Mathematical Modeling to Inform Implementation of HIV Prevention Programs in the United States

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Abstract

Mathematical modeling to inform implementation of HIV prevention programs in the United States

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Despite advances in the detection and treatment of HIV, the incidence of infection in the United States has increased in some subgroups over the past decade and remained stable in others. These trends point to a need for improved strategies for prevention that take into account the social, behavioral, and clinical context of different target populations.

We conducted an internet-based survey to measure sexual behavior and use of pre-exposure prophylaxis (PrEP) among men who have sex with men (MSM) in Washington State (Chapter 1). Among 1,080 cisgender MSM respondents, 79% had heard of PrEP, 19% reported current use, and 36% of PrEP-naïve men reported that they wanted to start taking it. Among high-risk men recommended to initiate PrEP, 31% were taking it. With the data from this survey, in combination with secondary data from local surveillance systems and other surveys, we developed a dynamic network-based mathematical model to evaluate the potential impact of PrEP on HIV incidence in Washington MSM (Chapter 2). In the context of the high levels of testing and treatment in Washington, our model estimated that HIV incidence at the end of the 10-year simulation would be 48-83% lower with continued or increasing use of PrEP relative to a counterfactual scenario with no PrEP use.

In chapter 3, we constructed a static linear mathematical model to estimate the impact and optimal age for one-time routine HIV screening in terms of case detection, person-years of

undiagnosed infection, and progression to symptomatic HIV/AIDS. When added to prenatal, risk-based, symptom-based, and partner notification testing, our model estimated that the impact of routine screening is likely to be modest. The percent of tests resulting in new diagnoses exceeded the recommended minimum of 0.1% only in a setting with high HIV incidence in groups that don't engage in repeat, targeted testing.

The results from these three projects provide important insights to inform local policies and HIV prevention strategies, demonstrating the value of applying mathematical modeling to inform public health practice. Our findings highlight the influence of epidemiologic context on the impact of interventions such as PrEP and HIV screening, underscoring the importance of using local data to define context-specific prevention strategies.

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DEDICATION

To my mother, Linda White, who encouraged me to be curious and pursue my passions.

To my daughter, Mika Rao, to whom I hope to pass on my mother's wisdom, and from whom I have much still to learn.

INTRODUCTION

In the 38 years since the start of the HIV epidemic, advances in prevention and treatment have resulted in significant decreases in incidence, AIDS diagnoses, and HIV/AIDS-associated mortality in the United States.[1–3] However, these gains have not been uniform by region or sociodemographic group.[3–6] Among men who have sex with men (MSM), who account for two-thirds of new HIV infections,[7] incidence has been increasing in certain age groups and among Hispanics.[4] To curb these trends and accelerate progress in controlling the epidemic, the US Department of Health and Human Services launched an initiative in 2019 with a focus on improving HIV diagnosis, engagement in care, and access to HIV pre-exposure prophylaxis (PrEP).[8] In light of pronounced geographic heterogeneity in transmission risk and clinical outcomes,[3,9–11] the initiative calls for context-specific policies and programs informed by local data.[8]

Historically, the only prevention tools available to HIV-negative individuals targeted sexual risk behavior change, with limited practical effectivenes.[12,13] The availability of PrEP, which has demonstrated >90% efficacy with adequate dosing,[14,15] presents an opportunity to achieve substantial reductions in incidence among MSM. Interest and investment in the intervention is growing rapidly,[1,2][16–19] signaling a need to develop reliable methods to monitor changes in awareness and utilization. The impact of PrEP on population-level transmission dynamics will depend on uptake, adherence, discontinuation, changes in risk behavior, use of other prevention interventions, HIV clinical care, and the sexual network structure in targeted populations. Variability in these factors may lead to important differences in the potential contribution of PrEP to prevention efforts at the subnational level.

Questions remain about the optimal implementation of secondary prevention efforts as well, such as timely testing and treatment of persons found to be HIV-positive. In 2015, the median time from infection to diagnosis in the United States was 3 years.[20] To improve clinical outcomes[21] and reduce the number of transmission events resulting from undiagnosed, untreated infection,[22,23] identifying strategies to shorten this window is a key objective. The Centers for Disease Control and Prevention recommends that all persons aged 13-64 test for HIV at least once in their lifetime regardless of risk factors (routine screening).[24] The US Preventative Services Task Force has issued a similar recommendation.[25] However, the impact of this non-targeted testing has been unclear,[26–29] and in any given jurisdiction it will depend on the distribution and magnitude of HIV incidence and existing patterns of risk-based, prenatal, symptom-based, and partner notification testing.

To inform policy and program design, mathematical models can be used to evaluate and project the impact of interventions such as PrEP and HIV screening. By taking a systems-level view, models allow us to understand how biology, behavior, and factors operating at levels beyond the individual interact to shape epidemiologic outcomes.[30–32] With explicit representation of the key processes and variables relevant to the outcomes of interest, we can use models to test alternative scenarios and make context-specific projections. To support these analyses, detailed behavioral, demographic, and clinical data are needed at the local level.

Chapters 1 and **2** of this dissertation were conducted in collaboration with partners at the Washington State Department of Health and Public Health—Seattle & King County to monitor and evaluate the impact of PrEP among MSM in Washington State. Compared to much of the rest of the United States,[11] Washington has uniquely high levels of HIV treatment and viral suppression.[33] An estimated 89% of diagnosed cases in 2017 were engaged in care and 80% had evidence of a suppressed viral load.[33] In King County, which is home to 53% of persons living with diagnosed HIV in Washington, 92% were in care and 85% were virally suppressed.[33] Despite these successes, the rate of new HIV diagnoses declined only 5% from 2014 to 2017,[33] falling below the pace required to meet the State's goal for a 50% decline by 2020.[34] As part of a comprehensive strategy to improve prevention outcomes, the Department of Health has invested in increasing access to PrEP, and Washington was the first state to launch a drug assistance program to help remove financial barriers to uptake.[34] To support and maximize the impact of these efforts, the Department of Health identified a need to develop systems to monitor PrEP use and evaluate the long-term impact on HIV incidence.

In **Chapter 1**, we present the findings from an internet-based survey that was designed to measure awareness, interest, and use of PrEP among MSM in Washington State. Key outcomes from this survey include the proportion of men with indications for PrEP according to local guidelines,[35] levels and correlates of PrEP use, patterns of discontinuation, and reported barriers to uptake and retention. The survey also collected data on sexual partnerships and partner-specific behavior, which were used to parameterize a dynamic network-based mathematical model of HIV transmission among Washington MSM. With this model, we estimated the potential impact of PrEP on HIV incidence and diagnoses over 10 years (**Chapter 2)**. To explore a range of possible outcomes, we evaluated scenarios defined by varying levels of uptake, adherence, and decreases in condom use associated with PrEP (risk compensation).

Chapter 3 uses a static linear mathematical model to assess the population-level impact of adding one-time routine HIV screening to existing practices of targeted testing of high-risk MSM, pregnant women, partners of newly diagnosed cases, and persons presenting with AIDS-associated symptoms. The model was parameterized at the national level and for two jurisdictions distinguished by the rates and distribution of infection: King County, Washington, and Philadelphia County, Pennsylvania. For each model, we evaluated the optimal ages for one-time routine HIV screening in terms of the percent of tests that yield new diagnoses, the cumulative population-level years of undiagnosed infection, and the number of cases that progress to symptomatic HIV/AIDS. To assess the relative contribution of routine vs. targeted screening, we compared the incremental impact of implementing prenatal, risk-based, and routine screening with respect to these outcomes.

The work presented in this dissertation demonstrates the value of integrating public health surveillance with mathematical modeling to advance public health practice. Using local data, mathematical models can provide context-specific estimates of intervention effectiveness and efficiency and identify areas where more research is needed. These insights can be used to improve strategies to curb HIV incidence and improve public health outcomes.

CHAPTER 1: Monitoring HIV pre-exposure prophylaxis use among men who have sex with men in Washington State: findings from an internet-based survey

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ABSTRACT

Background: Many state and local health departments now promote and support the use of HIV pre-exposure prophylaxis (PrEP), yet monitoring use of the intervention at the population level remains challenging.

Methods: We report the results of an online survey designed to measure PrEP use among men who have sex with men (MSM) in Washington State. Data on the proportion of men with indications for PrEP based on state guidelines and levels of awareness, interest, and use of PrEP are presented for 1,080 cisgender male respondents who completed the survey between January 1 and February 28, 2017. We conducted bivariate and multivariable logistic regression to identify factors associated with current PrEP use. To examine patterns of discontinuation, we conducted Cox Proportional Hazards regression and fit a Kaplan Meier curve to reported data on time on PrEP.

Results: Eighty percent of respondents had heard of PrEP, 19% reported current use, and 36% of men who had never used PrEP wanted to start taking it. Among MSM for whom state guidelines recommend PrEP, 31% were taking it. In multivariable analysis, current PrEP use was associated with older age, higher education, and meeting indications for PrEP use. Our data suggest that 20% of PrEP users discontinue within 12 months, and men with lower educational attainment were more likely to discontinue.

Conclusions: Despite high levels of use, there is significant unmet need for PrEP in Washington. Our experience indicates that internet surveys are feasible and informative for monitoring PrEP use in MSM.

INTRODUCTION

Expanding access to HIV pre-exposure prophylaxis (PrEP) has become a pillar of the HIV prevention strategy in the United States,[36] supported by strong evidence of the intervention's efficacy and effectiveness from clinical trials and observational studies.[37] The potential population-level impact of PrEP is particularly significant for men who have sex with men (MSM), who experienced 70% of new HIV diagnoses nationally in 2016.[38] The U.S. Public Health Service has issued guidelines recommending PrEP for high-risk MSM and other priority populations,[39] but large gaps have been reported between eligibility, interest, and use.[40–42] To inform efforts to improve PrEP delivery, reliable data are needed to describe the populations at risk, monitor use, and characterize the barriers to uptake and retention in care.

Measuring PrEP use among MSM is methodologically challenging due to the lack of efficient and unbiased sampling methods for this population. In the U.S., data on MSM's use of prevention interventions have primarily come from clinic samples,[42,43] which are limited to persons who seek care in selected clinics or healthcare organizations, and venue- and event-based samples,[44,45] which are often expensive and limited in geographic scope. Internet-based recruitment has gained popularity as an alternative strategy for sampling MSM,[46–50] but this approach has not yet been widely adopted by state and local health departments for purposes of public health monitoring.

In this paper, we present the findings from the 2017 Washington HIV Prevention Project (WHPP), an internet-based survey developed to monitor the success of Washington State's efforts to promote PrEP use among high-risk resident MSM. To evaluate the consistency of WHPP findings with data from offline samples, we compare our estimates of PrEP use to estimates from an in-person survey administered at the 2017 Seattle Pride parade.[51]

METHODS

We recruited participants to complete an online cross-sectional survey between January 1 and February 28, 2017. Participants accessed the survey through banner and text-based pop-up advertisements on social media, male-male geosocial networking, and general LGBTQ-interest apps and websites. Upon clicking past a landing webpage with information on the purpose of the survey, participants were randomly shown one of three informed consent pages that differed only in the stated incentive: a $10 Amazon gift certificate, a $10 donation to charity, or no monetary incentive. Through daily monitoring of IP addresses and timestamps (described in Supplemental Appendix 1), we identified a pattern of seemingly fraudulent responses that led us to discontinue the gift certificate incentive after nine days.

Consenting participants were shown a set of questions to screen for eligibility. Persons were ineligible if they were female sex at birth, age <16 years, lived outside of Washington, did not have oral or anal sex with a man in the past 12 months, reported ever testing positive for HIV, or had an Internet Protocol (IP) address outside the U.S. Additional details on survey methods are provided in Supplemental Appendix 1. Because this work was conducted as a public health surveillance activity, it was determined not to be human subjects research by the University of Washington Institutional Review Board.

Key Measures

Prior to answering questions about PrEP, respondents were presented with the following description: "PrEP is a pill taken every day by HIV-negative people to reduce the risk of getting HIV. It is currently available under the brand name Truvada®." Respondents who had heard of PrEP were asked if they were currently taking or had taken it in the past. Men who had never taken PrEP were asked if they were interested in taking it, with response options of "Yes, I want to start taking PrEP", "I am not sure about PrEP, but I would like to learn more about it," and "No, I am not interested in taking PrEP." Follow-up questions asked why they were not interested or had not yet initiated (see Supplemental Appendix 1 for response options). Current and past PrEP users reported the month and year they most recently started PrEP, and men who had discontinued additionally reported the month and year in which they last took PrEP. We measured self-reported adherence over the past 30 days and defined high adherence as taking ≥4 pills per week on average.[14] Men who had discontinued PrEP indicated why they stopped their medication and whether they were interested in taking it again. All participants were asked how effective they thought PrEP is at preventing HIV infection if taken every day.

PrEP candidacy was defined according to guidelines developed by Public Health – Seattle and King County and the Washington State Department of Health (WADOH).[35] These guidelines were adapted from those issued by the U.S. Public Health Service,[39] the International Antiviral Society—USA,[52] and the World Health Organization[53] to reflect the local epidemic context, and were informed by analyses that identified factors associated with HIV acquisition. The guidelines define two tiers of risk: persons for whom medical providers should recommend PrEP, and persons with whom providers should discuss PrEP (Table 1.1).

To assess heterogeneity in PrEP uptake across the state, we categorized respondents as residing in one of three regions based on reported ZIP codes: King County (which includes Seattle), other counties in western Washington, and eastern Washington (see Figure 1.1 for a regional map).

Analyses

Duplicate and invalid responses were flagged and removed using a modified version of a published protocol,[54] described in Supplemental Appendix 1. Data are presented from respondents who completed the survey at least through initial questions about PrEP awareness and use. To identify factors associated with current PrEP use, we conducted logistic regression. We first examined associations for a base model including the following covariates, which were defined *a priori*: region, age, race/ethnicity, sexual orientation, education, income, and PrEP candidacy. In an exploratory analysis, we examined bivariate associations with other factors measured in our survey, including health insurance, perceived effectiveness of PrEP, and specific HIV risk indicators. Our multivariable exploratory model included base model social and demographic variables and additional factors that were significant in bivariate analyses.

We estimated time to PrEP discontinuation by fitting a Kaplan Meier curve to reported data on dates of first and last PrEP use. Current users' time on PrEP was censored at the date of survey completion. Time-invariant predictors of discontinuation (age at PrEP initiation, race/ethnicity, education, and region of residence) were explored using multivariable Cox Proportional Hazards regression, employing the exact marginal method to adjust for ties.

To assess the consistency of WHPP findings with data from sources using offline (in-person) recruitment, we compared estimates of PrEP awareness and use with those from a sample of MSM who completed a self- or interviewer-administered paper questionnaire at the Seattle Pride Parade in June 2017.[16] In this analysis, both samples were restricted to cisgender males living in the Seattle metropolitan area. To account for differences in the HIV risk profile of the two samples, we tabulated the proportion reporting PrEP use among high-risk men for whom state guidelines recommend the intervention. Because the Pride survey did not measure current partnerships with HIV-positive partners, this indication is not included when defining risk groups for this comparison. Analyses were conducted using Stata version 13.1 (StataCorp, College Station, TX). An alpha of 0.05 was used for significance testing.

RESULTS

Recruitment, response rates, and cost

In the two-month recruitment period, 2,767 unique individuals consented to the survey, 44% of whom (1,225) met inclusion criteria. Seventy-nine percent (973) of eligible participants completed the survey. The costs of recruitment, survey administration, and incentives totaled $23.69 per complete response (see Supplemental Appendix 1 for details on response rates and expenses). For this analysis, we excluded respondents who reported a gender other than male (n=32), resulting in 1,080 responses from cisgender males who completed the survey through initial questions about PrEP, of whom 924 completed the entire survey.

Sample characteristics

The median age in the sample was 30 (range: 16-82), and 61% of respondents were below the age of 35 (Table S.2). Two-thirds of the sample (68%) identified as non-Hispanic white, and 49% reported a 4-year college degree or higher education. Fifty-six percent of respondents reported residence in King County. Based on reported behaviors and experiences within the past 12 months, 33% of men met criteria indicating that medical providers should recommend PrEP initiation. Another 30% of men met criteria indicating that a medical provider should discuss PrEP with them.

Awareness, interest, and use of PrEP

Eight in ten respondents (79%) had heard of PrEP, 19% reported current use, and 4% had used PrEP in the past (Table S.2). By Washington State PrEP candidacy category, 31% of men for whom PrEP is recommended and 25% of those with whom it should be discussed reported current use, compared to only 4% of those for whom PrEP is not indicated. Among men in the "recommend" category, current PrEP use was reported by 37% in King County, 20% in other western Washington counties, and 22% in eastern Washington.

More than one third (36%) of men who had never used PrEP indicated that they wanted to start taking it, and 33% weren't sure but wanted to learn more. Among never-users for whom PrEP is recommended, 56% wanted to start PrEP and 23% weren't sure; among those with whom PrEP should be discussed, 51% wanted to start and 32% weren't sure. Reported reasons for not using or not being interested in PrEP are presented in Figure 1.2, stratified by PrEP candidacy category and interest. Overall, the most common barriers to uptake among PrEP-naïve men for whom PrEP is recommended were a perception of being at low risk for HIV (29%), concern about side-effects (26%), and cost or insurance coverage issues (23%).

Correlates of current PrEP use

In bivariate analyses, current PrEP use was associated with residence in King County, older age (relative to 18-24), identifying as gay or homosexual, higher education, higher income, and meeting criteria for PrEP being recommended or discussed (Table 1.3). In the base multivariable model adjusting for *a priori* covariates, only age, education, and PrEP candidacy remained significantly associated with current use. In a multivariable exploratory model, older age, having health insurance, diagnosis with rectal gonorrhea or syphilis, reporting ≥10 anal sex partners in the past 12 months, having a current HIV-positive male partner, CAS with a partner who was not main/primary or whose HIV status was positive or unknown, poppers use, and perceiving PrEP to be ≥90% effective were positively associated with current PrEP use.

PrEP adherence and discontinuation

Current PrEP users reported high adherence, with 93% having taken an average of 4 or more pills per week in the past 30 days and 66% reporting perfect adherence. Current users reported having started PrEP a median of 12 months prior to survey completion (interquartile range (IQR): 5-20), and past users reported a median of 5 months of use (IQR: 2-8.5). The most common reasons for stopping PrEP were a perception of no longer being at high risk for HIV (52%), concern about long-term health effects (27%), not being able to afford PrEP or having lost insurance (23%), and side-effects (20%). In a Kaplan-Meier analysis (Figure 1.3), we estimated that 20% of men discontinue PrEP within 12 months of initiation (95% CI: 15%-26%). Discontinuation was associated with having a high school education or lower (adjusted hazard ratio (aHR): 4.86, 95% CI: 1.77-13.38) or having completed some college or vocational school (aHR: 2.08, 95% CI: 1.02-4.25), relative to having a 4-year college degree or higher, but was not significantly associated with age, race/ethnicity, or region. Fifty-three percent of men who had discontinued PrEP wanted to start taking it again, and 28% were unsure about taking PrEP again.

Comparison with the 2017 Seattle Pride Parade survey

Awareness of PrEP was similar among the 739 Seattle-area WHPP respondents (82%) and the sample of 297 HIV-negative cisgender MSM who completed the 2017 Seattle Pride Parade survey (86%; chi-square $p=0.073$). In both samples, 26% of men reported lifetime use of PrEP, with 21% of WHPP and 22% of Pride survey respondents reporting current use ($p=0.853$). A higher proportion of men in the WHPP sample reported behaviors indicating that PrEP should be recommended (33% vs. 19%; $p<0.001$). Among those in this high-risk category, 39% of WHPP respondents and 36% of Pride survey respondents reported lifetime use of PrEP ($p=0.739$), and 33% and 27% reported current use, respectively ($p=0.398$).

DISCUSSION

In this sample of internet-recruited Washington State MSM, awareness and interest in PrEP were high, with more than half of high-risk men who had never used PrEP indicating that they wanted to start taking it. Current PrEP use was associated with sexual and drug-related HIV risk indicators in multivariable regression, and nearly one-third of men classified by state guidelines as having the strongest indication for PrEP reported current use. However, the gaps between reported interest and use of PrEP reveal substantial unmet need, and our analyses indicate sociodemographic disparities in uptake.

Previous surveys of MSM in the United States, conducted between 2014 and 2016, have reported 4%-10% current or past-12-month use of PrEP[40,55,56] and 10%-15% lifetime use.[49,57] Among higher risk men, these studies have found that 6%-13% report current or past-12-month use.[41,58] The differences between these estimates and our findings are likely partially attributable to increased PrEP uptake in the years over which these data were collected. However, the 23%-26% lifetime and 19%-22% current use of PrEP reported by men in the WHPP and Seattle Pride survey samples suggest that PrEP use is higher in Washington State than in many other parts of the county.

Despite the high uptake of PrEP reported by men at high risk for HIV, many respondents reported barriers to PrEP initiation. Thirty percent of PrEP-naïve men who met indications for PrEP being recommended or discussed perceived themselves to be at low risk. Although Washington State guidelines may misclassify some individuals, our findings suggest a potential disconnect between perceived and actual risk. Among men recommended to initiate PrEP who wanted to start taking it, reported barriers suggest that many men face real or perceived financial barriers to PrEP, lack sufficient information about the intervention or how to receive it, or live somewhere where access is inadequate.

In particular, PrEP use was lower among younger, less educated, and uninsured men. Of note, we did not observe disparities in PrEP use by race/ethnicity, though our sample of black respondents was small. Some previous surveys of MSM have similarly reported no significant differences in PrEP use by race/ethnicity,[49,58] but others have reported lower use among black and other minority MSM.[41,57,59] In light of the high incidence of HIV among black and Hispanic MSM,[4] concerted efforts are needed to ensure that PrEP reaches these at-risk populations.

We estimated that in our population, 20% of men who initiate PrEP will discontinue by 12 months. This estimate is similar to that derived from a cohort study of patients in northern California,[60] but substantially lower than estimates from studies focusing on STD clinic patients and other high-risk populations.[61,62] As in prior studies,[49,61] the primary reasons for discontinuation reported by WHPP participants included no longer being at high risk, concern about long-term health effects, and financial barriers. While discontinuation may be indicated for some men, these findings point to a need for more consistent follow-up to encourage patients to discuss their concerns before discontinuing their medication. More than half of men who had discontinued PrEP expressed interest in starting it again, highlighting the need for clinicians and public health staff to serially discuss the intervention with men whose risks may be dynamic.

