection associated with the behavioral pattern to be 6% over one year.

One possible intervention for HIV-uninfected MSM with no discernible strategy is PrEP. Randomized controlled trials have demonstrated that a once-daily regimen of tenofovir diso-

proxil fumarate and emtricitabine generally involves few side effects and helps prevent HIV infection among MSM.[27,28] Efficacy is, however, highly dependent on persistence,[27,36,37] which has been demonstrated to be less than perfect in real-world settings. For example, at 3 American clinics between 2014 and 2015, only 81% of MSM who received PrEP prescriptions initiated use within 6 months and only 57% remained in care at 6 months.[38] Meanwhile, a longitudinal study of PrEP-initiating MSM and transwomen, iPrEx OLE, estimated persistence to be 72% 12 weeks after initiation[39] while a demonstration project among MSM estimated persistence to be 80% 48 weeks after initiation.[40] Persistence in these studies was possibly even lower than the estimates suggest, since the estimates derive from observed follow-up visits only.

The dependence of PrEP efficacy on persistence and the low levels of persistence in real-world settings raise questions about the suitability of the PrEP strategy for no-discernible-strategy MSM. Indeed, the very definition of the risk population involves non-persistence: non-persistence of—or disinterest in—sexual-behavioral strategies such as condom use or serosorting. Fortunately, some research suggests that high-risk MSM may in fact be suitable candidates for PrEP. Two longitudinal studies—iPrEx OLE and the demonstration project—found that condomless receptive anal intercourse is associated with greater, not lower, PrEP persistence.[37,40] The iPrEx OLE study additionally suggests that individuals with one or more HIV-infected partner are more likely to persist with PrEP.[37] Though these findings offer reason for optimism regarding the appropriateness of PrEP for MSM who do not engage in behavioral harm reduction, neither of the behaviors studied—condomless receptive anal intercourse or sex with an HIV-infected partner—is sufficient to define no discernible strategy. An additional concern is the possibility that the studies may have over-

sampled highly motivated high-risk MSM or experienced a disproportionate loss to follow-up of low-motivated high-risk individuals.

In this chapter, we present a study examining whether possible predictors of PrEP initiation or persistence are commonly found among sexually active, HIV-uninfected San Francisco MSM with no discernible strategy. Predictors of PrEP persistence identified in prior studies include age,[37,41] race or ethnicity,[40] education,[37] city of residence,[40] health insurance,[40] and living situation.[40] The Centers for Disease Control and Prevention (CDC)'s guideline for PrEP use additionally mentions financial stability, depression, substance use, and social support. The role of providers in maintaining persistence is also emphasized: the guideline encourages providers to educate patients about PrEP and its possible side effects and to help patients establish and maintain pill schedules.[10] In our study, we focus on risk factors that HIV prevention programs might be able to address, such as substance abuse. The aims are to assess the suitability of PrEP as a broad prevention strategy for no-discernible-strategy MSM and to gather information that could inform research regarding possible campaigns or interventions to increase PrEP initiation or persistence among this subpopulation.

4.2 Methods

We used data from San Francisco's fourth implementation of the CDC's National HIV Behavioral Surveillance System for MSM. Recruitment occurred in 2014 via time-location sampling.[25] We restricted analysis to sexually active, HIV-uninfected MSM who had not access PrEP within the last year.

The survey included measures on various factors possibly associated with PrEP initiation or persistence among MSM,[10,37,40,41] and variables closely related to such factors. We

classified these factors into four categories: health care, engagement in HIV prevention, environmental instability, and mental health or substance use. The measures of health care are: having health insurance, having a usual source of health care, accessing a provider within the last year, and being able to afford care within the last year. Our measures of HIV prevention are: access to one-on-one HIV prevention within the last year, access to group-based HIV prevention within the last year, having heard of PrEP, and being willing to persist with daily anti-HIV medication. The measures of environmental instability are: poverty (defined by US Census Bureau thresholds, using measures of income and financial dependents), history of homelessness, history of incarceration, and low social support (measured via questions adapted from a prior scale[42]). Finally, our measures of mental health and substance use are: recent indication of major depressive syndrome (via the PHQ-9,[43] with a recall period of 2 weeks) and methamphetamine use, cocaine use, or binge drinking more than once a month in the last year.

The survey additionally collected detailed behavioral information from each respondent on up to five recent sexual partnerships. We used these responses to measure no discernible strategy, which we defined as condomless receptive anal intercourse with one or more potentially HIV-serodiscordant partner within the last 6 months.

We computed frequencies of the possible predictors of PrEP initiation or persistence among no-discernible-strategy MSM, and compared these frequencies to the corresponding frequencies among other HIV-uninfected MSM. We conducted all analysis in R.

4.3 Results

The surveys recruited 192 sexually active, HIV-uninfected San Francisco MSM who had not accessed PrEP within the last year, 21 of whom had no discernible strategy.

Table 4.1 summarizes possible predictors of PrEP initiation and persistence, by behavioral pattern (no discernible strategy or other). We estimate that 85.7% of no-discernible-strategy MSM have health insurance, 81.0% have a usual source of care, and 76.2% saw a provider in the last year. These levels are comparable to the corresponding levels among other HIV-uninfected MSM. An estimated 76.5% of no-discernible-strategy MSM are willing to take daily medication to prevent HIV infection.