Our approach to PrEP monitoring has implications for diverse public health HIV programs. To inform implementation and evaluate the success of efforts to promote PrEP and other interventions, state and local health departments need to establish systems to monitor patterns of utilization and related behaviors at the population level. Alongside data from general population probability samples, event-based surveys, partner services interviews, and in-person surveys of high-risk groups (i.e., the National HIV Behavioral Surveillance System), internet-based surveys can be a valuable component of a comprehensive HIV surveillance strategy. Internet-based surveys have several advantages over other methods, particularly for recruitment of MSM: they can efficiently collect data over broad geographic areas; avoid linking PrEP monitoring to STI surveillance activities, which likely results in biased estimates since persons on PrEP are screened for asymptomatic STIs as part of their care; and are relatively inexpensive, at approximately $24 per completed response. Collaboration between public health and academic partners could facilitate expansion of internet-based public health monitoring to jurisdictions with limited time or expertise, a factor that was key to the success of this project.

Our findings have several limitations. First, our sample may not be representative of all Washington State MSM. As with other internet-based samples,[48,49,63] WHPP participants were young, highly educated, and reported high engagement in HIV risk behaviors. The fact that the prevalence of PrEP use was similar in the WHPP and Pride samples lends credibility to the estimates, though the representativeness of the Pride survey sample is also uncertain. Second, the relative anonymity afforded to participants in online surveys makes it difficult to verify their eligibility and prevent duplicate responses. Through monitoring of IP addresses, time stamps, and response patterns, we detected 851 apparently invalid entries, but this approach is not foolproof. Third, our analyses of time to PrEP discontinuation assumed uninformative censoring (i.e. that current and past PrEP users were comparably likely to complete the survey), and used data on dates of PrEP use during a period of increasing awareness and uptake. These data may not be generalizable to men starting PrEP now or in the future. Additionally, our estimates of time to discontinuation might overestimate the duration of PrEP use, since our cross-sectional design may be more likely to collect data on longer periods of PrEP use among respondents who have gone on and off PrEP multiple times (length time bias).

The 2017 WHPP survey suggests high use of PrEP among MSM in Washington State, particularly among those at highest risk for HIV. Despite this success, there is substantial unmet need for PrEP; many men – particularly young, less educated MSM – require additional information or assistance to access PrEP, and our region has not yet achieved our defined 2020 objective of 50% PrEP use among MSM at highest risk.[51] Our experience indicates that internet-based monitoring to measure PrEP utilization is feasible, relatively low cost, and allows for collection of statewide data which may not otherwise be available. Particularly if they are repeated at regular intervals, the data such surveys generate can play a critical role in monitoring the uptake of public health interventions over time and in identifying populations with disproportionate unmet need.

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Table 1.1: PrEP candidacy categories based on Washington State PrEP implementation guidelines

Recommend PrEP for MSM with any of the following risk factors:

- Diagnosis of rectal gonorrhea or syphilis[a] in the past 12 months
- Methamphetamine or poppers use in the past 12 months
- History of exchanging sex for money or drugs in the past 12 months
- Ongoing sexual partnership(s) with HIV-positive partners(s) who are not on antiretroviral therapy (ART), started ART ≤6 months ago, or are not virologically suppressed

Discuss PrEP with MSM who do not meet the above criteria for recommending PrEP and who report any of the following[a]:

- Diagnosis of urethral gonorrhea or rectal chlamydia in the past 12 months
- Condomless anal sex (CAS) with a partner not considered to be main/primary, or with a partner of unknown or positive HIV status in the past 12 months[b]
- Non-prescription injection drug use in the past 12 months
- Ongoing sexual partnership(s) with HIV-positive partners(s) who have been on ART >6 months and are virologically suppressed

[a]The guidelines refer to diagnosis of *early* syphilis. Due to the difficulty of measuring stage of infection via self-report, for this analysis we included any diagnosis of syphilis as an indication for recommending PrEP; [b]Three indications for discussing PrEP with MSM were not measured in the survey: having an HIV-positive female partner with intentions to conceive, completing a course of post-exposure prophylaxis for non-occupational exposure, and seeking a prescription for PrEP; [c]Proxy measure for CAS outside of a long-term, mutually monogamous relationship with a partner who is HIV-negative;

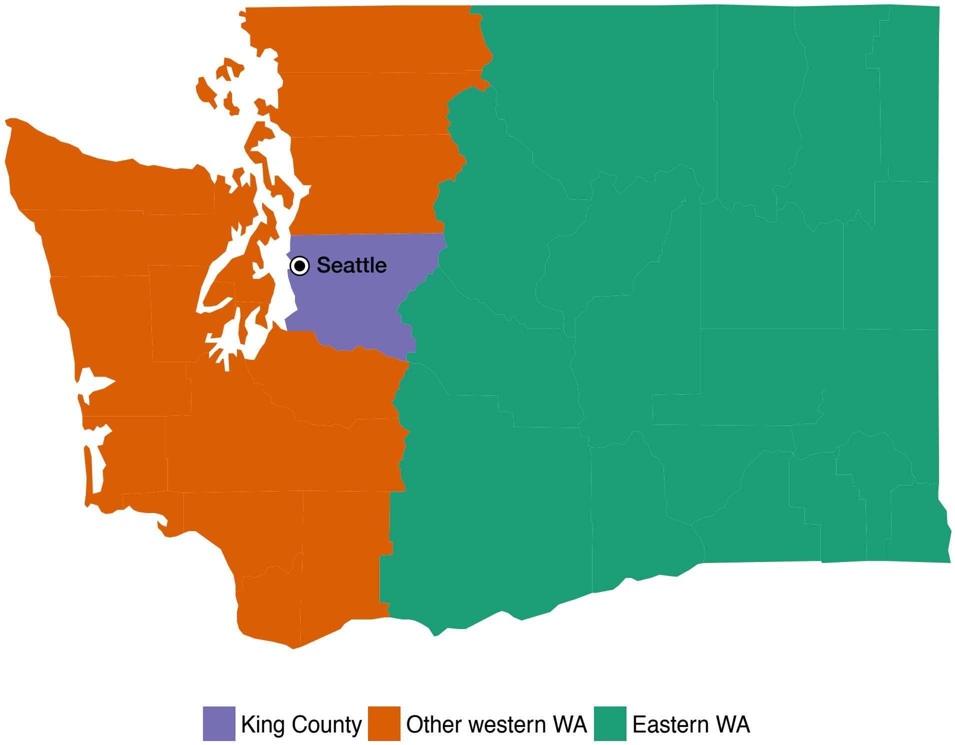

Figure 1.1. Map of the regions of Washington State defined for survey analysis

King County is home to an estimated 55% of the state's MSM population[64] and 59% of prevalent MSM HIV/AIDS cases.[65] This figure was created using the 'maps'[66] and 'ggplot2'[67] packages in R version 3.4.2.[68]

Table 1.2: Sample characteristics

	n/N[a]	%
Recruitment platform		
Social media	806/1,080	74.6%
Geosocial networking	211/1,080	19.5%
General LGBTQ interest	63/1,080	5.8%
Demographic and social characteristics		
Region		
King County	610/1,080	56.5%
Other counties in western Washington	308/1,080	28.5%
Eastern Washington	162/1,080	15.0%
Age		
16 to 24	313/1,080	29.0%
25 to 34	351/1,080	32.5%
35 to 44	167/1,080	15.5%
45 to 54	128/1,080	11.9%
55 and older	121/1,080	11.2%
Race/ethnicity		
Hispanic	198/1,067	18.6%
Non-Hispanic white	725/1,067	67.9%
Non-Hispanic black	42/1,067	3.9%
Non-Hispanic other	102/1,067	9.6%
Gay/homosexual identity	889/1,076	82.6%
Education		
High school or less	176/1,065	16.5%
Some college/vocational school	364/1,065	34.2%
4-year college or higher	525/1,065	49.3%
Income		
Less than $15,000	110/930	11.8%
$15,000 to $29,999	111/930	11.9%
$30,000 to $49,999	167/930	18.0%
$50,000 to $99,999	278/930	29.9%
$100,000 or more	215/930	23.1%
Prefer not to answer	49/930	5.3%
Has health insurance	929/1,037	89.6%
HIV and STI testing		
HIV testing history		
Never tested	219/1,074	20.4%
Tested in the past 12 months	657/1,074	61.2%
Tested >12 months ago	198/1,074	18.4%
STI diagnosis (past 12 months)		
Rectal gonorrhea	47/1,025	4.6%
Syphilis	57/1,025	5.6%
Any bacterial STI[b]	189/1,025	18.4%
Sexual behaviors and drug use (past 12 months)		
Anal sex role		
No anal sex	103/1,000	10.3%
Exclusively bottom	197/1,000	19.7%
Versatile	578/1,000	57.8%
Exclusively top	122/1,000	12.2%
≥10 anal sex partners	162/1,013	16.0%

Current main/primary male partner	443/998	44.4%
Current HIV-positive male partner	79/979	8.1%
CAS with a non-main partner	476/980	48.6%
CAS with an unknown status partner	280/975	28.7%
CAS with an HIV-positive partner	145/979	14.8%
Injection drug use	57/938	6.1%
Methamphetamine use	81/926	8.7%
Poppers use	211/926	22.8%
History of exchange sex	36/935	3.9%
PrEP awareness and use		
PrEP awareness	852/1,080	78.9%
Perceived effectiveness of PrEP		
Less than 75%	260/1,036	25.1%
75% to 89%	174/1,036	16.8%
90% or higher	524/1,036	50.6%
Unsure/Prefer not to answer	78/1,036	7.5%
Use of PrEP		
Never	832/1,080	77.0%
Current	200/1,080	18.5%
Past	48/1,080	4.4%
WA State PrEP guideline category		
Recommend[c]	303/912	33.2%
Discuss[d]	271/912	29.7%
Not indicated	338/912	37.1%

Acronyms: STI, sexually transmitted infection; CAS, condomless anal sex; PrEP, pre-exposure prophylaxis

[a]Includes data from 924 complete and 156 partial responses that completed the survey at least through questions about PrEP use. Denominators may vary due to missing data; [b]Diagnosis of gonorrhea (pharyngeal, urethral, or rectal), chlamydia (pharyngeal, urethral, or rectal), or syphilis; [c]MSM who reported a diagnosis of rectal gonorrhea or syphilis, use of methamphetamine or poppers, or history of exchange sex in the prior 12 months, and those in ongoing sexual relationships with HIV-positive male partners who are not on ART, on ART <6 months, or not virologically suppressed; [d]MSM who do not meet criteria for recommending PrEP and who reported CAS with a partner who is not main/primary, CAS with an HIV-positive or unknown status partner, diagnosis of urethral gonorrhea or rectal chlamydia, or injection drug use in the past 12 months, and those in ongoing sexual relationships with HIV-positive male partners who have been on ART ≥6 months and who are virologically suppressed.

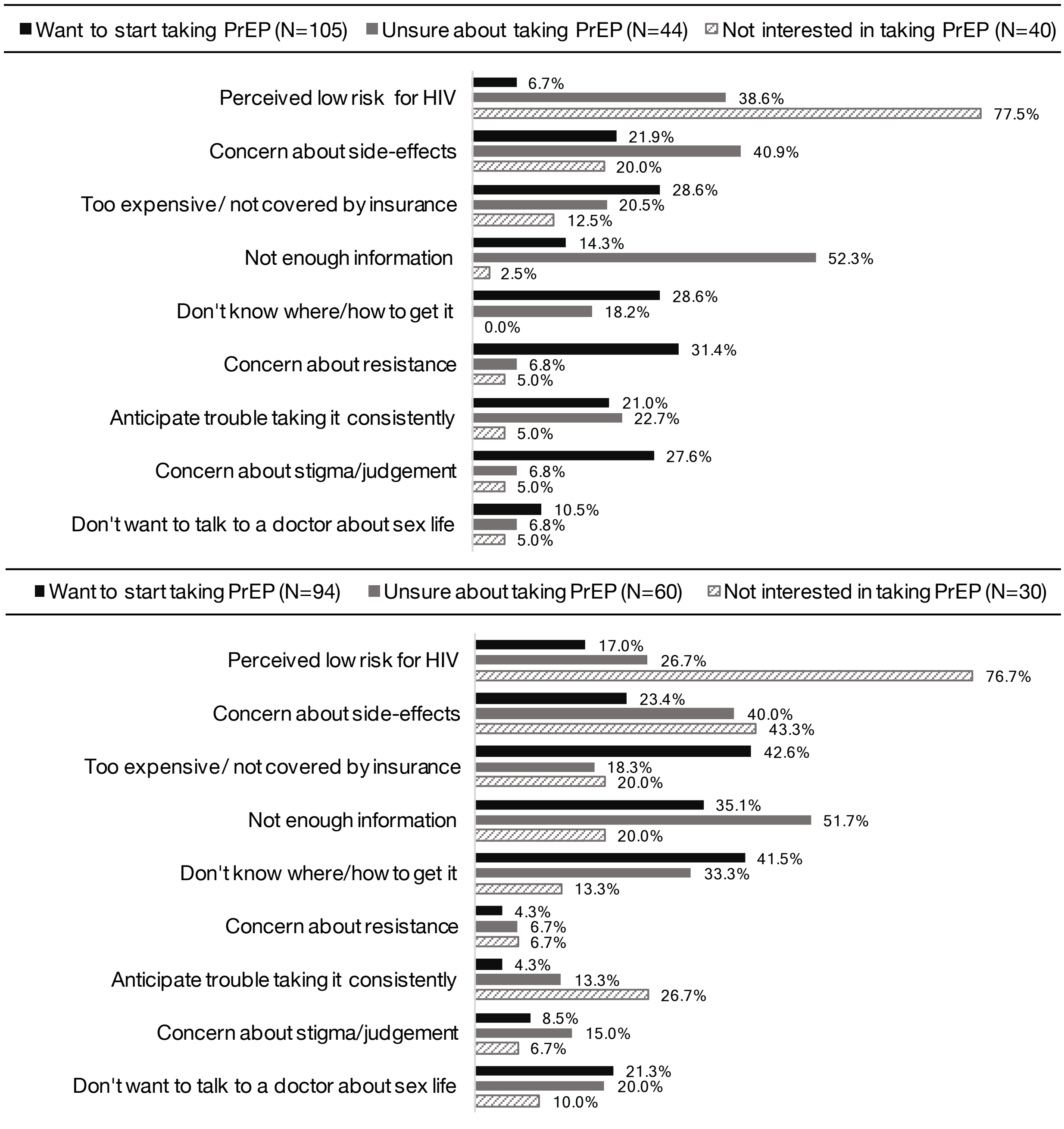

Figure 1.2: Reasons for not taking or not being interested in PrEP among PrEP-naïve MSM who meet local indications for PrEP being recommended[a] (top panel) or discussed[b] (bottom panel), by reported interest in starting PrEP (N=373).

[a]MSM who reported a diagnosis of rectal gonorrhea or syphilis, use of methamphetamine or poppers, or history of exchange sex in the prior 12 months, and those in ongoing sexual relationships with HIV-positive male partners who are not on ART, on ART <6 months, or not virologically suppressed; [b]MSM who do not meet criteria for recommending PrEP and who reported CAS with a partner who is not main/primary, CAS with an HIV-positive or unknown status partner, diagnosis of urethral gonorrhea or rectal chlamydia, or injection drug use in the past 12 months, and those in ongoing sexual relationships with HIV-positive male partners who have been on ART ≥6 months and who are virologically suppressed.

Table 1.3: Correlates of current PrEP use (N=850)[a]

	Using PrEP		Unadjusted associations		Adjusted associations Base model[b]		Exploratory model[c]	
	n	%	OR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
A priori covariates								
Region of residence				<0.001		0.260		0.676
King County	123	25.2%	Reference		Reference		Reference	
Other western Washington	32	13.4%	0.46 (0.30, 0.70)		0.67 (0.41, 1.09)		0.80 (0.45, 1.44)	
Eastern Washington	18	14.5%	0.50 (0.29, 0.86)		0.82 (0.44, 1.53)		1.13 (0.53, 2.42)	
Age				<0.001		<0.001		0.043
16 to 24	18	7.2%	Reference		Reference		Reference	
25 to 34	70	25.4%	4.36 (2.51, 7.57)		3.97 (2.19, 7.18)		2.99 (1.43, 6.25)	
35 to 44	44	33.1%	6.34 (3.48, 11.57)		5.23 (2.66, 10.27)		3.09 (1.33, 7.23)	
45 to 54	29	28.7%	5.17 (2.71, 9.85)		4.17 (2.03, 8.57)		3.34 (1.32, 8.41)	
55 and older	12	13.2%	1.95 (0.90, 4.23)		2.06 (0.87, 4.88)		2.31 (0.83, 6.41)	
Race/ethnicity				0.717		0.784		0.858
Non-Hispanic white	125	21.3%	Reference		Reference		Reference	
Hispanic	26	17.4%	0.78 (0.49, 1.25)		0.76 (0.45, 1.29)		0.96 (0.50, 1.84)	
Non-Hispanic black	7	21.9%	1.03 (0.44, 2.45)		0.86 (0.32, 2.33)		0.60 (0.19, 1.91)	
Non-Hispanic other	15	18.3%	0.83 (0.46, 1.50)		0.95 (0.47, 1.90)		0.98 (0.44, 2.17)	
Gay/homosexual identity	160	22.3%	2.68 (1.47, 4.87)	0.001	1.90 (0.96, 3.75)	0.063	1.50 (0.67, 3.39)	0.326
Education				<0.001		0.002		0.126
High school or less	7	5.2%	Reference		Reference		Reference	
Some college/vocational school	41	15.0%	3.23 (1.41, 7.41)		2.00 (0.82, 4.89)		1.50 (0.52, 4.33)	
4-year college or higher	125	28.3%	7.21 (3.28, 15.86)		3.66 (1.55, 8.66)		2.34 (0.83, 6.55)	
Income				<0.001		0.319		0.534
Less than $15,000	7	7.1%	Reference		Reference		Reference	
$15,000 to $29,999	13	12.6%	1.90 (0.72, 4.98)		2.07 (0.73, 5.86)		1.76 (0.53, 5.87)	
$30,000 to $49,999	34	23.1%	3.95 (1.68, 9.33)		2.80 (1.09, 7.14)		2.84 (0.98, 8.29)	
$50,000 to $99,999	59	22.8%	3.88 (1.71, 8.82)		2.37 (0.96, 5.86)		1.96 (0.68, 5.62)	
$100,000 or more	54	27.3%	4.93 (2.15, 11.30)		2.90 (1.13, 7.46)		1.84 (0.62, 5.50)	
I prefer not to answer	6	13.6%	2.08 (0.65, 6.58)		1.94 (0.54, 7.01)		1.77 (0.39, 8.12)	
WA State PrEP guidelines category				<0.001		<0.001		
Not indicated	13	4.1%	Reference		Reference			
Discuss[d]	69	27.2%	8.81 (4.74, 16.37)		10.14 (5.31, 19.37)			
Recommend[e]	91	33.0%	11.62 (6.32, 21.36)		13.91 (7.35, 26.34)			
Exploratory covariates								

Has health insurance	170	21.9%	6.74 (2.10, 21.67)	0.001			6.16 (1.57, 24.14)	0.009
Diagnosis with rectal gonorrhea or syphilis	27	41.5%	3.11 (1.84, 5.26)	<0.001			3.35 (1.49, 7.49)	0.003
Anal sex role				<0.001				0.364
No anal sex	1	1.0%	0.03 (0.00, 0.24)				0.28 (0.03, 2.33)	
Exclusively bottom	20	12.1%	0.41 (0.21, 0.78)				0.74 (0.31, 1.74)	
Versatile	127	25.9%	1.04 (0.63, 1.70)				1.13 (0.58, 2.20)	
Exclusively top	25	25.3%	Reference				Reference	
≥10 anal sex partners	83	60.6%	10.64 (7.08, 16.00)	<0.001			2.99 (1.73, 5.14)	<0.001
Current HIV-positive male partner	30	41.1%	3.09 (1.88, 5.10)	<0.001			3.63 (1.52, 8.69)	0.004
CAS with a partner who was not main/primary or whose HIV status was positive or unknown	153	33.8%	9.61 (5.89, 15.69)	<0.001			4.78 (2.63, 8.70)	<0.001
Injection drug use	5	9.3%	0.38 (0.15, 0.97)	0.044			0.33 (0.09, 1.19)	0.092
Methamphetamine use	10	13.5%	0.59 (0.30, 1.17)	0.130				
Poppers use	77	41.4%	4.18 (2.91, 6.01)	<0.001			1.91 (1.17, 3.13)	0.010
History of exchange sex	1	3.1%	0.12 (0.02, 0.89)	0.038			0.32 (0.03, 3.02)	0.321
Perceived effectiveness of PrEP ≥90%	153	36.0%	11.39 (6.97, 18.61)	<0.001			4.83 (2.62, 8.89)	<0.001

Acronyms: OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; CAS, condomless anal sex; PrEP, pre-exposure prophylaxis

[a]This analysis is restricted to respondents who have never or are currently using PrEP and provided responses to all covariates; [b]The base model includes only *a priori* covariates (region, age, education, race/ethnicity, sexual orientation, income, and PrEP candidacy based on Washington state guidelines); [c]The exploratory model includes base model social and demographic variables and exploratory variables that were significant in biviariate analyses. The Washington state PrEP guideline category variable was not included in the exploratory model because it is derived from the specific HIV risk indicators included as exploratory covariates; [d]MSM who do not meet criteria for recommending PrEP and who reported CAS with a partner who is not main/primary, CAS with an HIV-positive or unknown status partner, diagnosis of urethral gonorrhea or rectal chlamydia, or injection drug use in the past 12 months, and those in ongoing sexual relationships with HIV-positive male partners who have been on ART ≥6 months and who are virologically suppressed; [e]MSM who reported a diagnosis of rectal gonorrhea or syphilis, use of methamphetamine or poppers, or history of exchange sex in the prior 12 months, and those in ongoing sexual relationships with HIV-positive male partners who are not on ART, on ART <6 months, or not virologically suppressed.

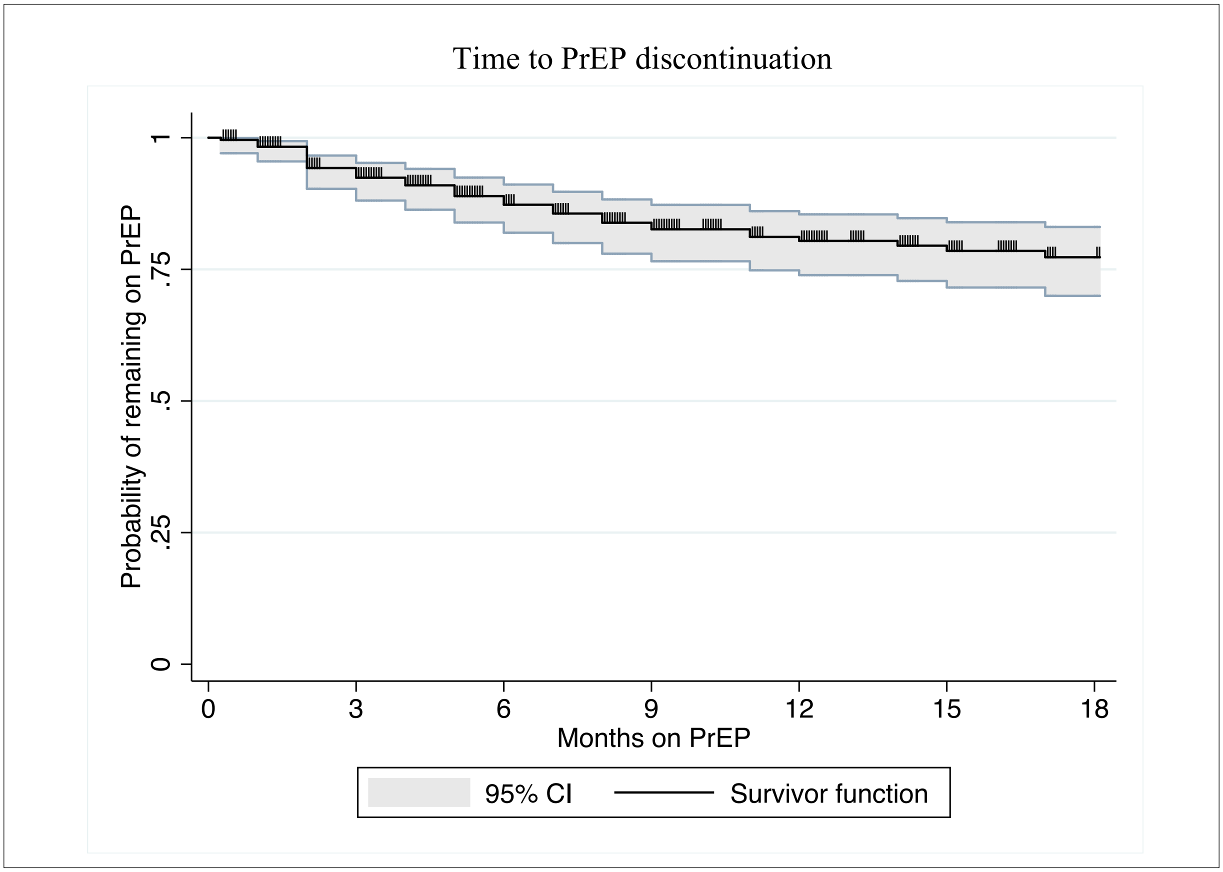

Figure 1.3: Time to PrEP discontinuation

Includes data from 194 current and 44 past PrEP users who provided data on their dates of PrEP use. Tic marks indicate censoring times for current PrEP users. The graph is truncated at 18 months; 60 men reported having taken PrEP for 18 months or longer.

CHAPTER 2: A network-based mathematical model to evaluate the impact of pre-exposure prophylaxis on HIV incidence in Washington State MSM

ABSTRACT

Background: With high preventative efficacy against HIV infection, pre-exposure prophylaxis (PrEP) has the potential to contribute to substantial declines in HIV transmission at the population level. However, the impact of the intervention will depend on individual, structural, and network-level factors, which are heterogeneous across the United States.

Methods: We constructed a stochastic network-based mathematical model to estimate the impact of PrEP among men who have sex with men (MSM) in Washington State, using local data for model parameterization and calibration. To evaluate the range of possible outcomes with PrEP, we defined scenarios with varying uptake, adherence, and risk compensation, each of which we simulated 500 times over 10 years. PrEP scenarios were evaluated in terms of annual diagnosis and incidence rates, the incidence rate ratio (IRR) relative to a scenario with no PrEP, the cumulative percent of infections averted, and the number needed to treat to avert one infection.

Results: Relative to a scenario with no PrEP, our model estimated that PrEP use would result in a 48-83% reduction in the annual HIV incidence rate at the end of 10 years. With uptake increased from observed 2017 levels to 50% coverage among eligible men by 2020, 62-65% of infections would be averted over 10 years. Our model indicates that the HIV prevention benefits of PrEP are robust to risk compensation resulting in decreases in condom use.

Conclusions: Grounded in local data, our model indicates that sustained use of PrEP over 10 years could have a substantial impact on HIV incidence in Washington State. Decreases in condom use and modest variations in adherence are unlikely to undermine the population-level benefits of the intervention.

INTRODUCTION

Antiretroviral medications have been shown to be highly effective for both prevention and treatment of HIV,[69] spurring goal-setting and discussions of the path towards elimination of the virus in the United States.[8,9,70] Men who have sex with men (MSM) bear a disproportionate burden of infection, and incidence in this group has remained relatively stable over the past decade.[4,7] Prevention strategies relying on sexual risk behavior change have been shown to have limited practical effectiveness,[12,13,71,72] and there is evidence that use of condoms has decreased in recent years.[50,73] With pre-exposure prophylaxis (PrEP), men who maintain high adherence have a >90% reduced risk of acquiring HIV through male-male sexual contact.[114,15] However, the population-level impact of PrEP on the trajectory of the epidemic will depend on levels of uptake and adherence, changes in risk behavior, engagement in care, and patterns of sexual contact.

The HIV epidemic in the United States is demographically and geographically heterogeneous,[7,74–78] with the estimated prevalence of infection among MSM ranging from 4% in South Dakota to 32% in the District of Columbia.[77] Within geographic regions, further disparities in HIV prevalence and transmission risk reflect differences in behavior, access to care, and in the size, composition, and structure of sexual networks.[79] For sexually transmitted infections such as HIV, the rate of partnership formation and temporal overlap in partnerships (concurrency) are important drivers of transmission.[80–87] The degree to which individuals form partnerships with persons similar to themselves on attributes such as race/ethnicity and age also has a strong influence on transmission dynamics and resulting disparities.[88,89] To the extent that these features vary across the United States, so too will the impact of PrEP.

When parameterized using appropriate local data, mathematical models provide a valuable framework for assessing the context-specific impact of interventions such as PrEP, accounting for both individual- and network-level factors that influence transmission.[30–32] A growing number of studies have used mathematical modeling to estimate the epidemiologic impact and cost-effectiveness of PrEP in MSM.[90–108] However, most of these studies have used compartmental model frameworks, which have limited ability to account for individual heterogeneity and structural features of the sexual network.[82,109,110] Of the U.S.-based models designed to represent the dynamic properties of the sexual network, all but one[99] have been parameterized using national-level data, which limits the relevance of model predictions to any given jurisdiction.

In this paper, we present findings from a network-based mathematical model developed to estimate the impact of PrEP on HIV transmission among Washington State MSM. Washington has high levels of diagnosis and engagement in care, with an estimated 91% of persons living with HIV diagnosed and 73% virally suppressed in 2017.[33] These features make Washington a unique setting in which to assess the potential contribution of adding PrEP to the existing prevention portfolio. Using empirical data on the sexual networks, behaviors, clinical epidemiology, and patterns of PrEP use of Washington MSM, our model provides policy-relevant insights on effective strategies to control the HIV epidemic locally.

METHODS

Model overview

We constructed a network-based mathematical model to represent the demographic, sexual network, and epidemiologic processes that influence HIV transmission among MSM in Washington State using the EpiModel software platform.[109] EpiModel provides functions for estimation and simulation of network-based mathematical models using the statistical framework of exponential family random graph models (ERGMs).[111] For this project, we modified and adapted previous models of HIV transmission among men who have sex with men[94,112] for the

Washington State context. The model's structure and parameter values were informed by analyses of data from local surveys of MSM and surveillance records.

Our model represents an open population of MSM aged 18 to 59. Upon entry at age 18, individuals are assigned fixed attributes, such as race/ethnicity, region of residence, and circumcision status. Dynamic attributes, such as age, treatment status, and viral load are updated in weekly time steps. Pairs of individuals form and dissolve partnerships according to probabilities dependent on their attributes and the presence of other ties, which are estimated from observed data using ERGMs.[109,111,113] Within these partnerships, the model simulates sex acts, condom use, and HIV transmission stochastically. Full details on the methodology and derivation of parameters are provided in Supplemental Appendix 2.

Data sources

The primary source of data on sexual partnerships and behaviors within partnerships was the 2017 Washington HIV Prevention Project (WHPP), an internet-based survey of MSM in Washington State (Chapter 1).[114] As this survey excluded men who reported a positive HIV diagnosis, we supplemented it with data on HIV-positive MSM from three sources. Where possible, we used local data from the Washington site of the 2014 Medical Monitoring Project (MMP), an annual probability-based survey of persons living with diagnosed HIV who are in care.[115] For parameters not measured in the MMP, we used data from HIV-positive respondents to an online survey of MSM in the U.S. (ARTnet) and from a previous analysis of Atlanta-based cohort studies.[94] Data from the WHPP, MMP, and ARTnet surveys were weighted to match the demographic composition of males in Washington, as detailed in Supplemental Appendix 2.

Parameters relating to HIV testing were derived from the WHPP survey and Washington State surveillance data on late diagnoses. Engagement in care, viral suppression, and HIV-associated mortality rates were estimated from surveillance data, and HIV natural history and transmission probability parameters were drawn from published studies. We used data from the WHPP survey to estimate PrEP coverage and discontinuation, and PrEP adherence and efficacy were defined from the literature.

Sexual network

To account for heterogeneity in partnership dynamics and behaviors, we modeled three overlapping partnership networks distinguished by partner type. Main partners were defined as individuals whom respondents feel "committed to above all others." Partners with whom men have ongoing sexual relationships but whom they do not classify as main were categorized as "persistent," and partners with whom men have sex only once were represented in the "instantaneous" network. For each of these networks, partnership formation depended on the race/ethnicity and region of residence of the individuals involved, patterns of sexual mixing by age, race/ethnicity, and region, and each individual's number of ongoing partnerships. For instantaneous partnerships, an additional term specified heterogeneity based on membership in one of four risk groups with varying propensity for instantaneous partnerships. Main and persistent partnerships dissolved as a function of the estimated median duration of each partner type.

HIV transmission and disease progression

Within serodiscordant partnerships, we simulated receptive and insertive anal sex acts according to data on mean coital frequency by partnership type. For a given sex act, transmission depended on condom use, the susceptible partner's sexual position, circumcision status, and CCR5-Δ32 genotype, and the infected partner's stage of infection and viral load. Time to diagnosis was controlled by a fixed attribute that assigned men to either screen for HIV at regular intervals or test only with progression to symptomatic HIV/AIDS, which was assumed to occur after 7.5 years of infection.[116,117] All diagnosed individuals were assumed to initiate ART, with levels of viral suppression and rates of cycling on and off treatment determined by an adherence profile attribute. Persons living with HIV were subject to elevated age- and race-specific mortality rates.

PrEP

Men were eligible to initiate PrEP at the time of HIV screening if they tested HIV-negative and met at least one behavioral indication defined based on guidelines developed by the Washington State Department of Health and Public Health—Seattle and King County:[35] 1) being in an ongoing partnership with a known HIV-positive partner, or 2) having condomless anal sex in the past 12 months outside of the context of a mutually monogamous relationship with a main partner who had tested negative for HIV. While the guidelines also recommend initiation or discussion of PrEP with men who report drug use, exchange sex, or STIs, these indications function as proxy measures of HIV risk, which, for sexual exposure, our model tracks directly.

To examine a range of potential outcomes with PrEP, we defined scenarios with varying levels of uptake, adherence, and changes in risk behavior with use of PrEP (risk compensation). Eligible men were started on PrEP in a given timestep if current coverage was below the defined threshold. The first uptake scenario assumed stable coverage at 33% of eligible men, the level of PrEP use among high-risk respondents to the 2017 WHPP survey.[114] A second scenario increased coverage linearly to a maximum of 50% in 2020, aligning with Washington State goals.[33] In the third scenario, we increased coverage linearly to 66%, corresponding to the proportion of eligible MSM in Washington who reported use of or interest in starting PrEP in 2017.[114] Acknowledging that selection and response biases may impact survey data on PrEP coverage (i.e., if PrEP users were more likely to complete the survey than men not on PrEP), in our final scenario we set PrEP coverage to 25% for the duration of the simulation. Figure 2.1 displays PrEP coverage over time under these four scenarios.

Men who initiated PrEP were assigned one of three adherence profiles, corresponding to mean adherence of <2 doses per week, 2-3 doses per week, or ≥4 doses per week. PrEP use was assumed to lower the per-contact probability of HIV transmission by 31%, 81%, and 96% for each of these respective levels of adherence.[14,15] In our baseline scenario, the proportion of men in each of these groups was 5%, 30%, and 65%, based on data from demonstration projects and open-label studies that measured tenofovir diphosphate concentrations over time using dried blood spot samples.[10,15118,119] In sensitivity analyses, we evaluated the impact of higher adherence, with levels drawn from self-reported data, medication possession ratios, and cross-sectional dried blood spot samples taken closer to the time of PrEP initiation.[114,118–123] The proportions of men with low, medium, and high adherence in these analyses were 3%, 7%, and 90%, respectively.

Although data on risk compensation attributable to PrEP have been inconsistent,[15,118,119,121,123–131] there is strong evidence that PrEP use is associated with increased engagement in condomless anal sex.[119,121,123–125,127,129,132] We simulated risk compensation by decreasing the probability of condom use across partnership types from 0% to 100% with use of PrEP.

We modeled discontinuation of PrEP coinciding with HIV diagnosis, changes in risk behavior resulting in the intervention no longer being indicated, and spontaneously. In scenarios with risk compensation, we explored the impact of men maintaining on-PrEP levels of condom use following spontaneous discontinuation.[133]

Calibration, simulation, and analysis

We calibrated the model in the absence of PrEP to the prevalence of diagnosed HIV in 2017 among Washington State MSM aged 18-59, which we estimated at 8.18% using data on the size of the MSM population from Grey et al.[134] to define the population denominator. We selected two variables with substantial uncertainty for use as tuning parameters: condom use and per-act HIV transmission probability. Prior distributions were informed by assessment of the magnitude and direction of potential bias in survey data and the range of estimates from the literature.[135–138] Posterior distributions were estimated using approximate Bayesian computation with sequential Monte Carlo sampling,[96,139] and we selected the set of values that resulted in equilibrium prevalence within 0.1% of the target.

Using these calibrated parameters, we simulated network, demographic, and epidemic dynamics in a starting network of 10,000 MSM. After allowing the model to burn-in to an equilibrium state, we simulated each PrEP use scenario 500 times over 10 years, from 2017 to 2027, for comparison with a baseline counterfactual scenario of no PrEP. For each scenario, we calculated the annual number of new HIV diagnoses, mean incidence rates per 100 person-years, incidence rate ratios (IRRs) relative to the baseline scenario, the cumulative percent of infections averted, and the number needed to treat (NNT) with PrEP to avert 1 new infection. The NNT is defined as the total person-years on PrEP divided by the number of infections averted. For assessment of the marginal impact of each PrEP uptake scenario, we assume 20% risk compensation.[119,124,127,140] Outcomes are summarized as the median and interquartile range (IQR) across simulations.

RESULTS

In the absence of PrEP, our model estimated an annual incidence rate of 0.54 cases per 100 person-years (IQR: 0.44, 0.65). Figure 2.2 shows the projected annual incidence rates over time with varying PrEP uptake, baseline adherence, and a 20% reduction in condom use among PrEP users. In the scenario with stable PrEP coverage at observed 2017 levels (33% of eligible men), the HIV incidence rate was reduced by 41% in the first year (IRR: 0.59, IQR: 0.44, 0.80) and by 58% in 2026 relative to the no-PrEP scenario (IRR: 0.42; IQR: 0.32, 0.57; Table 2.1). With increased coverage up to 50% of eligible men by 2020, the HIV incidence rate decreased by 71% by 2026 (IRR: 0.29; IQR: 0.21, 0.40). Decreases in new diagnoses were similar in magnitude, though with a slight delay (Figure 2.3). In the first year of stable 33% coverage, new diagnoses declined by 14% (IQR: -15%, 31%), and were 41% lower than the no-PrEP scenario in the second year (IQR: 24%, 55%).

Over the 10-year period, PrEP use under the modeled scenarios with 20% risk compensation would avert 40% to 70% of new infections (Table 2.1). In the scenario with stable PrEP coverage at 33% of eligible men, 50% of all new infections would be averted with baseline adherence levels (IQR: 41%, 57%). Higher adherence would increase the impact of PrEP slightly to avert 52% of all new infections over 10 years (IQR: 44%, 59%). With uptake increased to 50% coverage among eligible men in 2020, 62% (IQR: 55%, 67%) and 65% (IQR: 59%, 70%) of infections would be averted with baseline and high adherence, respectively. With higher coverage, the number of person-years on PrEP required to avert one infection would increase (Table 2.1). With baseline adherence, stable 25% coverage would avert one infection for every 85 person-years on PrEP (IQR: 74, 99), compared to one infection averted for every 118 person-years on PrEP under the maximal coverage scenario (IQR: 112, 125).

As shown in Figure 2.4, prevention gains with PrEP were fairly insensitive to risk compensation. With condom use returning to pre-PrEP levels for men who discontinue spontaneously, the percent of infections averted in a scenario with 50% coverage by 2020 and baseline adherence levels ranged from 62% (IQR: 56%, 67%) with no risk compensation to 60% (IQR: 53%, 66%) with 100% risk compensation. If condom use were to remain at on-PrEP levels following spontaneous discontinuation, the percent of infections averted would be reduced by up to 7% with 100% risk compensation (55% of infections averted; IQR: 48%, 62%).

DISCUSSION

Our model indicates that substantial declines in HIV incidence are possible with continued use of PrEP among Washington State MSM. With stable coverage over 10 years at observed 2017 levels,[114] approximately half of the incident cases predicted in the absence of PrEP would be averted. If coverage were to increase to meet State goals of 50% uptake among eligible men by 2020, an estimated 60% of infections would be averted. Incidence rates were still declining at the end of the simulation after PrEP coverage stabilized, suggesting even greater long-term benefits with sustained PrEP use. These findings provide strong support for further investment in programs to promote and facilitate uptake of PrEP among MSM at high risk of infection in Washington.

The predicted impact on HIV incidence from our model is higher than suggested by previous models of MSM in the US.[94,98,99,103,141,142] In a national-level dynamic network model, Jenness et al.[94] estimated that 30% coverage of PrEP among eligible men would result in 27% fewer incident cases over 10 years, and 50% coverage would avert 37% of cases. However, in this model, 21% of PrEP users were assumed to be fully non-adherent, lowering effective coverage. Other models have reported 16% to 33% of infections averted with mid-range coverage,[99,103,141] although a model of MSM in San Francisco predicted a 50-86% decline in incidence if PrEP uptake is concentrated among men at highest risk.[120]

One reason for the higher estimated impact of PrEP from our model may be the high engagement in care in Washington State. Prior models have represented populations with 20% to 67% of diagnosed cases virally suppressed,[94,99,101,103,120,141] whereas 82% of diagnosed MSM aged 18-59 in Washington were suppressed in 2017. In this context, acutely infected and undiagnosed cases are likely to account for a relatively greater proportion of transmission events, and the impact of preventing new infections will be accentuated. By representing temporal overlap in partnerships, a network-based model is well-suited to capture the chain of transmissions that arise, or are averted, during this window of high risk. Empirical data from New South Wales, Australia, where engagement in care is similar to Washington State, indicate that new diagnoses declined by 25% from the 12 months before to the 12 months after roll-out of a large-scale PrEP project.[143] Diagnoses with recent infection, used as indicator for incidence, fell by 32%. These declines coincided with scale-up to 20% coverage among all MSM in the region and were comparable to our model projections of a 32% decline in incidence and a 12% decline in new diagnoses over 12 months of PrEP at 25% coverage among eligible men (19% coverage overall).

Our findings highlight the cascading, non-linear effects of PrEP at the population level. In the scenario with PrEP coverage increasing to 50% among eligible men by 2020, 36% of all person-years at risk were covered by PrEP and 62% of infections were averted. With higher coverage, the efficiency of PrEP, measured as the number needed to treat to avert one infection, declined. Other models have reported similar declining marginal returns with increasing coverage,[98,141] which reflect the benefits of PrEP in averting downstream infections; with use of PrEP, fewer people acquire HIV, thereby decreasing the force of infection at the population level.

Adherence to PrEP has been found to be an important determinant of effectiveness in clinical trials,[37] with the relative reduction in incidence in trials of MSM ranging from 44% to 86% depending on levels of adherence in the cohorts.[125,144,145] In our simulations, increasing the proportion of men who maintain adherence of ≥4 doses per week from 65% to 90% conferred only a modest improvement to population-level outcomes. In both of these scenarios, ≥95% of men were assumed to take at least 2 doses per week, which corresponds to a 76%-99% reduction in the risk of infection.[14,15] While the population-level impact of PrEP would be reduced if more men took PrEP with low adherence, there is consistent evidence from observational studies that levels of adherence are high, with very few reported seroconversions among MSM with ongoing use of PrEP.[118,127,140,143,146]

Although concerns about risk compensation tempered early enthusiasm about PrEP,[147] our model aligns with previous simulation analyses in demonstrating that the benefits of PrEP are robust to even large decreases in condom use.[90,97,104,108] A previous network-based model estimated that complete cessation of condom use among PrEP-using men would result in 1 percentage point fewer infections averted relative to a scenario with no risk compensation.[97] If men who discontinue PrEP while still at high risk maintain lower levels of condom use, our model indicates that up to 7% fewer total infections would be averted over 10 years. One reason for the relatively small impact of risk compensation in our model is low baseline levels of condom use. By partner type, the average probability of condom use was 17% in main partnerships, 41% in persistent partnerships, and 51% in instantaneous partnerships. With 60% risk compensation, the proportion of sex acts within PrEP-using dyads that were protected decreased to 7%, 16%, and 20% for each partnerships type, respectively. Counterbalancing the resulting increased transmission risk for these individuals, lower condom use among the partners of PrEP users expands the pool of men who meet condom-based indications for PrEP.[97] As a result, the model assumes that uptake will increase to maintain the same level of coverage among eligible men.

A limitation of our model is that we do not model transmission of other sexually transmitted infections, which could increase HIV transmission. STI incidence is high among PrEP-users,[148] and some studies have reported increasing incidence with use of PrEP.[121,128,149,150] A recent mathematical modeling study revealed that PrEP may end up decreasing STI incidence in the population if it leads to higher rates of STI screening and treatment as components of PrEP care.[96] However recent evidence suggests that provider adherence to STI screening guidelines is low. A study in New York City found that only half of PrEP users reported receiving a rectal or oral swab for STI screening at their last visit,[151] and a study in San Francisco similarly reported low STI screening at PrEP care visits.[152] Future models should examine the impact of risk compensation on both STI and HIV incidence in the context of suboptimal STI screening. It would also be valuable for future models to examine the impact of community-level risk compensation, whereby increases in risk behavior may spill over to populations not taking PrEP.[153] As awareness of and confidence in the effectiveness of PrEP become more widespread, increases in risk behavior may become more pronounced.[130]

Although we predict strong declines in HIV incidence among Washington State MSM with use of PrEP, our model cannot be used to forecast when or if we might achieve elimination of HIV. Surveillance data show that new diagnoses were decreasing in Washington before the introduction of PrEP,[33] reflecting the effects of improvements in the care cascade and more effective ART regimens. In calibrating our model to sustain the estimated 2017 prevalence of diagnosed HIV among MSM in the absence of PrEP, we do not account for these pre-existing trends in transmission, nor for possible early effects of PrEP on prevalence. As such, our findings should be interpreted with caution regarding implications for the trajectory of the epidemic. Future work is needed to improve calibration and validation, possibly by collecting longitudinal network and behavior data to support fitting models to observed epidemic trends.