We estimate that 25.0% of no-discernible-strategy MSM meet the US Census Bureau's thresholds for poverty and 14.3% have a history of homelessness. An estimated 14.3% of no-discernible-strategy MSM have symptoms consistent with major depressive syndrome, 9.5% use methamphetamine more than once a month, and 76.2% engage in binge drinking more than once a month. These levels are all higher than the corresponding levels among other MSM.

4.4 Discussion

Reassuringly—given the importance of no-discernible-strategy MSM, as suggested in the last chapter—this study suggests high levels of access to health care among no-discernible-strategy MSM: we estimate that 86% of no-discernible-strategy MSM have health insurance, 81% have a usual source of care, and 76% see a provider once a year or more. These levels, which are comparable to those for MSM with other behavioral patterns, point to widespread

Table 4.1: Frequencies of possible predictors of PrEP initiation or persistence among HIV-uninfected San Francisco men who have sex with men in 2014, by behavioral group.

	Count (Percent)	
Characteristic	No-discernible-strategy MSM	Other MSM
Health care		
Health insurance	18 (85.7)	148 (86.5)
Usual source of care	17 (81.0)	134 (78.8)
Saw provider*	16 (76.2)	152 (88.9)
Afford care*	17 (81.0)	149 (87.1)
HIV prevention		
One-on-one discussion*	3 (14.3)	37 (21.6)
Group discussion*	2 (9.5)	14 (8.2)
Heard of PrEP	15 (88.2)	149 (87.1)
Willing to take PrEP	13 (76.5)	97 (58.1)
Environmental instability		
Poverty	5 (25.0)	22 (12.9)
Ever homeless	3 (14.3)	14 (8.2)
Ever incarcerated	4 (19.0)	25 (14.6)
Low social support	11 (52.4)	63 (37.1)
Mental health		
Major depressive syndrome	3 (14.3)	7 (4.1)
Methamphetamine use†	2 (9.5)	7 (4.1)
Cocaine use†	3 (14.3)	26 (15.2)
Binge drinking†	16 (76.2)	98 (57.3)

*In the last year. †More than once a month in the last year.

potential clinical support for PrEP initiation and persistence among no-discernible-strategy MSM. Also encouraging is the high level of interest in PrEP in the subpopulation: we estimate that more than two-thirds of MSM with no discernible strategy are willing to take regimens such as PrEP to prevent HIV infection.

On the other hand, viewing our findings less optimistically, the non-universal levels of health care and willingness to use PrEP among no-discernible-strategy MSM represent possible barriers to bringing incidence to 0 in cities such as San Francisco. We thus recommend efforts to increase access to care among high-risk MSM, such as those with no discernible strategy. These might include, for example, dissemination of information regarding insurance options or campaigns to encourage routine visits with providers. Increased access to care will allow for greater opportunities to educate MSM—with no discernible strategy or otherwise—about PrEP and to support PrEP initiation and persistence.[10,11]

Another area of concern is our study's findings of high frequencies of binge drinking among no-discernible-strategy MSM, and minorities of no-discernible-strategy MSM with unstable housing, depressive symptoms, and recreational drug use. These findings suggest caution regarding the suitability of PrEP for no-discernible-strategy individuals, since the CDC's clinical guidelines on PrEP use specifically mention substance use, depression, and unstable housing as characteristics to screen for.[10,11] Though some studies have failed to find that substance use or depression impede PrEP persistence,[37,40,44] we recommend that clinicians continue to assess for these patterns, particularly among no-discernible-strategy MSM. Our rationale for our recommendation, despite the aforementioned findings, are twofold. First, the conclusions from the studies may be dependent on the measures. For example, the alcohol studies may have been dependent on the defining thresholds of frequency of use. Second, it

is possible that at least some of the studies over-sampled highly motivated exposed MSM or experienced a disproportionate loss to follow-up of low-motivated, exposed individuals.

A limitation of our study is the self-reported nature of the data. We acknowledge, for example, that it is unclear whether the reported willingness of no-discernible-strategy MSM to use PrEP would actually translate to initiation and persistence. However, the high levels of access to care we estimate among no-discernible-strategy MSM lessen that concern, since access to care can help ensure that individuals are well-informed about PrEP and that PrEP initiators persist with the treatment regimen.[10,11]

We believe that our study succeeds in addressing its aims. It suggests that no-discernible-strategy individuals—a crucial risk group—are suitable targets for PrEP: they have high levels of access to health care, appear willing to persist with daily anti-HIV medication, and do not appear to have high frequencies of possible obstacles to treatment persistence (with the exception of binge drinking). Nevertheless, we recommend interventions to improve access to care among MSM, with the goal of reaching all no-discrnible-strategy MSM. An additional challenge to halting the epidemic is binge drinking, which appears to occur with high frequency among no-discernible-strategy MSM. We encourage research regarding interventions that may address such barriers. For example, it is possible that interventions for reducing binge drinking[45] may help improve persistence to PrEP. Finally, we reiterate the CDC's recommendations that providers routinely assess for behavioral or environmental factors that may disrupt PrEP persistence and work with patients to develop solutions to these barriers.[10,11]

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