Better data on patterns of sexual behavior and PrEP use would also improve the accuracy of modeled projections. Our parameter estimates were largely derived from internet-based surveys, which tend to over-sample young, highly-educated, white, and high-risk men.[63,114] We re-weighted the survey samples to match the demographic profile of Washington males, but this procedure does not account for all sources of bias. However, in the absence of population-based methods for recruitment of MSM, internet-based surveys provide a feasible, efficient means for collecting valuable data at the county, state, or national level.[50,114] It is worth noting that estimates of PrEP use from the WHPP survey were consistent with estimates derived from local event- and venue-based surveys.[33] An additional limitation of our approach is that we estimated parameters relating to sexual mixing and behavior within partnerships using data on the most recent partnership, which may not capture the range of typical behaviors. Because condom use is a key determinant of HIV transmission risk and eligibility for PrEP, models could be improved with better data on heterogeneity in condom use within and between individuals, and on how individual-level preferences influence condom use at the dyad-level. With models that span a wide age range, it is also important to consider how behaviors change over the life course. This could be particularly informative for interpreting the implications of PrEP discontinuation. A recent Netherlands-based model found that incorporation of data on risk trajectories increased the projected impact of PrEP.[154] To support further research into these dynamics, new data collection is needed.

In 2019, the US Department of Health and Human services established new targets to reduce HIV incidence by 90% by 2029,[8] and increasing uptake of PrEP is a core component of the proposed strategy. In light of the geographic heterogeneity in the HIV epidemic, the national plan calls for data-driven policies tailored to the local level.[8] Grounded in local data on behavior, sexual network dynamics, and clinical care, our model indicates that efforts to support and increase uptake of PrEP in Washington State will be a valuable investment, yielding long-term reductions in transmission. In the context of high levels of testing and treatment in Washington, scale-up of PrEP to 50% coverage among eligible men by 2020 could avert nearly two-thirds of incident cases over 10 years. Within the range of observed levels of adherence, decreased condom use among PrEP users will do little to diminish these prevention gains. Future models are needed to identify the optimal allocation of prevention resources and to assess the potential for elimination of HIV in Washington State if PrEP uptake is paired with concurrent improvements in the HIV care cascade.

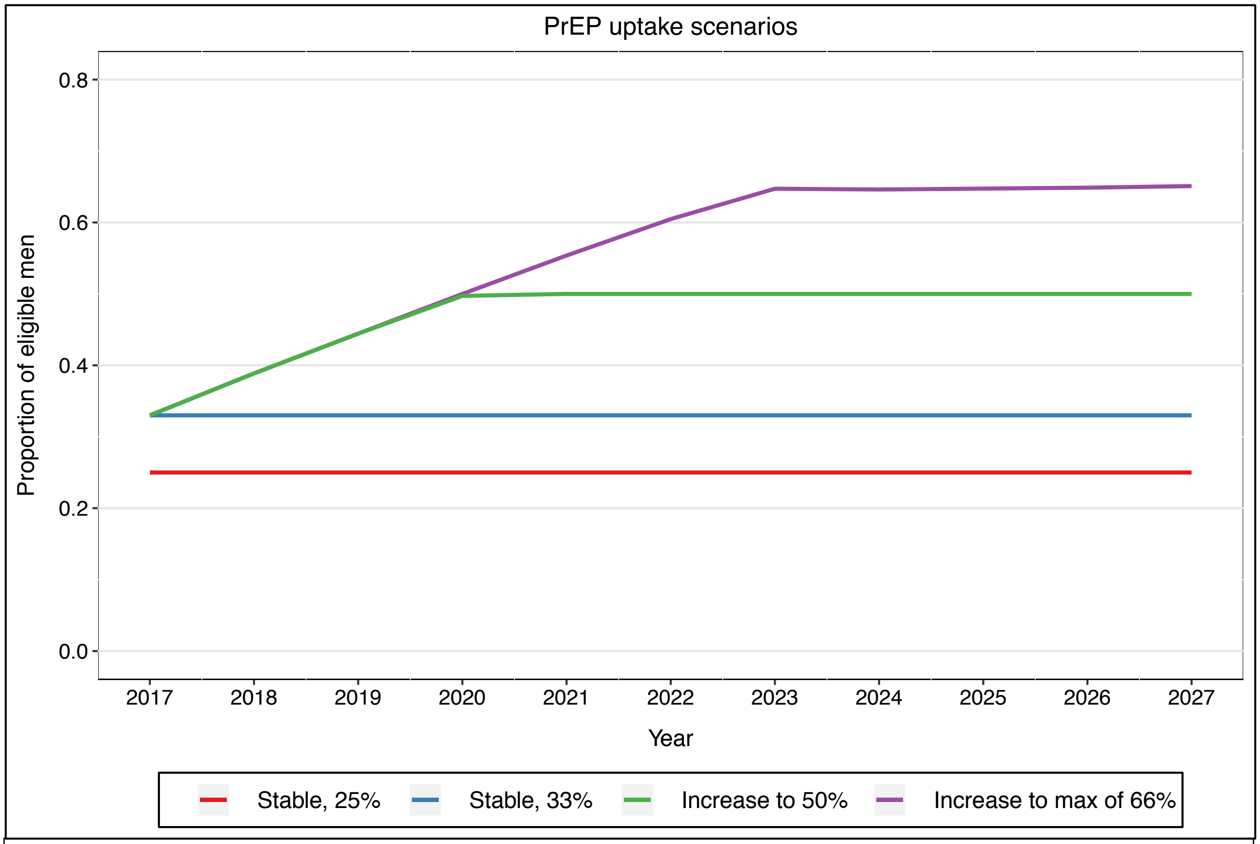

Figure 2.1: PrEP uptake scenarios

PrEP uptake is controlled in the model with thresholds defining the proportion of men with indications for PrEP who can use it at any point in time. We model four scenarios: two with stable coverage over the course of the simulation and two with increased coverage up to specified maximums.

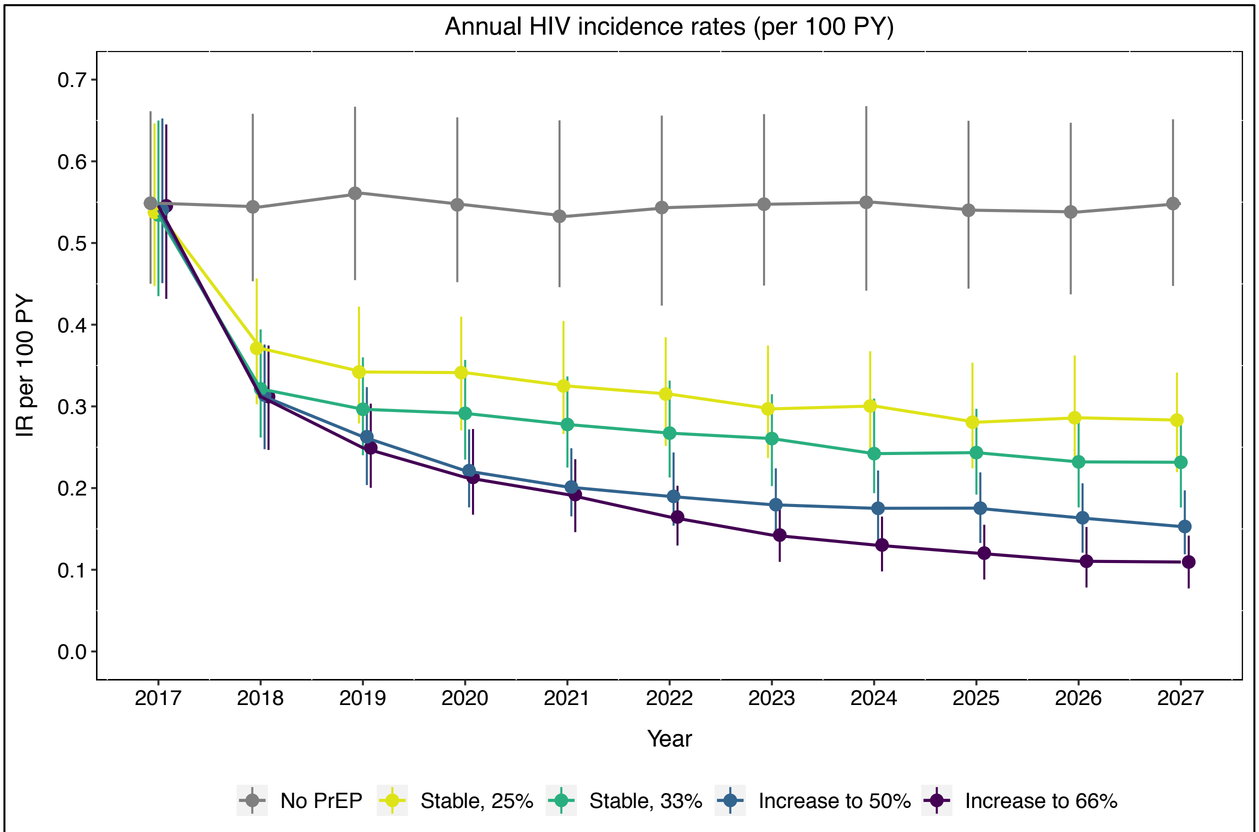

Figure 2.2: Annual HIV incidence rates (per 100 person-years) over 10 years, by PrEP uptake scenario

The solid lines connect median annual HIV incidence rates over time across 500 simulations, and the vertical lines span the interquartile range. Coverage thresholds are defined among men who meet indications for PrEP use. The scenarios presented assume baseline adherence levels and 20% reduction in condom use among PrEP users.

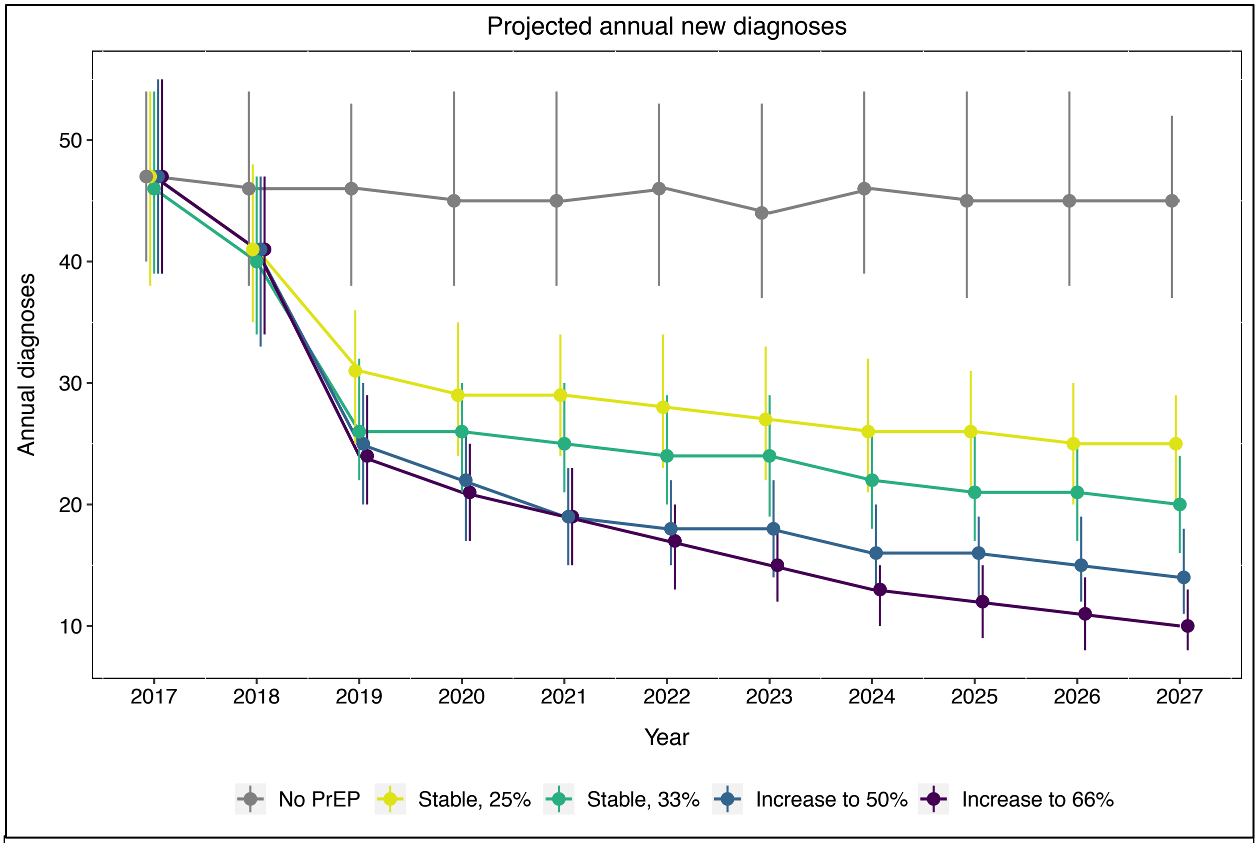

Figure 2.3: Annual HIV diagnoses by PrEP uptake scenario

The points indicate the median annual number of new diagnoses, and the vertical lines span the interquartile range from 500 simulations of each uptake scenario. Coverage thresholds are defined among men who meet indications for PrEP use. The scenarios presented assume baseline adherence levels and 20% reduction in condom use among PrEP users. Over the simulated period, the number of persons at risk in the presented scenarios ranged from 8,919 to 9,167.

Table 2.1: Projected impact of PrEP on HIV incidence in Washington State over 10 years with varying uptake[a] and adherence

	2026 HIV incidence rate (per 100 PY)[b] *Median (IQR)*	2026 Incidence rate ratio (IRR)[b] *Median (IQR)*	Percent of infections averted *Median (IQR)*	Number needed to treat (NNT) *Median (IQR)*
No PrEP	0.54 (0.44, 0.65)	Ref	Ref	Ref
PrEP with baseline adherence[c]				
Stable, 25% coverage	0.27 (0.22, 0.35)	0.52 (0.38, 0.69)	40.4% (32.1%, 49.2%)	84.6 (74.2, 98.8)
Stable, 33% coverage	0.23 (0.19, 0.29)	0.42 (0.32, 0.57)	50.2% (41.4%, 57.3%)	93.0 (83.7, 103.4)
Increase to 50% coverage	0.16 (0.12, 0.20)	0.29 (0.21, 0.40)	61.8% (55.2%, 67.9%)	107.9 (100.4, 116.9)
Increase to 66% coverage	0.11 (0.08, 0.14)	0.20 (0.15, 0.27)	67.0% (61.7%, 71.9%)	118.1 (111.6, 124.8)
PrEP with higher adherence[c]				
Stable, 25% coverage	0.27 (0.21, 0.34)	0.49 (0.35, 0.68)	44.1% (33.6%, 52.1%)	80.5 (69.2, 95.5)
Stable, 33% coverage	0.22 (0.16, 0.27)	0.41 (0.29, 0.55)	52.0% (44.4%, 59.9%)	89.0 (80.8, 98.8)
Increase to 50% coverage	0.15 (0.11, 0.19)	0.27 (0.19, 0.37)	64.8% (58.6%, 70.3%)	103.2 (97.6, 109.1)
Increase to 66% coverage	0.09 (0.07, 0.12)	0.17 (0.12, 0.24)	70.1% (63.5%, 74.5%)	113.5 (108.1, 119.4)

[a]Coverage thresholds are defined among men who meet indications for PrEP. The presented scenarios assume 20% risk compensation; [b]Incidence rates are calculated over the last year of the simulation; [c]In the baseline adherence scenario, 5% of men have low adherence (<2 doses/week), 30% have mid-level adherence (2-3 doses/week), and 65% have high adherence (4 doses/week). In the higher adherence scenario, these proportions are 3%, 7%, and 90%, respectively.

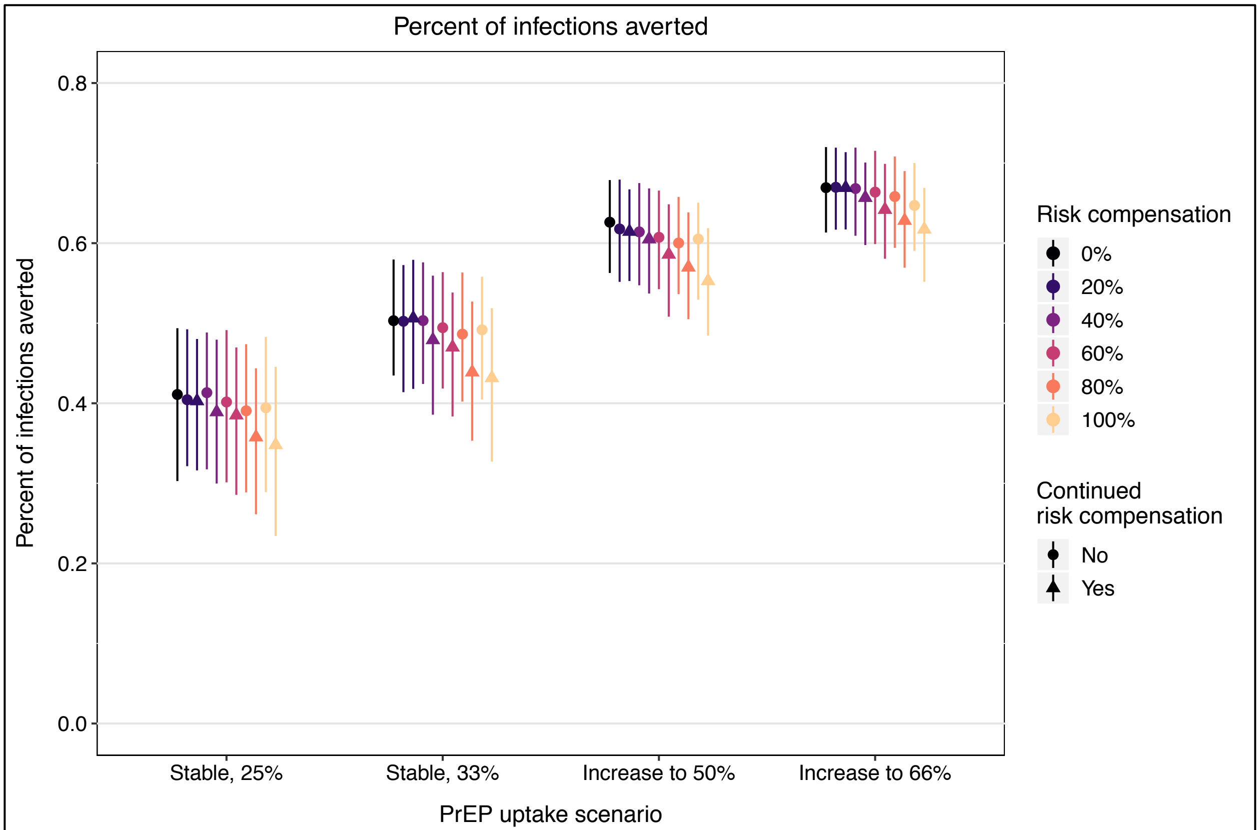

Figure 2.4: Percent of infections averted by 2027 relative to a scenario with no PREP, by PrEP uptake scenario, level of risk compensation, and whether risk compensation continues after spontaneous discontinuation

The points indicate the median percent of infections averted over 10 years of PrEP use, and the vertical lines span the interquartile range from 500 simulations of each uptake scenario. Coverage thresholds are defined among men who meet indications for PrEP use, and the plotted scenarios are with baseline levels of adherence. Risk compensation is modeled as a percent reduction in condom use across all partner types. In scenarios with continued risk compensation, on-PrEP levels of condom use are assumed to continue with spontaneous discontinuation of PrEP.

CHAPTER 3: The potential impact of routine one-time HIV screening in the United States: a model-based analysis of case finding strategies in two settings

ABSTRACT

Background: To improve clinical and prevention outcomes through earlier HIV diagnosis, US guidelines recommend routine screening of all adults and adolescents at least once (routine screening). The impact and efficiency of this strategy will vary across the US and will depend on patterns of targeted HIV screening.

Methods: We constructed a static linear model to estimate the optimal age and incremental impact of adding routine screening to risk-based and prenatal screening and testing prompted by symptom onset or partner notification. The model represents the processes of infection and diagnosis in a cohort of 100,000 persons aged 16-64. Using surveillance data and published studies, we parameterized the model at the national level and for two settings representing subnational variability in the rates and distribution of infection: King County, WA and Philadelphia County, PA. Screening strategies were evaluated in terms of test positivity, change in cumulative person-years of undiagnosed infection, and the number of cases that progress to symptomatic HIV/AIDS. To account for uncertainty in model inputs, we conducted 500 Monte Carlo simulations for each scenario.

Results: Depending on levels of risk-based screening, the optimal age for routine screening ranged from 30-34 in the national model, 26-27 in King County, and 44 in Philadelphia County. At these ages, test positivity with routine screening exceeded the established cost-effectiveness threshold of 0.1% only in Philadelphia County. Across settings, routine screening resulted in an incremental 2-7% reduction in years of undiagnosed infection and a 3-11% reduction in symptomatic cases, compared to reductions of 36-68% and 39-74% attributable to risk-based screening.

Conclusion: One-time routine HIV screening in the general population is likely to have a modest impact on population-level outcomes, though test positivity may be sufficient for the intervention

to be cost-effective in settings with high incidence in groups not typically the focus of risk-based screening.

INTRODUCTION

Reducing the time from HIV infection to diagnosis is central to efforts to control the HIV epidemic. Early diagnosis and treatment initiation is associated with improved clinical outcomes[21] and substantially reduced risk of transmission to susceptible partners.[22,23,155–157] In 2015, an estimated 15% of persons living with HIV in the United States were undiagnosed, and the median time from infection to diagnosis was 3 years.[20] To improve primary and secondary prevention endpoints, more work is needed to define effective strategies to identify individuals earlier in the course of infection.

The Centers for Disease Control and Prevention (CDC) and the US Preventative Services Task Force recommend that all adults and adolescents undergo screening for HIV at least once in their lifetime regardless of risk.[24,25] This recommendation for opt-out (routine) screening is in addition to guidelines calling for screening of high-risk persons at least annually, screening the sex and injection partners of diagnosed cases, screening pregnant women as part of prenatal care, and testing patients with HIV/AIDS-associated symptoms. Modeling studies have indicated that one-time routine screening is cost-effective in settings where the prevalence of undiagnosed infection exceeds 0.05%-0.2%.[158,159]

However, data suggest that the impact of routine screening has been limited.[26–28] In the years following the 2006 revision to the CDC HIV testing guidelines, the proportion of people who had ever tested for HIV in the United States remained largely unchanged.[29] Although some analyses of the case detection yield from routine screening programs have reported increases in diagnoses,[160,161] others have reported equivalent or lower case detection compared to targeted and symptom-driven testing.[26,162] An analysis comparing rates of testing and diagnosis pre- and post-implementation of a routine screening program in North Carolina STD clinics reported decreases in HIV testing among some sub-groups at high risk of infection.[27] To identify settings where routine screening is likely to be beneficial, analyses need to account for existing patterns of screening and the risk profile of the population.

In this paper, we evaluate the population-level impact of adding routine screening to other established screening strategies in terms of case detection, cumulative years of undiagnosed infection, and the number of cases that develop HIV/AIDS symptoms prior to diagnosis. Building on a previous model that did not account for targeted screening strategies,[163] we estimate the optimal ages for routine screening with respect to these outcomes. To highlight the dependence of the impact of routine screening on the local epidemic context, we compare three models: a national model, a model representing a jurisdiction with infection concentrated among MSM (King County, WA), and a model representing a jurisdiction with a more diverse distribution of infection (Philadelphia County, PA).

METHODS

Model overview

We constructed a static linear mathematical model using Microsoft Excel (Version 16.9) to represent the processes of HIV infection, testing, and diagnosis in a hypothetical population of 100,000 persons. To account for heterogeneity in HIV risk and patterns of testing, we divided the population into four groups: high- and low-risk men who have sex with men (MSM), men who have sex with women only (MSW), and women. All persons enter the model at age 16 and progress in yearly time steps through age 64 or HIV diagnosis, at which point they exit the model.

Our model evaluates the incremental impact of adding one-time routine screening to four baseline targeted HIV testing strategies: 1) repeat screening of those at high risk of infection; 2) prenatal screening; 3) testing prompted by partner notification, and; 4) diagnostic testing at the onset of HIV/AIDS-associated symptoms. Routine screening was implemented at specific ages, with all persons who had not engaged in risk-based or prenatal screening in that year offered routine screening. To examine the tradeoff between targeted and routine screening, we defined scenarios with low, mid-range, and high risk-based screening. Because repeat HIV testing among MSW and women is not common,[164] our model represents risk-based testing only among MSM.

To account for uncertainty in parameter estimates, we conducted Monte Carlo simulation using @RISK software (version 7.6, Palisade Company, Ithaca, NY). Distributions were defined based on the range of estimates in the literature or expert opinion (see Table 3.1 and Supplemental Appendix 3). Additional details about the model, including a model schematic and equations describing the modeled processes and outcomes, are presented in the Supplemental Appendix.

Parameters and data sources

Model inputs and sources are summarized in Table 3.1. To parameterize the model to King and Philadelphia Counties, we used local data to define the risk group distribution, HIV incidence rates, and birth rates. All other parameters were held at the values used in the national model.

<u>Risk group distribution</u>: To distribute the modeled cohort by gender, we used American Community Survey (ACS) data on the number of individuals ages 16-64 at the national level and in King and Philadelphia Counties.[165,166] For each setting, we applied estimates of the proportion of males who have had sex with men in the past 5 years to define the size of the MSM population.[134,167] Uncertainty intervals for the proportion of males who are MSM were defined to encompass 95% confidence intervals and estimates from other sources.[33] The percent of MSM who are high risk was informed by estimates of the percent with indications for PrEP use.[10]

<u>HIV incidence</u>: For the national-level model, we used published estimates of the number of incident HIV cases attributable to male-male sex, including MSM who also reported injection

drug use, and heterosexual contact among males and females in 2016.[7] The age distribution of infection for MSM, males, and females was defined as the weighted average of race/ethnicity-specific distributions. We derived the age distribution specific to MSW from the calculated distributions for all males and for MSM. We used 2016 ACS data[165] to define denominators for calculation of incidence rates, assuming the proportion of males who are MSM to be uniform across age groups.

For the King County model, we obtained estimates of the number of incident infections in 2016 using a back-calculation method that uses data on the number of new diagnoses and the date of the last negative test to measure undiagnosed infection.[168] Incident infections were calculated for MSM and other non-injection adult cases, and we apportioned non-MSM cases by gender according to the distribution of new diagnoses.[33] For the Philadelphia model, we used incidence estimates for 2016 published by the Philadelphia Department of Public Health.[169] For both jurisdictions, we applied the same age distribution as in the national model. We defined population denominators using 2016 ACS data in combination with estimates of MSM population sizes, described above.

In all three models, we assumed that all infections in individuals aged 13 and older occur between the ages of 16-64. Incidence rates for high- and low-risk MSM were calculated assuming the incidence rate among high-risk MSM to be 2.5 times that of low-risk MSM,[170] with a uniform uncertainty interval ranging from 2 to 3 times higher. With these inputs for incidence, the mean percent of infections in MSM was 71% in the national model, 77% in the King County model, and 57% in the Philadelphia County model. The lifetime risk of infection was 1 in 135, 1 in 225, and 1 in 62 for the three models, respectively.

Risk-based screening: We modeled patterns of risk-based screening by dividing the MSM population into three groups: men who do not engage in risk-based screening, men who screen every year, and men who screen less than once a year. The screening interval for non-annual testers was sampled from a normal distribution with a mean of 3 years and a standard deviation of 0.51 (Table 3.1). The proportion of men in each group varied by age, with mid-range estimates defined based on data from national surveys of MSM.[171–174] High-risk MSM were more likely to screen annually and less likely to never screen compared to low-risk MSM.[175] In the low risk-based screening scenario, the proportion of men assumed to screen annually was reduced and the proportion who do not regularly screen was increased, both by 30%. In the high risk-based screening scenario, annual screening was increased and never screening was reduced by 30%. Figure 3.1 displays the proportion of men in each screening group by age for the low, mid, and high screening scenarios.

Prenatal screening: Birth rates were used to define the number of women who become pregnant at each age.[176–178] We used data from surveys and medical records to define a plausible range for the proportion of pregnant women screened for HIV.[179–182]

Partner notification testing: For every 100 newly diagnosed cases, we estimated that an average of 8 additional persons would be diagnosed through partner notification.[183] To account for uncertainty in this estimate, we sampled values from a normal distribution with a standard deviation defined based on the range of published estimates.[183–186]

Symptom-based testing: Diagnostic testing was assumed to occur for all HIV-positive individuals upon CD4+ cell count depletion below 200 cells/mm^3. Following the approach adopted by Golden et al.,[163] we assumed that 8.8% of persons develop a CD4+ cell count <200 cells/mm3 within the first year of infection, after which the risk of dropping below this threshold is linear at a rate of 6.08% per year.[117] Symptom onset was assumed to coincide with CD4+ depletion.

Routine screening coverage: For consistency with previous models of routine screening,[158,187–189] we assumed that 80% of eligible individuals are offered and accept routine screening.

Analyses

To identify the optimal age for routine screening, we examined the impact of adding one-time screening at each age in the model. For each specified age, all persons who had not been tested through risk-based or prenatal screening in that year were considered eligible for routine screening. Outcomes were defined as the percent of tests that result in a new diagnosis (test positivity), the population-level person-years of undiagnosed infection, and the number of cases that progress to symptomatic HIV/AIDS before diagnosis in each modeled scenario. We assessed the optimal ages for routine screening as the ages at which test positivity was maximized and/or years of undiagnosed infection and symptomatic cases were minimized. We also report the range of ages for which these outcomes were within 10% of the optimal values.

For comparison with the impact of more targeted screening strategies, we evaluated the incremental impact of implementing prenatal, risk-based, and routine screening. For this analysis, we defined a series of nested screening scenarios. In the baseline scenario, diagnosis occurred only as a result of symptom-based testing and partner notification. We then added prenatal screening, with continued partner notification and symptom-based testing. The third and fourth scenarios added low- and high-level risk-based screening to these strategies. The fifth and sixth scenarios added routine screening to scenarios with low- and high-level risk-based screening, respectively. For each scenario, we report the test positivity for the added screening strategy and the percent change in person-years of undiagnosed infection and symptomatic HIV/AIDS cases relative to the baseline scenario.

In all analyses, we assumed 100% HIV test sensitivity and no window period. Outcomes are presented as the mean and 95% uncertainty intervals (UI) from 500 Monte Carlo simulations.

RESULTS

Optimal age for routine screening

In the national-level model, the test positivity from routine screening increased with age up to a peak of 0.06% (95% UI: 0.05%, 0.07%) at 31 years in a scenario with mid-range risk-based screening (Figure 3.1). Screening between the ages of 26 and 36 resulted in test-positivity within 10% of optimal. The cumulative population-level years of undiagnosed infection and symptomatic HIV/AIDS cases were both minimized with routine screening at age 34. Compared with test positivity, these latter two outcomes were less sensitive to the age of routine screening, with screening between the ages of 16 to 62 and 20 to 57, respectively, resulting in outcomes within 10% of optimal (Table 3.2).

The optimal age for routine screening was lower in King County, with test positivity maximized at 0.04% (95 % UI: 0.04%, 0.05%) at age 26 in the mid-range screening scenario (note that y-axes differ across plots in Figure 3.1). In Philadelphia County, routine screening at age 44 yielded a test positivity rate of 0.16% (95% UI: 0.14%, 0.19%). The age ranges for which test positivity was within 10% of optimal for these scenarios were 24 to 33 in King County and 38 to 52 in Philadelphia County.

By gender, test positivity was projected to be higher for males than for females across modeled settings (Figure 3.1). In the national and King County models, where MSM account for >70% of prevalent cases, the overall estimated routine screening test positivity by age more closely tracked that of males, for whom peak test positivity occurred at ages 28 and 25, respectively, compared to age 44 for females in both models. In the Philadelphia County model, where MSM account for an estimated 57% of prevalent cases, test positivity was optimized at age 44 for both males and females.

Relative impact of routine and targeted screening strategies

Test positivity with risk-based screening was high for all three modeled settings, ranging from 0.22% (95% UI: 0.18, 0.28) with high-level screening in King County to 1.20% (95% UI: 0.87%, 1.58%) with low-level screening in Philadelphia County (Table 3.3). Relative to a scenario with only symptom-based and partner notification testing, the mean incremental impact of adding low-level risk-based screening was a 50% (95% UI: 45%, 54%) reduction in person-years of undiagnosed infection and a 55% (95% UI: 49%, 60%) reduction in symptomatic HIV/AIDS cases in the national model. With high-level risk-based screening, these outcomes were reduced by 60% (95% UI: 57%, 63) and 66%, (95% UI: 62%, 69%) respectively. In King County, the incremental impact of risk-based screening was of a similar magnitude, while in Philadelphia County the impact was slightly lower, with mean estimates of 40-48% reductions in person-years of undiagnosed infection and 44-53% reductions in symptomatic cases.

Test positivity with routine screening at the national level was 0.07% (95% UI: 0.06%, 0.09%) when added to low-level risk-based screening and 0.05% (95% UI: 0.04%, 0.06%) when added to high-level risk-based screening (Table 3.3). Mean estimates for routine screening test positivity were 0.04% and 0.03% in King County, and 0.17% and 0.15% in Philadelphia County. Incorporating uncertainty intervals, the percent reduction in person-years of undiagnosed infection with routine screening ranged from 2-7% and the percent reduction in symptomatic cases ranged from a 3-11%. For comparison, increasing risk-based screening from low to high levels in the national model resulted in a 10% reduction in person-years of undiagnosed infection (95% UI: 8%, 13%) and an 11% reduction in symptomatic HIV/AIDS cases (95% UI: 8%, 14%). These gains were achieved with an average of 4.75 times fewer screening tests than in the scenario adding routine screening to low risk-based screening.

DISCUSSION

By accounting for heterogeneity in HIV risk and explicitly representing established screening practices, our model provides more realistic estimates of the potential impact of routine screening in different contexts in the United States. Even at optimal ages with high test acceptance, we estimated that one-time routine HIV screening in the general population will have limited impact on cumulative years of undiagnosed infection and the number of cases who develop HIV/AIDS symptoms prior to diagnosis. Although the test positivity values at the national level and in King County were below the established threshold of cost-effectiveness,[24,158,159] this threshold may have shifted with adoption of test and treat policies,[190,191] and willingness to pay may be higher as jurisdictions work towards meeting the goals of the Ending the HIV Epidemic Initiative.[8] Our results indicate that routine screening may be an effective case finding strategy particularly in settings with high HIV incidence and a relatively high proportion of cases in females and non-MSM males, such as Philadelphia County.

Our analyses demonstrate that the optimal age for routine screening depends on the local epidemic context. In King County, where HIV infection is concentrated in men who have sex with men, the optimal age range was younger and more narrowly defined than in Philadelphia, where the epidemic is more diverse. The range of ages resulting in a test-positivity within 10% of the optimal was also narrower with a more concentrated epidemic, driven by heightened incidence at younger ages for men who have sex with men. At the national level, our results are comparable with a previous model of the optimal age for routine screening in adults and adolescents,[163] and reinforce the conclusion that one-time screening before age 24 is not an efficient use of resources.[189]

Consistent with previous models,[187,192] our findings highlight a tradeoff between targeted and non-targeted screening. With higher practice of risk-based screening, the incremental impact of adding routine screening is diminished. However, the relative benefits of risk-based and routine screening depend on the epidemiologic context. In settings with transmission largely concentrated in MSM, increasing from low- to high-level risk-based screening resulted in shorter time to diagnosis and fewer symptomatic cases than adding routine screening to a scenario with low-level risk-based screening. In Philadelphia County, these scenarios were more comparable, although increased risk-based screening required far fewer screening tests to achieve the same results across all settings. Of note, our outcomes do not account for downstream effects of screening, in that earlier diagnosis would be associated with reduced risk of transmission.[22,23] Taking these effects into account would likely amplify the relative population-level benefits of targeted screening strategies, as improving diagnosis in groups with high rates of partner turnover and among pregnant women will avert more infections.

A key advantage of routine screening is that it does not depend on risk assessment and captures people who are not the typical focus of targeted testing campaigns.[27,162] Survey data indicate that 23% to 39% of MSM do not disclose to their healthcare providers that they have sex with men,[193,194] and providers do not always offer HIV tests to those with indications for repeat testing.[195] As a result, many high-risk individuals fall through the cracks with risk-based screening.[28,196] However, evaluations of routine screening programs have reported low rates of testing,[26,162,197] with perceptions of low risk reported as a common reason for screening not being offered or accepted.[198] Perceived and actual risk are often mis-aligned,[197,199,200] such that over-reliance on opt-out routine screening may miss opportunities to identify cases and engage persons at risk of infection in effective prevention strategies like pre-exposure prophylaxis. More research is needed to develop and test improvements in clinic procedures to prompt and facilitate screening of at-risk patients, which have been shown to outperform universal routine screening in some settings.[160,201,202]

A limitation to our model is the reliance on estimates of HIV incidence, which is measured with substantial uncertainty. A recent analysis suggested that HIV cases are over-counted by 26% in New York City and may be over-counted by as much as 100%-200% in other jurisdictions.[203] King County implements a rigorous de-duplication procedure,[33] but incidence estimates from Philadelphia and at the national level may be biased, resulting in an over-estimation of the impact of routine screening. Improvements in surveillance systems and methods to estimate incidence could improve the accuracy of model predictions. The age of infection is also subject to a high degree of uncertainty, and small numbers for some subgroups make these estimates unreliable.[7] Lacking data on the risk-group-specific age distribution of infection in King and Philadelphia Counties, we assumed the age distributions to be the same as in the national model. Future models should seek to incorporate data on how age at infection varies across contexts. Incidence rates are also influenced by uncertainty in the size of the MSM population, although results produced by sampling within a range of plausible values were not meaningfully different.

Our model made a number of simplifying assumptions. Based on data indicating low levels HIV testing in non-MSM populations,[164] we modeled risk-based screening only in MSM. To the extent that females and MSW engage in regular screening, our model will overestimate the impact of routine screening. We assumed that diagnostic testing occurs for all individuals with progression to CD4 count <200 cells/mm^3. Although we modeled heterogeneity in the time to reach this immunologic threshold, we do not fully capture variability in the timing of symptom onset and resulting diagnosis.[116,204] However, we do not expect variability in this process to meaningfully affect modeled outcomes. We also did not account for transmission attributable to injection drug use among non-MSM males and females, which contributed 5% of incident cases in 2016.[7] Although injection drug users engage in risk-based screening,[205,206] recent increases in diagnoses in this population[33,207] highlight the importance of improving case finding and may add value to routine screening programs.

Even with a relatively modest impact on HIV prevention and care outcomes, making HIV testing a routine component of healthcare provision is valuable to help normalize HIV testing and detect cases who would not be tested through other modalities. Together with modeled estimates from Golden et al.[163] and Neilan et al.,[189] our findings can be used to inform more efficient and impactful implementation of routine screening at optimal ages in different contexts. Ultimately, the question of whether routine screening is indicated for any particular clinical setting is an empirical question, but at the population level our model demonstrates that the impact will be modest in comparison to more targeted testing strategies. It will be important to ensure that implementation of the policy does not detract from targeted testing efforts. With data on HIV incidence and patterns of targeted HIV screening, other jurisdictions could use similar models to inform local HIV screening strategies.

Table 3.1: Model parameters and sources

Parameters varied across modeled settings							
	National		King County		Philadelphia County		
Parameter	*Base value*	*Distribution*[a]	*Base value*	*Distribution*[a]	*Base value*	*Distribution*[a]	*Refs*
Population composition							
Proportion female	0.502		0.491		0.522		165, 166
Proportion MSM	0.019	Normal (σ=0.001)	0.080	Uniform(0.064, 0.096)	0.061	Uniform(0.049, 0.073)	33,134,167
HIV incidence (per 100,000)							134,165,166, 169,208
MSM (overall)[b,c]							
16-24	881	σ = 64.1	311	σ = 49.3	1,149	σ = 181.3	
25-34	1,329	σ = 97.1	309	σ = 47.3	1,335	σ = 210.9	
35-44	586	σ = 41.5	145	σ = 22.7	815	σ = 124.8	
45-54	357	σ = 26.1	100	σ = 15.7	535	σ = 83.1	
55-64	188	σ = 13.2	58	σ = 8.92	286	σ = 44.2	
MSW[c]							
16-24	1.37	σ = 0.169	1.30	σ = 0.135	7.90	σ = 0.810	
25-34	3.85	σ = 0.475	2.40	σ = 0.246	17.06	σ = 1.743	
35-44	3.81	σ = 0.472	2.55	σ = 0.261	23.41	σ = 2.399	
45-54	2.93	σ = 0.362	2.22	σ = 0.228	19.42	σ = 1.980	
55-64	2.39	σ = 0.296	1.99	σ = 0.203	16.05	σ = 1.641	
Women							
16-24	4.36	Normal(σ = 0.29)	2.07	Normal(σ = 0.21)	9.57	Normal(σ = 0.98)	
25-34	8.67	Normal(σ = 0.57)	2.86	Normal(σ = 0.29)	14.39	Normal(σ = 1.47)	
35-44	6.98	Normal(σ = 0.46)	2.50	Normal(σ = 0.26)	16.16	Normal(σ = 1.65)	
45-54	5.19	Normal(σ = 0.34)	2.11	Normal(σ = 0.22)	13.03	Normal(σ = 1.33)	
55-64	4.20	Normal(σ = 0.28)	1.85	Normal(σ = 0.19)	10.38	Normal(σ = 1.06)	
Age-specific birth rates (per 1,000)							166,176-178
16-17	8.8		5.1		17.7		
18-19	37.5		16.7		46.4		
20-24	73.8		37.4		76.5		
25-29	102.1		65.6		73.2		
30-34	102.7		109.4		86.1		
35-39	52.7		69.7		51.4		
40-44	11.4		16.2		12.8		
45-49	0.9		1.7		0.8		

50+	0.0	0.0	0.0
Parameters applied to all modeled settings			
Parameter	*Base value*	*Distribution*[a]	*Refs*
MSM: proportion high-risk	0.247	Normal (σ=0.072)	[10]
Risk-based screening in MSM (mid-range scenario estimates)			[171,172,174,209,210]
Proportion who screen annually			
16-24	0.46		
25-34	0.55		
35-44	0.50		
45-54	0.38		
55-64	0.32		
Proportion who do not screen			
16-24	0.28		
25-34	0.09		
35-44	0.10		
45-54	0.12		
55-64	0.15		
Risk-based screening interval for MSM who screen <once/year	3	Normal(σ=0.51)	
Relative risk of annual screening for high- vs. low-risk MSM	1.5	Uniform(1.0, 2.0)	
Relative risk of no screening for high- vs. low-risk MSM	0.7	Uniform(0.5, 1.0)	
Proportion of pregnant women screened for HIV	0.8	Normal(σ=0.089)	[179-182]
Rate of symptom development			[117,163]
Year 1 of infection	0.0880	Normal($\sigma = 0.003$)	
Years 2-16 of infection	0.0608	Normal($\sigma = 0.003$)	
Partner notification: new diagnoses per index case	0.082	Normal($\sigma = 0.03$)	[183-186]
Routine screening acceptance	0.80		

[a]Prior distribution used for Monte Carlo simulation, for variables with substantial uncertainty; [b]Combined incidence for high- and low-risk MSM; [c]For MSM and MSW, uncertainty is modeled separately for the numerator and denominator. In this table, we present the mean and standard deviation from the resulting distribution of sampled values across 500 Monte Carlo simulations.

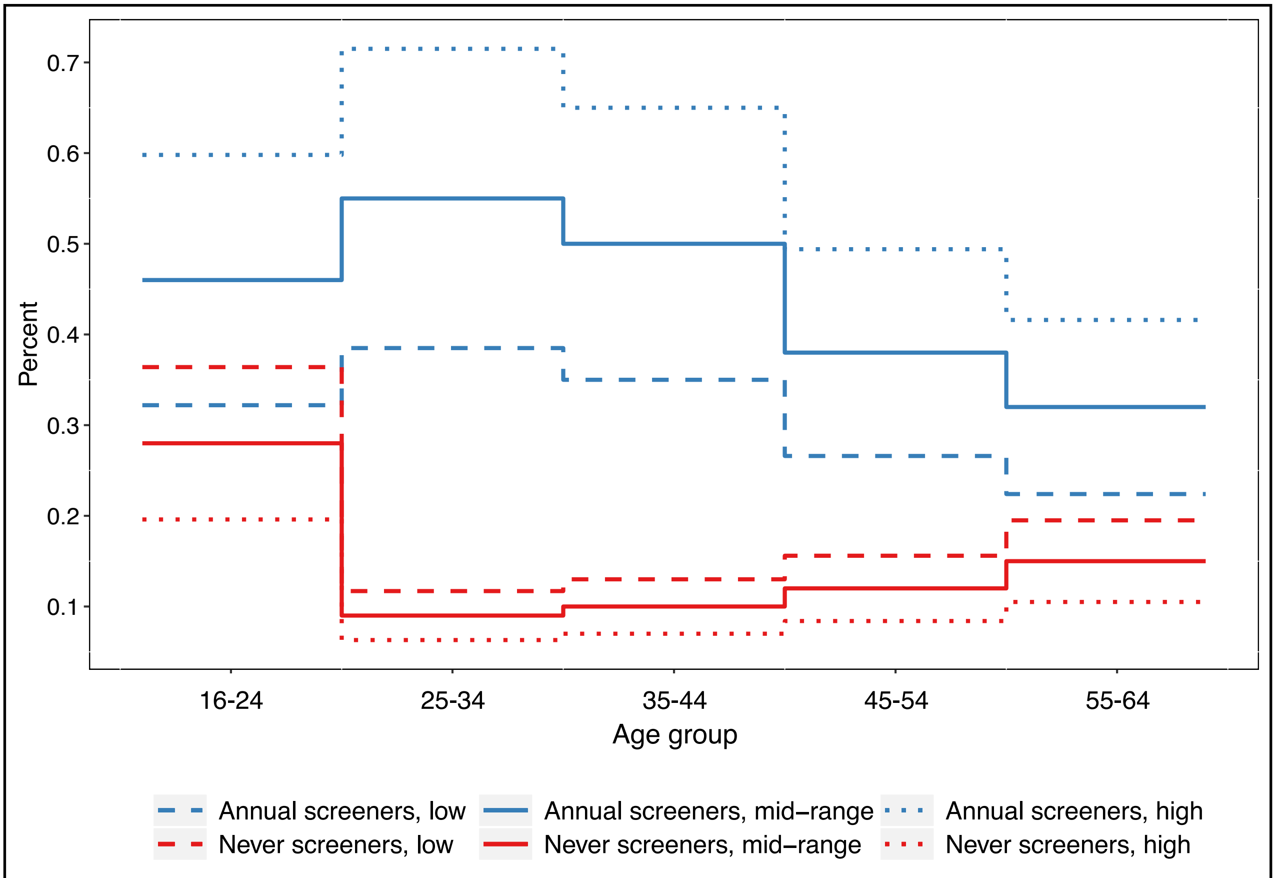

Figure 3.1: Levels of risk-based screening among men who have sex with men by age group in low, mid-range, and high screening scenarios.

All men who are not annual or never screeners are assumed to screen at an interval sampled from a normal distribution with a mean of 3 years and a standard deviation of 0.51 years.

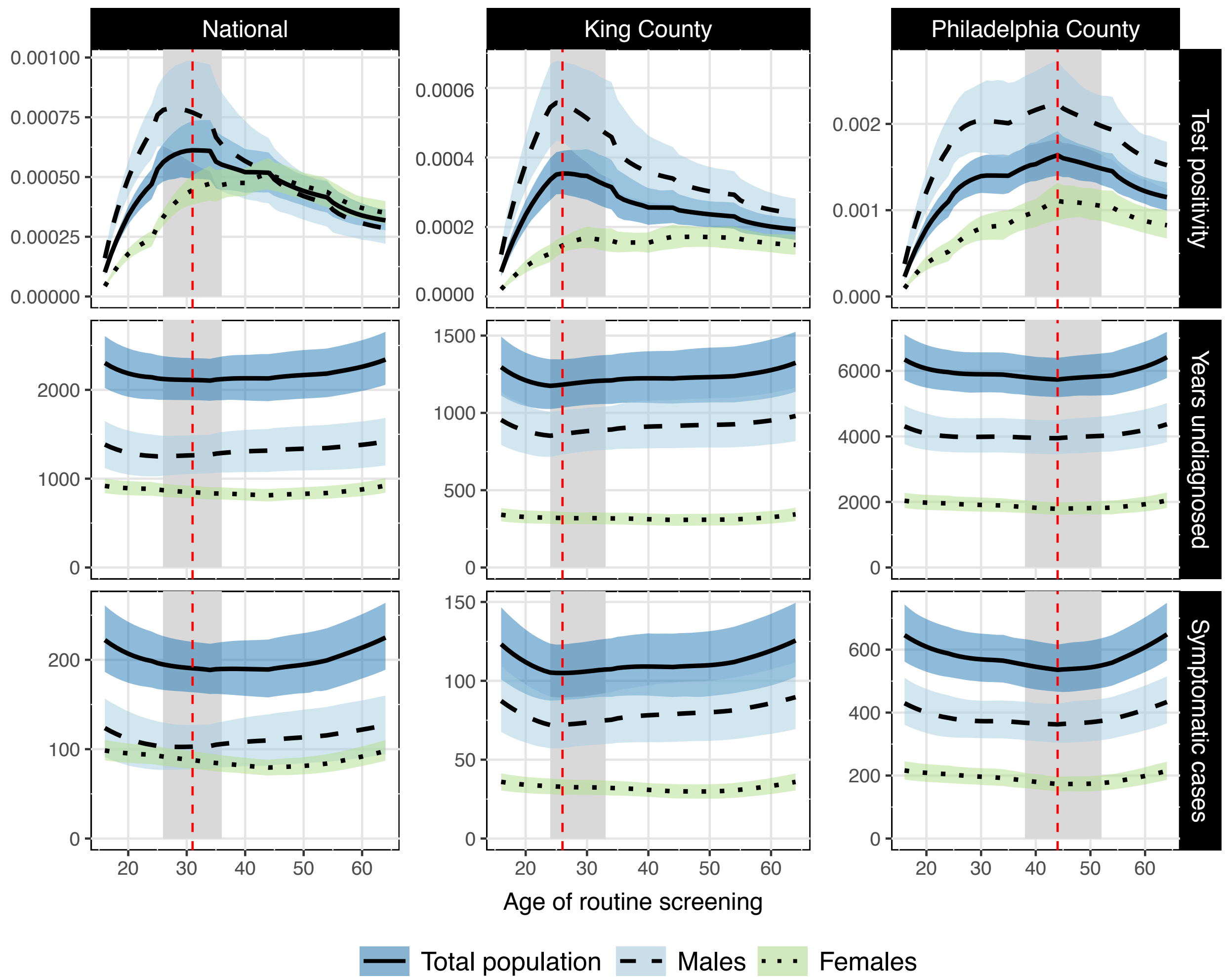

Figure 3.2: Impact of adding routine screening to targeted testing strategies by age of screening

Routine screening is implemented at specific ages with 80% coverage, added to scenarios with mid-level risk-based screening among MSM, prenatal screening, and testing prompted by symptom onset and partner notification. The top row of figures presents the proportion of screening tests that result in a new diagnosis. The middle row presents the cumulative population-level years of undiagnosed infection, and the bottom row presents the total number of symptomatic HIV/AIDS cases. The black lines show the mean across 500 Monte Carlo simulations and the shaded area corresponds to the 95% uncertainty interval from the simulations. The vertical doted red lines indicate the optimal age in terms of test positivity, and the grey area highlights the ages that resulted in a test positivity within 10% of the optimal. Note that the y-axes differ across plots.

Table 3.2: Optimal age for routine screening, by risk-based screening scenario and model setting

	Low risk-based screening *Optimal age (range[a])*	Mid-range risk-based screening *Optimal age (range[a])*	High risk-based screening *Optimal age (range[a])*
Test positivity			
National	30 (26, 34)	31 (26, 36)	34 (27, 46)
King County	26 (24, 32)	26 (24, 33)	27 (24, 34)
Philadelphia County	44 (28, 51)	44 (38, 52)	44 (39, 54)
PY undiagnosed infection			
National	34 (16, 62)	34 (16, 62)	44 (16, 63)
King County	24 (17, 59)	24 (17, 61)	25 (16, 63)
Philadelphia County	44 (17, 62)	44 (17, 62)	44 (17, 62)
Symptomatic cases			
National	34 (20, 55)	34 (20, 57)	44 (23, 57)
King County	25 (19, 54)	26 (19, 57)	44 (18, 60)
Philadelphia County	44 (22, 58)	44 (24, 57)	44 (28, 57)

[a]Corresponds to the ages at which the outcome is within 10% of optimal

Table 3.3: Estimated incremental test positivity, change in person-years (PY) of undiagnosed infection and symptomatic HIV/AIDS cases from different HIV screening scenarios

	Test positivity[a]	Percent reduction in PY of undiagnosed infection[b]	Percent reduction in symptomatic HIV/AIDS cases[b]
	Mean (95% UI)[c]	*Mean (95% UI)*[c]	*Mean (95% UI)*[c]
National			
A) Prenatal screening[d]	0.04% (0.03%, 0.04%)	3% (2%, 4%)	4% (3%, 5%)
B) A + low risk-based screening	0.99% (0.80%, 1.19%)	50% (45%, 54%)	55% (49%, 60%)
C) A + high risk-based screening	0.82% (0.71%, 0.96%)	60% (57%, 63%)	66% (62%, 69%)
D) B + routine screening[e]	0.07% (0.06%, 0.09%)	5% (4%, 6%)	7% (5%, 9%)
E) C + routine screening[e]	0.05% (0.04%, 0.06%)	4% (3%, 4%)	5% (4%, 6%)
King County			
A) Prenatal screening[d]	0.01% (0.01%, 0.02%)	2% (1%, 2%)	2% (2%, 3%)
B) A + low risk-based screening	0.26% (0.19%, 0.35%)	53% (48%, 58%)	58% (52%, 64%)
C) A + high risk-based screening	0.22% (0.18%, 0.28%)	64% (61%, 68%)	71% (66%, 74%)
D) B + routine screening[e]	0.04% (0.04%, 0.05%)	6% (5%, 7%)	7% (6%, 9%)
E) C + routine screening[e]	0.03% (0.02%, 0.03%)	3% (2%, 4%)	4% (3%, 5%)
Philadelphia County			
A) Prenatal screening[d]	0.07% (0.06%, 0.08%)	2% (2%, 3%)	3% (3%, 4%)
B) A + low risk-based screening	1.20 (0.87%, 1.58%)	40% (36%, 44%)	44% (39%, 49%)
C) A + high risk-based screening	1.00% (0.79%, 1.27%)	48% (45%, 52%)	53% (50%, 57%)
D) B + routine screening[e]	0.17% (0.14%, 0.20%)	6% (5%, 7%)	9% (8%, 11%)
E) C + routine screening[e]	0.15% (0.13%, 0.18%)	6% (5%, 7%)	9% (7%, 10%)

[a]Proportion of tests from each added screening strategy that are estimated to yield new HIV diagnoses, assuming 100% test sensitivity; [b]Relative to a baseline scenario with diagnostic symptom-based testing and testing resulting from partner notification; [c]Mean value and 95% uncertainty interval (UI) across 500 Monte Carlo simulations; [d]This scenario does not account for years of undiagnosed infection averted in infants; [e]Assuming screening at the optimal ages with 80% test acceptance

CONCLUSION

The findings from these three chapters provide valuable information to guide local public health decision-making and support implementation of high-impact HIV prevention strategies in the United States. To inform the design of evidence-based public health programs and policies, empirical data collection is necessary to describe the characteristics, behaviors, and prevention needs of the target population. However, individual-level behaviors and outcomes do not always scale linearly to the population level.[30,31] Mathematical models can play an important role in public health practice by providing a flexible framework with which to evaluate population-level outcomes, test alternative scenarios, and make long-term projections.

With high interest and investment in PrEP as a core component of the HIV prevention strategy across the US, data collection systems are needed to monitor patterns of utilization and evaluate the impact of efforts to increase uptake and retention. MSM are a primary target population for PrEP, but due to the lack of a sampling frame for probability-based recruitment,[211–213] collecting data on the behaviors of this population has proven challenging. In Chapter 1, we demonstrated the feasibility of an internet-based survey to measure PrEP use and HIV risk behaviors in a statewide sample of MSM in Washington State. As with most methods for recruitment of MSM, the data are subject to selection biases that limit the generalizability of the findings. However, advantages of internet-based recruitment for ongoing public health surveillance include the low cost, efficiency of data collection, and the ability to reach broad geographic areas, including men in rural areas and those who may be missed by venue-, event- and clinic-based samples.

Data from this survey indicate that PrEP use is high in Washington, with 19% of all MSM and 31% of those recommended to initiate PrEP reporting current use. After adjustment for differences in the samples, estimates from the internet-based survey and an event-based survey of MSM at the Seattle Pride parade were similar. Additional analyses comparing these two surveys with data from the 2017 Seattle-area NHBS survey found consistent estimates of PrEP use among high-risk men.[33] While this does not establish the representativeness of any of the samples, it provides support for the credibility of the estimates.

Looking forward, an important question for public health decision-makers is what impact current and future levels of PrEP use in Washington will have on HIV incidence. PrEP use has been shown to be highly effective for individuals who take it,[14,15,119,125,127,140,146] but the long-term impact on transmission at the population level cannot be estimated from empirical data. The network-based model in Chapter 2 used data on the sexual partnerships, behaviors, and engagement in care of MSM in Washington to simulate the potential impact of PrEP on HIV incidence. With representation of the timing and sequence of sexual contact that connects individuals over time,[109] this model captures the cascading benefits of PrEP use on averting infection along the potential chain of transmission. The model estimated that with PrEP uptake increasing to 50% among eligible men in 2020, corresponding to 36% coverage of total person-years at risk, nearly two-thirds of the incident cases projected in a scenario without PrEP would be averted.

In addition to PrEP, improvements in strategies to diagnose people earlier in the course of infection are needed to reduce transmission and morbidity from HIV. Routine screening of all adults and adolescents regardless of risk has been promoted as an important and cost-effective strategy to increase case finding,[124,25,214] but the model in Chapter 3 indicates that this approach may not be an efficient use of resources in all settings. In jurisdictions such as Philadelphia County, PA, where HIV incidence is high and a relatively low proportion of cases are MSM (60%),[169] one-time routine screening in the optimal age range of 28 to 51 was found to exceed the established cost-effectiveness threshold of 0.1% test positivity.[24] However, even in this setting, the impact on total years of undiagnosed infection and the number of cases that develop HIV/AIDS-associated symptoms prior to diagnosis was modest. Routine screening has other advantages, such as increasing equity by reaching populations not captured in targeted testing campaigns, but our model highlights the importance of continued investment in risk-based screening, which was estimated to reduce undiagnosed infection and symptomatic cases by 36% to 74%.

The models in Chapters 2 and 3 point to several areas where additional research is needed. The process of constructing a model requires synthesizing and summarizing available data and assumptions to represent the processes that influence transmission in the population, which can highlight potentially important gaps in knowledge. For the network-based model in Chapter 2, initial parameter estimates did not reproduce the observed HIV prevalence in equilibrium. We calibrated the model by applying scalars to adjust condom use and the per-act probability of transmission, two influential parameters with substantial uncertainty. However, simulations from our calibrated model did not match observed disparities in HIV prevalence by race/ethnicity or region of the state. Other models have similarly had difficulty reproducing racial disparities in HIV prevalence,[112] suggesting that more research is needed to investigate the causes of disparities. In the course of constructing the model, we noted a need for additional data on patterns of condom use and the factors that influence the decision to use condoms within a dyad. Better data on these dynamics, as well as how use of PrEP and ART influence partner selection,[215] could improve model fit. Additionally, in expanding the modeled age range from previous network-based MSM models, we were limited by inadequate data on how behaviors change over the life course. Studies to describe trajectories of sexual behavior could inform age-based targeting of interventions and recommendations for the duration of PrEP use.

The model in Chapter 3 revealed potential biases in estimates of HIV incidence. Using available estimates, our model projected a lifetime risk of infection of 1 in 62 in Philadelphia County, 1 in 225 in King County, and 1 in 135 at the national level. Among MSM, lifetime risk was estimated at 1 in 3 in Philadelphia County, 1 in 12 in King County, and 1 in 4 at the national level. Although previous studies have reported lifetime risks of infection in line with our estimates for Philadelphia County in some southern states and among black MSM,[74,216] there is indication that reported HIV cases may be overestimated.[203] More rigorous de-deduplication procedures in other jurisdictions, as have been implemented in King County,[33] could result in a lower projected yield from routine screening. Additionally, we lacked data on the age distribution of infection in the modeled jurisdictions. More complete records of HIV test history could improve efforts to estimate age at infection using local surveillance data.

Together, the chapters of this dissertation demonstrate the value of integrating mathematical models with public health practice. When constructed using appropriate data, models can be used to make projections to guide policy and prevention planning at the local level. Modeling can also inform areas where additional data collection is needed, which can be used to iteratively improve model projections. With prevention strategies tailored to the local context, significant reductions in HIV transmission may be achievable in the coming decade.

SUPPLEMENTAL APPENDIX 1: Recruitment, administration, and data cleaning protocol for the Chapter 1 survey

Recruitment methods and survey administration

To recruit participants, we placed banner and text-based pop-up advertisements in English and Spanish on social media, male-male geosocial networking, and general LGBTQ-interest apps and websites. Advertisements on all platforms were targeted based on location in Washington, and advertisements on social media were additionally targeted to males who reported an interest in relationships with men or expressed an interest in LGBTQ-related topics or groups. The design and content of the advertisements were informed by feedback from MSM visiting the Public Health—Seattle & King County STD clinic and from the University of Washington/Fred Hutch Center for AIDS Research Community Action Board. Example advertisements are presented in Figure S1.1, below.

Figure S1.1: Example survey advertisements

Let's talk about sex
surveygizmo.com
Take a confidential 10-minute survey to help improve sexual health and prevent HIV in WA.

Example pop-up ad:
Help improve sexual health in Washington
Share your experiences and opinions to help improve sexual health and HIV prevention programs in Washington. Your responses will be confidential, and you will have an opportunity to see how your answers compare to others in Washington at the end of the project. Click below for more information and to get started.

The survey was open to all individuals who clicked on posted advertisements between January 1st and February 28th, 2017. Upon clicking on an ad, individuals were linked to a webpage hosted by SurveyGizmo (Boulder, CO). The landing page stated that the survey was designed to collect information to improve efforts to prevent HIV and other sexually transmitted infections (STIs) in Washington State, with a focus on learning about awareness, interest in, and use of HIV pre-exposure prophylaxis (PrEP). This page additionally stated that the project was developed and conducted by the Washington State Department of Health, Public Health—Seattle & King County, and the University of Washington, and was not sponsored by or connected to any pharmaceutical company or private enterprise.

Individuals who clicked past this page were shown an informed consent page, which stated that the survey would take approximately 10 minutes to complete, participation is voluntary, and responses would be completely confidential. We informed participants that we would record their computer or device's Internet Protocol (IP) address, but that this would be used only to detect and screen out duplicate responses, would be deleted upon removal of duplicates, and no attempts would be made to identify individuals. We did not use web cookies to block repeat responses from the same browser.

The survey was programmed to randomly show one of three consent pages that differed only in the stated incentive. These pages stated either that individuals would receive a $10 Amazon gift certificate, could choose from one of five charitable organizations[*] to which we would donate $10, or would receive no monetary incentive. All individuals were informed that we would provide them with a link at the end of the survey where we would post a summary of results upon completion of the project, and they could request to have these results emailed to them. Email addresses for $10 Amazon gift certificates and communication of results were collected upon completion of the survey through separate electronic forms that were not linked to survey responses.

After nine days of data collection, we noticed a pattern of responses that led us to discontinue the $10 gift certificate incentive. Through monitoring of IP addresses and timestamps, we observed that individuals appeared to be clicking the advertisements repeatedly and providing consent only when presented with the $10 gift certificate incentive, and many individuals completed the survey for this incentive multiple times. We found no evidence that information about the survey and the opportunity to earn $10 had been posted on any websites other than those

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[*] Human Rights Campaign, the Latino Commission on AIDS, the It Gets Better Project, Equal Rights Washington, and the Northwest Network of Bi, Trans, Lesbian, and Gay Survivors of Abuse (The NW Network)

on which we posted advertisements, and we decided to drop this incentive. We removed duplicate entries according to the protocol described below, and for the remainder of the recruitment period, participants were randomized to the $10 donation or no monetary incentive. In sensitivity analyses, we excluded participants who completed the survey for the $10 gift certificate before this incentive was discontinued. The proportion of men who reported current (20%) and past (4%) PrEP use was comparable to findings from the full sample (19% and 4%). Among men for whom PrEP is recommended, a higher proportion reported current use (37% vs. 31% in the full sample) and a lower proportion reported interest (40% vs. 56%). The findings from analyses of time on PrEP, correlates of PrEP, and the comparison with the Seattle Pride survey were not meaningfully different.

Upon clicking to indicate consent, participants answered a set of screening questions. Persons were ineligible if they were female sex at birth, less than 16 years of age, reported residence outside of Washington State or did not provide a valid Washington zip code, did not have oral or anal sex with a man in the past 12 months, reported ever testing positive for HIV, or completed the survey from a device with an Internet Protocol (IP) address outside the United States. Eligible individuals were asked about their social and demographic characteristics, healthcare utilization, drug use, sexual behavior, and awareness, interest, and use of PrEP. Survey items were informed by review of the literature and adapted from existing measures,[210,217–221] and the instrument was tested and refined through cognitive interviewing with MSM attending the Public Health—Seattle & King County (PHSKC) STD clinic. All questions were required, though participants could indicate that they prefer not to answer for any question they were not comfortable with. The survey had an average of three questions per page. To minimize response burden, we used adaptive questioning to skip questions and pre-fill domains based on participants' previous responses. We programmed the survey to flag implausible or inconsistent responses and prompt participants to correct flagged entries. Participants could not otherwise go back to change answers on previous pages, and we did not ask them to review their answers prior to submission. An open text field was included at the end of the survey in which participants could clarify or correct previous responses and provide feedback. Respondents took a median of 11 minutes to complete the survey.

Protocol to remove invalid and duplicate responses

We used a modified version of a published protocol[54] to define four patterns of responses suggestive of invalid or duplicate entries. The first pattern identified responses from individuals who appeared to have clicked the link to open the survey repeatedly and consented only when they were randomized to receive a higher incentive. Observations that accessed the survey from the same recruitment platform, matched on the first three quadrants of the IP address, and were submitted for a higher incentive within 10 minutes of a previous entry were flagged, and all but the first entry were dropped. The second pattern of responses indicated a change in answers to screening questions to satisfy eligibility criteria. We flagged observations submitted within two hours of a disqualified response that matched on recruitment platform and the first three quadrants of the IP address. Through manual review, we excluded from analysis responses with similar answers to screening questions apart from one or two answers that may have been changed to meet eligibility criteria. Responses for which the survey language was changed were considered valid, and preceding responses were discarded. The two-hour window was defined after reviewing the distribution of time intervals between flagged responses and selecting the window that captured most of the entries that appeared invalid. Third, we flagged and removed duplicate responses. As above, we flagged responses for manual review if they matched on recruitment platform and the first three quadrants of the IP address and were submitted within two hours of a previous entry.

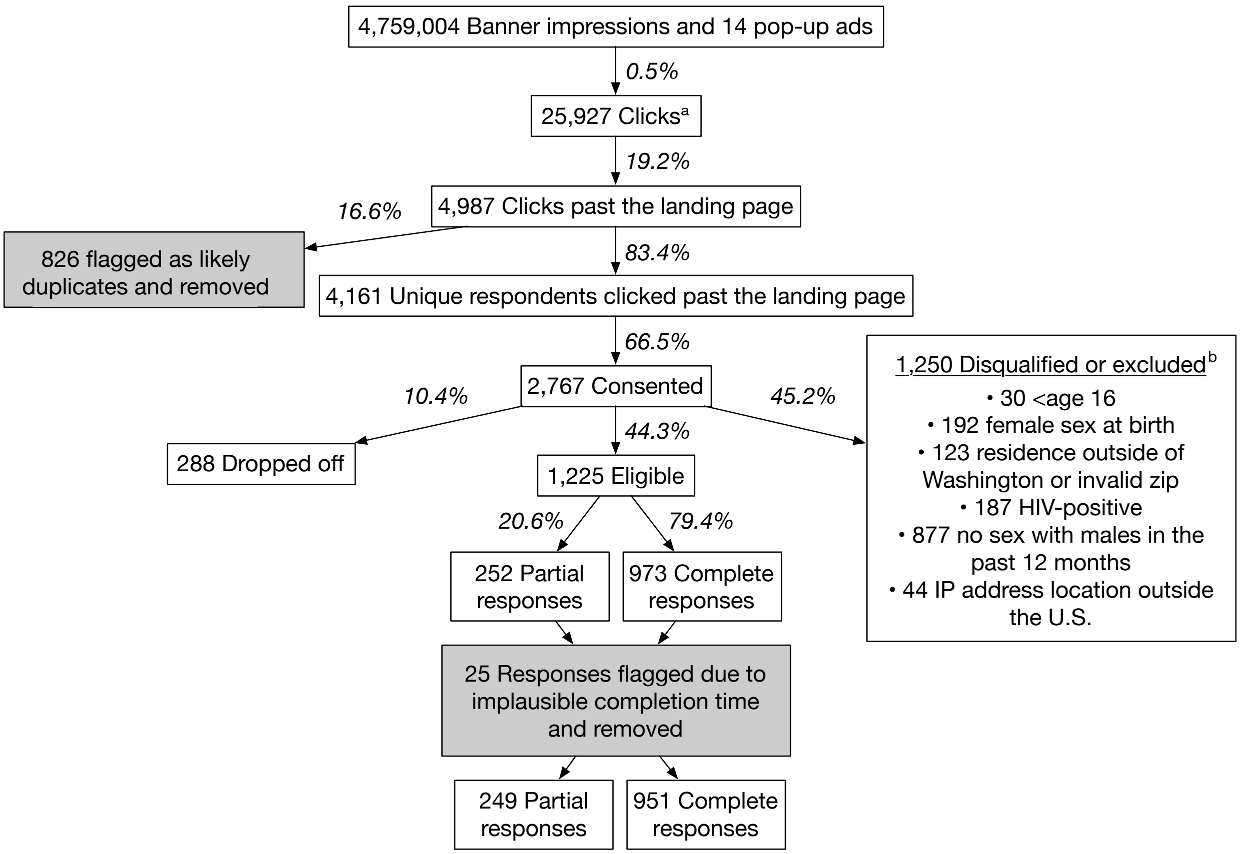
We considered responses with matching or similar data to be duplicates and retained only the first or most complete response. Fourth, to identify respondents who appeared to have clicked through without reading questions or contemplating their responses, we removed entries submitted in less than half the median time to completion.

Recruitment and response rates

From January 1 to February 28, 2017, we delivered 4,759,004 advertisement impressions and 14 broadcast ads, which generated 25,927 clicks to the survey, 4,987 of which (19%) proceeded past the landing page (Figure S1.2). Of these, 826 (17%) were flagged as duplicate entries and removed, leaving 4,161 unique visits past the landing page. Seventy-nine percent of eligible, consenting participants completed the survey, and after removing responses with implausible completion times, 951 complete and 249 partial responses were recorded. Recruitment costs totaled $11.24 per complete response; accounting for incentives, survey administration, and translation of the instrument and advertisements into Spanish, expenses totaled $23.69 per complete response (Table S1.1).

To assess response bias, we compared the characteristics of respondents who completed the survey to those who dropped off, using chi-square tests to assess statistical significance. Among the 1,157 eligible cisgender males who started the survey, drop-off was associated with not identifying as gay or homosexual ($p<0.001$), reporting less than a 4-year college degree ($p=0.003$), residence outside of King County ($p=0.002$), and accessing the survey in Spanish ($p=0.015$). Eligible respondents assigned to receive the $10 gift certificate were the most likely to complete the survey (126/140; 90%), followed by those assigned to the $10 donation incentive (413/507; 81%; $p=0.016$ for comparison with the gift certificate group), and those assigned to receive no monetary incentive (385/510; 75%; $p=0.021$ for comparison with the donation group).

Figure S1.2: Recruitment and response rates



To identify and remove duplicate and invalid responses, we flagged entries based on IP address, recruitment platform, time stamp, and answers to screening and basic demographic questions. Responses removed using this protocol are presented in grey boxes.

[a]One advertising platform, which delivered 1,096,094 impressions, recorded clicks that opened a pop-up display within the app, rather than clicks to the survey; [b]An additional 4 responses were wrongfully disqualified due to a programming error. Reasons for disqualification are not mutually exclusive.

Table S1.1: Survey expenses			
	Expenses[a]	Complete responses[b]	Cost per complete response
Recruitment			
Advertisement design	$364.00		
Advertisement placement			
Social media	$3,925.65	722	$5.44
Geosocial networking[c]	$4,000.00	172	$23.26
General LGBTQ interest	$2,400.00	57	$42.11
RECRUITMENT TOTAL	$10,689.65	951	$11.24
Incentives			
Amazon gift certificate	$2,970.00		
Donation	$5,170.00		
INCENTIVES TOTAL	$8,140.00		
Translation services[d]	$2,621.00		
Survey administration[e]	$1,080.00		
TOTAL	**$22,530.65**	**951**	**$23.69**

[a]Expenses do not include staff time developing or programming the survey instrument; [b]Excluding responses flagged as invalid. This does not account for the 163 partial responses that provided data at least through questions about current or past use of PrEP; [c]One of the geosocial networking platforms placed ads at no cost, but contributed only 30 complete responses; [d]Costs of translating the survey instrument and advertisements into Spanish; [e]Includes the costs of staff time to set up contracts with advertising partners, manage advertisements, and monitor survey performance.

SUPPLEMENTAL APPENDIX 2: Technical details on the Chapter 2 mathematical model

Table of Contents

1. Model overview

We constructed a stochastic network-based model to represent HIV transmission in sexual partnerships of men who have sex with men (MSM) in Washington State. Network-based models are a subset of individual (agent-based) models in which partnerships and are explicitly modeled and tracked over time.[82] In a given time step, the probability of a new partnership forming between any two individuals and the probability of an existing partnership dissolving are governed by exponential family graph models.[111] Over the past decade, advances in statistical methods have made it possible to estimate and simulate these models using egocentrically sampled data,[111,222,223] allowing for construction of context-specific models. Within the simulated sexual networks, the model represents individual anal sex acts, condom use, PrEP use, disclosure of HIV status, and disease transmission. These processes are described in detail in sections 5, 8, and 9, below. Separate modules track viral load, HIV diagnosis, and use of antiretroviral therapy, with the clinical attributes of HIV-positive individuals updated in weekly time steps (sections 6-7). The model represents an open network of men aged 18 to 59, with the rate of entry defined to maintain a stable population in the absence of HIV/AIDS mortality, as described in section 3.

The model was programmed in the R software language using the EpiModelHIV package,[224] which is an extension to the EpiModel platform (http://www.epimodel.org).[224] Foundational to both of these is a suite of packages developed to support network analysis, simulation, and visualization (statnet; http://www.statnet.org).[225] These tools have been used for previous network-based models of MSM in the United States.[94,112,226] Our model modifies and extends the code from these previously developed models for application to the Washington State context.

This work was facilitated though the use of advanced computational, storage, and networking infrastructure provided by the Hyak supercomputer system at the University of

Washington. Using functionality in the EpiModel package to run simulations in parallel, this system reduced the computation time required to run large numbers of simulations across a wide range of scenarios.

2 Data sources

2.1 Overview

To represent the partnership patterns, sexual behavior, and clinical profile of MSM in Washington, we estimated model parameters using data from local surveys and surveillance records, supplemented with data from a national survey where local data were unavailable. Line-level data from these surveys were raked to match the demographic profile of Washington males, described in more detail below. For parameters on changes in condom use with diagnosis and disclosure, we used estimates calculated from Atlanta-based studies for a previous model.[94] To define the demographic composition of the network and background mortality rates, we used vital statistics[227] and census data,[228] weighted by the estimated proportion of MSM by county in Washington State.[134] We reviewed the published literature for data on HIV natural history, transmission probabilities, and PrEP efficacy and adherence patterns. Table S2.1 summarizes the data sources used for each set of parameters in the model.

2.2 Survey samples

The primary source of data for this project was the 2017 Washington HIV Prevention Project (WHPP), an internet-based survey of MSM in Washington conducted in January and February 2017.[114] Respondents were recruited through banner and text-based pop-up advertisements on social media, MSM sexual networking apps, and general LBGTQ websites. Eligible respondents were Washington residents who were male sex at birth, aged 16 and older, reported oral or anal sex with a man in the past 12 months, and never tested positive for HIV. For the present analyses, we restricted the sample to 1,036 cisgender males aged 18 to 59. Respondents were asked questions about their demographic characteristics, HIV and STI testing, sexual behavior, and use of PrEP. Sexual behavior was measured with global questions summarizing behaviors and partnership counts in the past 12 months, as well as with detailed questions about the most recent anal sex partner in the past 12 months.

Because the WHPP survey did not include HIV-positive respondents, we incorporated data from two surveys that included HIV-positive men. With the goal of using local data sources, we used data from the Washington site of the Medical Monitoring Project (MMP) to the extent possible. The MMP is a national surveillance system that collects behavioral and medical record data from people receiving medical care for HIV in the United States on an annual basis.[229] The latest data available at the time of analysis were from the 2014 MMP questionnaire. Participants were recruited using a three-stage probabilistic sampling design to select HIV-positive individuals in care.[115] For this project, we analyzed survey data from cisgender male respondents aged 18-59 who had anal sex with males or identified as gay or bisexual (N=134). Relevant variables included respondent age and race/ethnicity, the age and race/ethnicity of the most recent male anal sex partner, and sexual position and HIV status disclosure with each of up to the most recent 5 male anal sex partners.

Table S2.1: Data sources	
Parameter set	Data source(s)
Demography	• Washington State Vital Statistics • 2011-2015 American Community Survey • Grey et al.[134] • 2014 Seattle MSM National HIV Behavioral Surveillance Survey • Published studies
Sexual network structure	• 2017 Washington HIV Prevention Project • 2014 Washington Medical Monitoring Project • 2017-2018 ARTnet survey
Behavior within partnerships	• 2017 Washington HIV Prevention Project • 2014 Washington Medical Monitoring Project • 2017-2018 ARTnet survey • Atlanta-based cohort studies
HIV natural history	• Published studies
Clinical epidemiology	• 2017 Washington HIV Prevention Project • Washington State HIV surveillance data
Transmission	• Published studies
PrEP	• 2017 Washington HIV Prevention Project • Published studies

For variables not measured in the MMP, we analyzed data from HIV-positive respondents to the 2017-2018 **ARTnet Study**, a nationwide internet-based survey of MSM. The ARTnet sample was recruited from respondents who completed the American Men's Internet Survey (AMIS).[50] For consistency with WHPP inclusion criteria, we restricted the sample to cisgender males aged 18-59 who reported oral or anal sex with a man in the past 12 months and reported a positive HIV diagnosis. We analyzed data on past-12-month sexual behavior and the characteristics of and behaviors with the most recent male anal sex partner.

Finally, we analyzed data from the Seattle project area of the 2014 **National HIV Behavioral Surveillance (NBHS)** survey of MSM[230] to obtain estimates of the prevalence of circumcision. The NHBS MSM cycle uses venue-based, time-space sampling to recruit participants from a sampling frame of site-specific venues attended by MSM and days and times when men are likely to be present. We analyzed self-reported circumcision status among 475 respondents aged 18-59.

2.3 Reweighting

To improve the consistency and representativeness of estimates from these surveys, we adjusted the samples to match the demographic composition of Washington males. As online convenience samples, the WHPP is subject to selection biases. While reweighting the samples does not remove all sources of bias, we sought to adjust for observed discrepancies in the distribution by region, age, and race/ethnicity. We defined three geographic regions of the state distinguished by the size of the MSM population,[134] racial/ethnic composition,[228] and engagement in care:[33] King County, which includes Seattle, other counties in western Washington, and eastern Washington.

To calculate the expected regional distribution, we used data from a 2016 analysis by Grey et al.[134] County-level data were obtained from Emory University's Coalition for Applied Modeling for Prevention website (http://www.emorycamp.org) and aggregated to the regional level to estimate the proportion of males who are MSM by region. We multiplied these proportions by the number of males aged 18 to 59 in each region from the 2011-2015 American Community Survey (ACS) 5-year estimates.[228]

We assumed that the distribution of MSM by age and race/ethnicity in each region mirrors the distributions for all males, again based on data from the 2011-2015 ACS.[228] Because the WHPP was administered only to men who had never tested positive for HIV, we subtracted the number of MSM living with diagnosed HIV by age, race/ethnicity and region from the population totals. We used estimates of the number of MSM living with diagnosed HIV as population targets for reweighting the MMP and ARTnet samples.

To reweight the sample compositions, we used the survey package[231] in R to rake to the joint distribution of race/ethnicity and region and the marginal distribution of age, categorized into the following groups: 18-24, 25-29, 30-34, 35-39, 40-49, 50-59. We grouped ages ≥40 into 10-year age groups to increase the stability of the estimates, as there were fewer respondents in these ages and the number of respondents in the component 5-year age groups were comparable. The MMP sample included only 7 MSM from eastern Washington and 15 from western Washington outside of King County, so we raked it to the marginal distributions of race, region, and age. Because the ARTnet sample was nationwide, we raked it to the margins of race/ethnicity and age only. The NHBS sample includes only Seattle-area men, so we raked it to the margins of race/ethnicity and age. Because the MMP and NHBS used complex sampling designs, we first applied the appropriate sampling weights, and then raked the resulting objects to the target distributions for consistency with the other samples.

3. Demography

The model represents an open population of MSM ages 18-59 distributed by race and region according to proportions derived from U.S. Census data on Washington males[228] and estimates of the proportion of males who are MSM by region,[134] as described in section 2, above. Individuals age through the model in weekly time steps and exit with death or at age 60. New entries arrive at age 18 and are assumed to be HIV negative.

3.1 Demographic composition of the network

At initialization, individuals in the model were assigned age, race/ethnicity and region attributes according to the estimated distribution of MSM in Washington (Figures S2.1 – S2.2). To represent key disparities in the Washington HIV epidemic, we defined three racial/ethnic groups: Hispanic, regardless of race, non-Hispanic black (alone or in combination with any other race), and non-Hispanic other. The non-Hispanic other group includes all non-Hispanic, non-black men, of whom 82% are white.

Figure S2.1: Age distribution

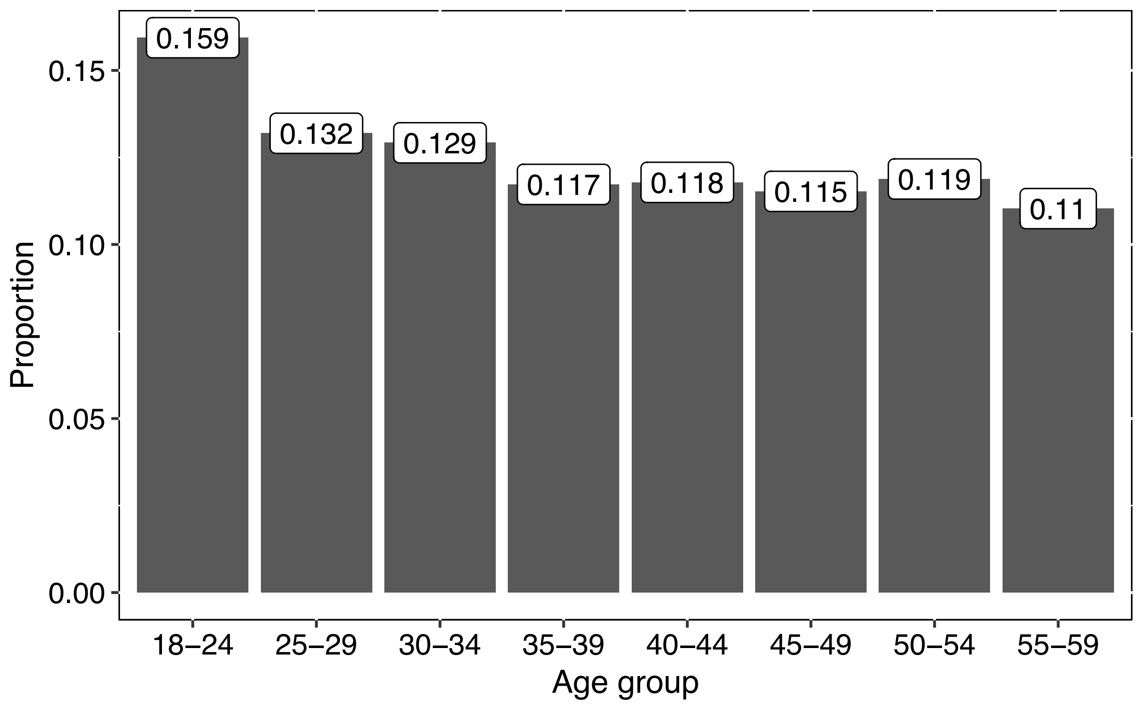
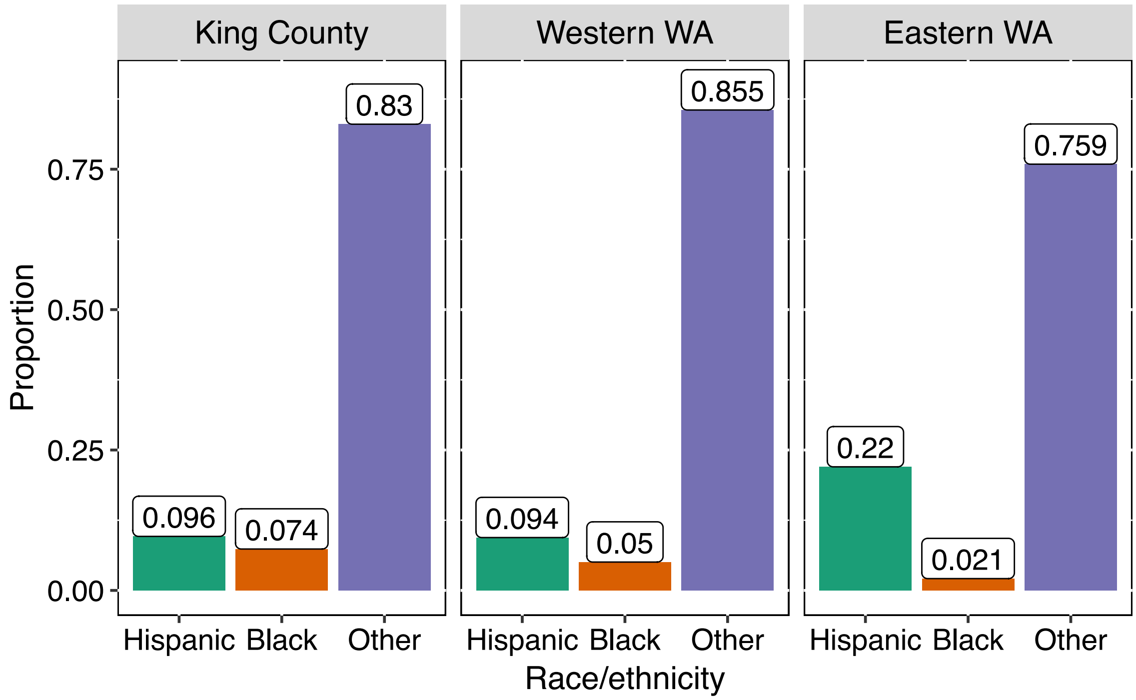


Figure S2.2: Racial/ethnic distribution by region



3.2 Entries and exits

Individuals exit the model deterministically at age 60 or stochastically according to age- and race/ethnicity-specific mortality rates. We defined background mortality rates for HIV-negative men using 2015 Washington vital statistics data[227] and population denominators from the 2011-2015 American Community Survey[228] (Table S2.2). HIV/AIDS-related mortality is represented by multiplying background mortality rates by age-specific scalars for men living with HIV. Using surveillance data on deaths from all causes among MSM living with HIV/AIDS, we defined mortality rates for men aged 18-44, 45-54, and 55-64. Assuming the mortality rate for HIV-positive men aged 55-64 applies to men aged 55-59, we calculated the relative excess mortality among persons living with HIV by age group. These scalars are assumed to apply uniformly across racial and ethnic groups.

Table S2.2 Age- and race/ethnicity-specific background mortality rates (per 100,000) and relative mortality for men living with HIV/AIDS				
	General population			HIV-positive
Age group	Black	Hispanic	Other	Relative rate
18-19	167.5	89.0	68.2	3.8
20-24	116.8	106.8	101.3	3.8
25-29	161.4	112.5	118.9	3.8
30-34	168.7	123.3	138.3	3.8
35-39	267.3	126.0	161.1	3.8
40-44	224.4	186.1	197.9	3.8
45-49	427.9	202.2	306.5	3.0
50-54	609.2	342.6	517.0	3.0
55-59	1322.3	503.2	780.4	2.0

Although there is evidence that HIV/AIDS mortality depends on treatment status and CD4 count,[232,233] because our model does not track CD4 cell count, these patterns would be difficult to implement. However, lifetable analyses indicate that, even for individuals with low CD4 cell count and no viral suppression, expected survival exceeds or comes close to the modeled age range.[234–236] There is evidence that survival has improved over time,[233,235,236] such that current estimates are likely even higher.

The rate of new entries to the model was defined to achieve a stable population in the absence of HIV/AIDS mortality. All new entries start at as HIV susceptible at age 18 and are assigned attributes according to specified distributions. Although the population in Washington is projected to grow in coming years,[237] much of this growth will be due to in-migration from out of the state, and we do not have data on the HIV status and other attributes of new entries from migration.

3.3 Other attributes

In addition to age, race/ethnicity, region, and HIV status, individuals in the network are assigned fixed and dynamic attributes that influence behavior and their risk of HIV transmission or acquisition. Two of the fixed attributes that influence HIV acquisition risk are circumcision status and CCR5-Δ32 genotype. Circumcision was assigned by race/ethnicity according to proportions calculated from 2014 Seattle are NHBS data (Table S2.3). Based on evidence of differential susceptibility to HIV infection associated with a mutation in the CCR5-Δ32 allele,[238] individuals were assigned a genotype with no mutations (wild type), one mutation (heterozygous), or mutations on both chromosomes (homozygous) according to prevalences reported by race/ethnicity in Marmor et al.[238] Other fixed and dynamic attributes are described in the relevant sections, below.

Table S2.3: Distribution of circumcision and CCR5-Δ32 genotype by race/ethnicity

	Black	Hispanic	Other
Proportion Circumcised	0.645	0.490	0.860
CCR5-Δ32 genotype			
Heterozygous	0.034	0.050	0.164[a]
Homozygous	0.000	0.003	0.017[a]

[a]Calculated as a weighted average of the reported prevalence for men of white and other racial groups, from Marmor et al.[238]

4. Sexual networks

To account for heterogeneity in partnership types, we modeled three overlapping partnership networks. Aligning with measures in the WHPP and ARTnet surveys, main partnerships were defined as partners men "feel committed to above all others" and whom they might refer to as a "boyfriend, spouse, husband, significant other, or life partner." Partners with whom respondents had anal sex only once and did not expect to have sex with again were classified as "instantaneous" (one-time) partners. All other partners were classified as "persistent," indicating non-main partnerships with duration.

Each of these partnership networks was estimated with a separate exponential family random graph model (ERGM), taking into account observed cross-network dependencies (i.e., the probability of forming a persistent partnership depends on main partnership status). Because the same statistical model is used for estimation and simulation, this approach has the advantage of preserving expected network features over time.[109] Section 4.1. describes the features of the sexual network our models were parameterized to represent, and section 4.2 presents the statistical methods used to implement them.

4.1 Modeled network features

The key features of the sexual network that our models represent are the expected number of active partnerships of each type men at any point in time (mean degree), partnership duration, and patterns of assortative mixing by age, race, and region. We include constraints to prohibit partnerships between two men who exclusively engage in receptive anal sex or two men who exclusively engage in insertive anal sex. Each of these features are described below, along with the approach used to derive target statistics for the model.

4.1.1 Active main and persistent partnerships

To estimate the distribution of active main and persistent partnerships, we combined the reweighted data from the WHPP and ARTnet samples into a single dataset representing all MSM in Washington. Active partnerships were defined as those in which the respondent expects to have anal sex again. We assumed that men can only have one main partnership at a time, and we truncated the number of concurrent persistent partnerships at 2. To represent the dependence of persistent partnership formation on main partnership status and vice versa, we fit our models to the joint distribution of active main and persistent partnerships (Figure S2.3). We also accounted for differential rates of partnership formation by race/ethnicity (Figure S2.4) and region (Figure S2.5) by calculating the mean number of active partnerships of each type stratified by these attributes. As described in section 4.5, the marginal effects of each of these variables are expressed as log-odds, which are combined to give an overall conditional probability of partnership formation for each time step.

Figure S2.3: Joint distribution of active main and persistent partnerships

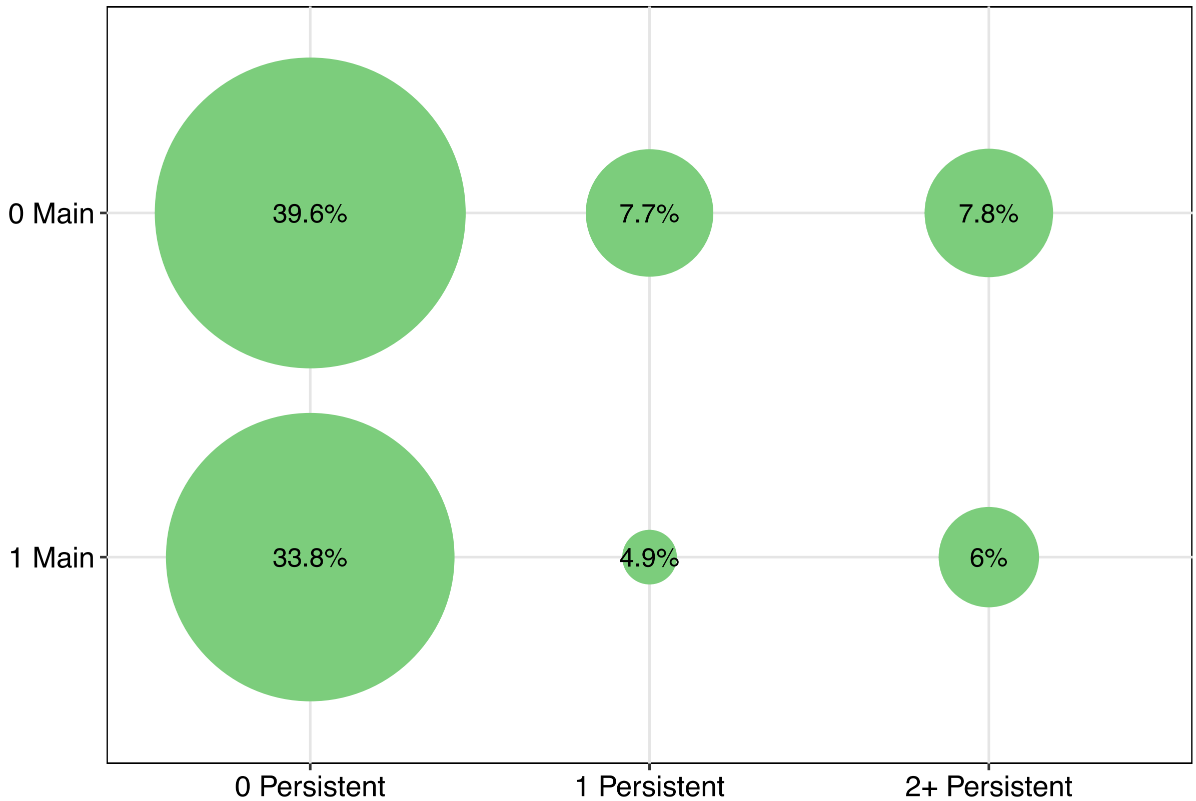


Figure S2.4: Mean active main and persistent degree by race/ethnicity

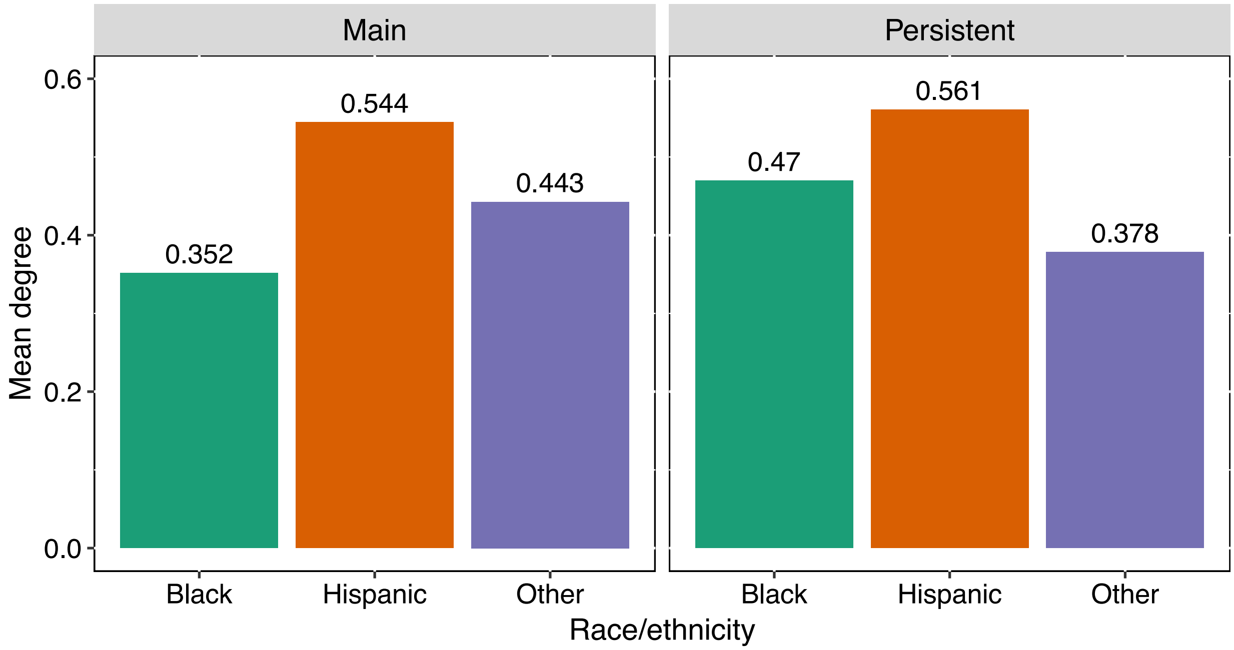
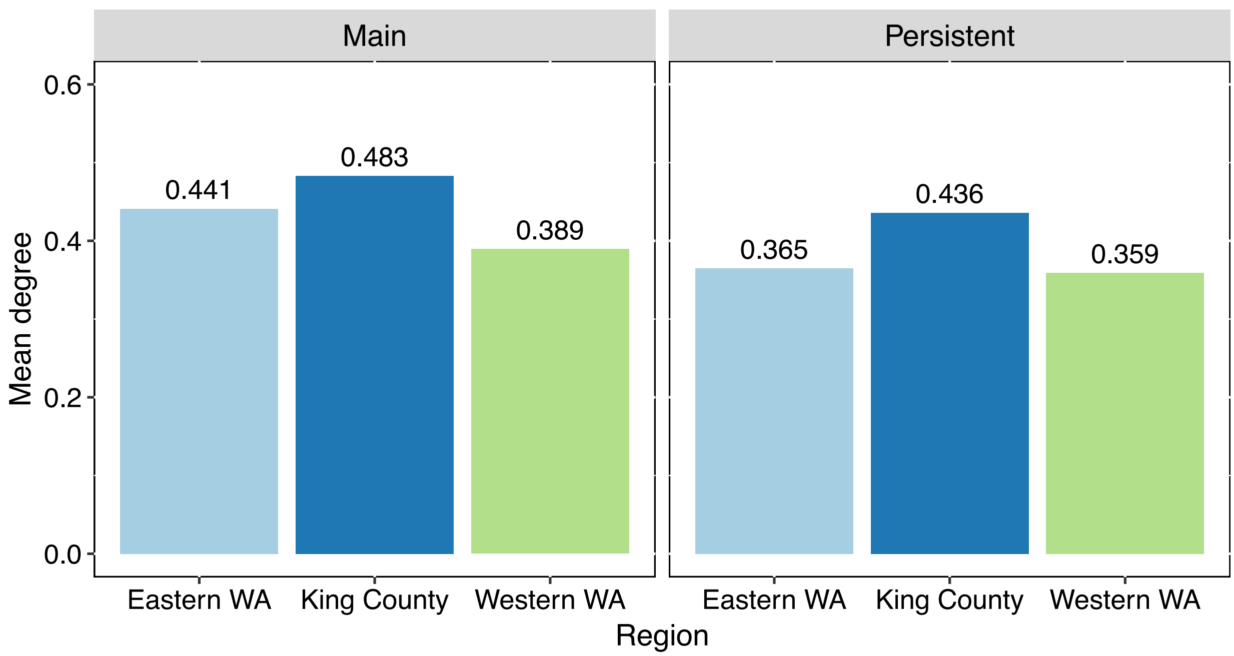


Figure S2.5: Mean active main and persistent degree by region



4.1.2 Instantaneous partnerships

For an individual in the model, the probability of forming an instantaneous partnership in a given time step is a function of his race/ethnicity, region of residence, current main and persistent partnership status, and a risk group attribute. Table S2.4 shows the expected numbers of instantaneous partnerships by race/ethnicity and region. Table S2.5 shows the expected number of instantaneous partnerships per time step by the joint cross-sectional distribution of active main and persistent partnerships.

The risk group attribute was informed by exploratory analyses, which indicated a right-skewed distribution, with a high proportion of men reported no instantaneous partnerships in the past 12 months. This distribution differed by age, with relatively more men over age 50 reporting no instantaneous partners in the past 12 months. To capture this effect, we defined a dynamic attribute assigning differential propensities for forming instantaneous partnerships within and across age groups. Data on the number of instantaneous partnerships in the past 12 months from the combined WHPP and ARTnet dataset were transformed into expected rates per time step. Men aged 18-49 were assigned one of four risk groups upon entry to the model with rates of instantaneous partnership formation calculated as the mean of each quartile of the distribution. Upon aging past 50 years, this attribute was updated by adjusting expected rates to the mean of the corresponding quartile of the distribution among men aged 50-59 in the survey data. The expected numbers of instantaneous partnerships per weekly time step for each quartile by age are presented in Table S2.6. For ease of interpretation, values in parentheses show the expected numbers of partnerships per year.

Table S2.4: Expected number of instantaneous partnerships per weekly time step (and per year) by race/ethnicity and region

Race/ethnicity	
Hispanic	0.138 (7.21)
Black	0.124 (6.49)
Other	0.088 (4.60)
Region	
King County	0.111 (5.78)
Western WA	0.074 (3.86)
Eastern WA	0.083 (4.31)

Table S2.5: Expected number of instantaneous partnerships per weekly time step (and per year) by active main and persistent partnership status			
	0 persistent partners	1 persistent partner	2+ persistent partners
0 main partners	0.109 (5.67)	0.047 (2.45)	0.174 (9.06)
1 main partner	0.051 (2.66)	0.077 (4.03)	0.241 (12.6)

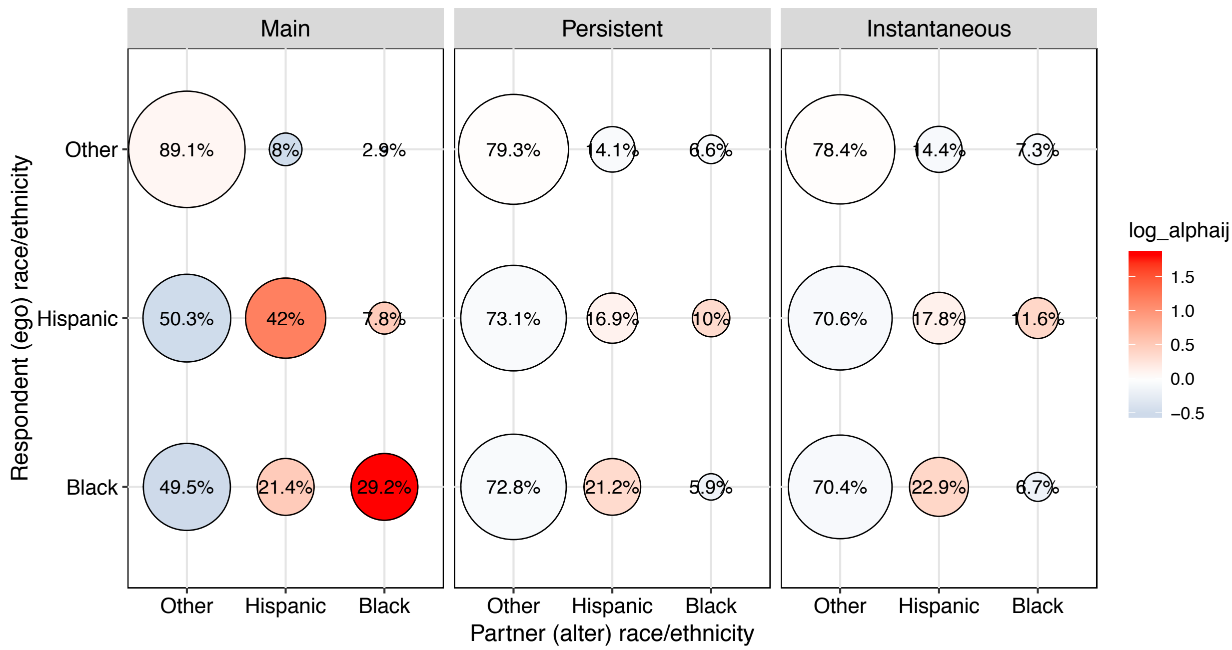
Table S2.6: Expected number of instantaneous partnerships per weekly time step (and per year) by risk group and age				
Age	First quartile	Second quartile	Third quartile	Fourth quartile
18-49	0.000 (0.000)	0.004 (0.222)	0.037 (1.92)	0.395 (20.63)
50-59	0.000 (0.0000	0.000 (0.000)	0.012 (0.625)	0.191 (9.98)

4.1.3 Racial/ethnic mixing

Patterns of selective mixing by race/ethnicity for each partnership type were defined using data on the race/ethnicity of the most recent partner from the WHPP and MMP samples. A challenge with using self-reported partnership data to obtain patterns of sexual mixing is that the number of partnerships reported by men in group A with men in group B may not match the number of partnerships reported by men in group B with men in group A. To account for imbalances in the data, we defined mixing matrices representing the expected number of partnerships for each combination of respondent (ego) and partner (alter) race/ethnicity based on observed data, and we averaged the off-diagonal elements. In the model, we represented the proportion of main, persistent, and instantaneous partnerships that are within-group (on the diagonal) for each racial/ethnic group.

Table S2.6 presents data on patterns of racial/ethnic mixing in each partnership type after adjusting for imbalances. The value labels and size of the circles indicate the row conditional probabilities that a partnership involving man of a given race/ethnicity is with a partner of the same or different race/ethnicity. To account for differences in the size of each group, the circles are colored to indicate how much more or less the observed probabilities are than we would expect with random (proportional) mixing. To quantify this, we took the log of the ratio of the observed cell count for partnerships between egos of race/ethnicity i and alters of race/ethnicity j to the expected cell count under random mixing: $log(\alpha_{ij}) = log(obs_{ij}/(exp_{ij}))$, where the expected cell count $exp_{ij} = (N_i * N_j)/N$. Larger (red) values indicate that the observed value is higher than expected, and lower (blue) values indicate that the observed value is less than expected.

Figure S2.6: Sexual mixing by race/ethnicity and partnership type



4.1.4 Age mixing

Following previous network-based models,[94,239,240] we modeled age mixing as the mean difference between the square root of the age of each partner. For each partnership type, we defined age mixing matrices in single years of age using egocentric data from the combined WHPP and MMP surveys, weighted by mean degree by age calculated from the WHPP and ARTnet datasets and the number of men of each age. We balanced the matrix by taking the average of off-diagonal elements. We then calculated the absolute difference between each combination of respondent (ego) and partner (alter) ages, weighted these differences by the edge count in the corresponding cell in the balanced mixing matrix, and took the mean of the non-zero elements.

For illustrative purposes, Figure S2.7 shows the balanced age mixing matrices for each partnership type, with age collapsed into 5-year age groups. As for racial/ethnic mixing, the value labels and size of the circles indicate the row conditional probabilities, and the color corresponds to the $log(\alpha_{ij})$ value. Red indicates that observed probability is higher than expected under random (proportional) mixing, and blue indicates that the observed probability is less than expected. Table S2.7 shows the mean absolute difference in the square root of ego and alter ages for each partnership type. These data indicate that men have stronger assortative tendencies by age in main partnerships than in persistent and instantaneous partnerships.

Figure S2.7: Sexual mixing by age and partnership type: conditional row probabilities

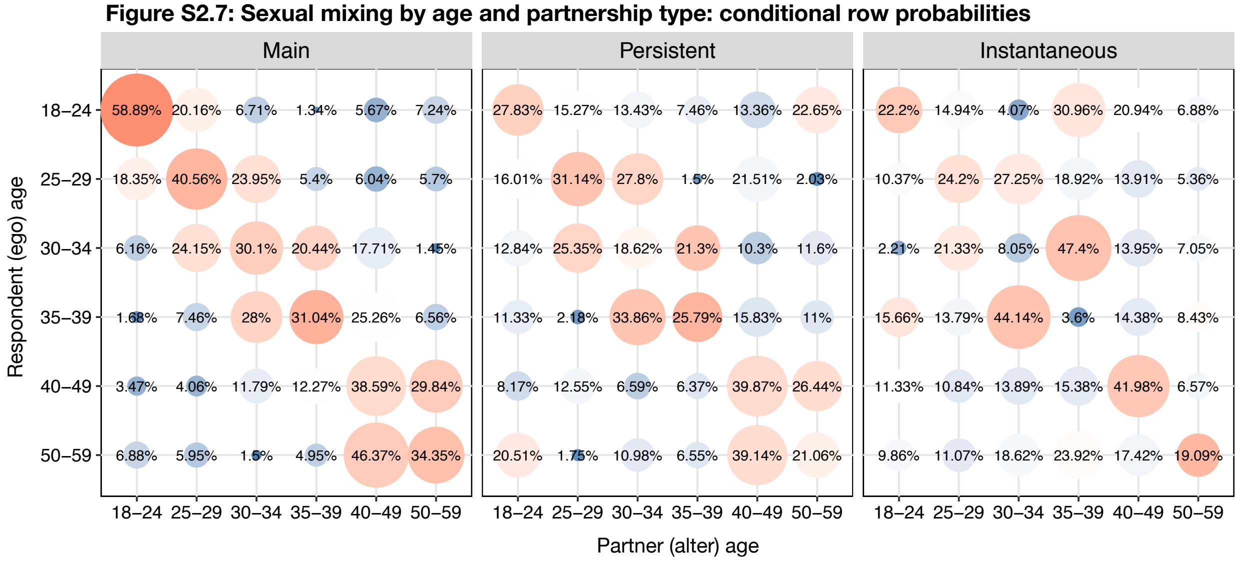


Table S2.7: Mean absolute difference in the square root of ego and alter ages, by partnership type	
Main partnerships	0.538
Persistent partnerships	0.825
Instantaneous partnerships	0.794

4.1.5 Regional mixing

In light of observed geographic differences in HIV prevalence and engagement in care in Washington, patterns of sexual mixing by region may be important for transmission dynamics. Because our surveys did not ask where sex partners live, we lacked data to inform this. However, not specifying region mixing terms in our model would allow partnerships to form randomly by region. We therefore assumed that all main partnerships and 80% of persistent and instantaneous partnerships are with men in the same region. Future work is needed to collect and use data on patterns of mixing by region to better represent these dynamics.

4.1.6 Mixing by sex role

Because the risk of HIV transmission is higher with receptive than insertive anal sex,[135,137] individuals in our model are assigned a fixed attribute determining their role in anal sex as exclusively receptive, exclusively insertive, or versatile. Sexual partnerships between two exclusively receptive or two exclusively insertive men are prohibited.

The distribution of this attribute, shown in Table S2.8, was informed by data from the WHPP and MMP surveys. In the WHPP survey, men were asked to characterize their role in anal sex with all of their male anal sex partners in the past 12 months, with options of: always a bottom (receptive partner), mostly a bottom (receptive partner), equally a bottom (receptive partner) and a top (insertive partner), mostly a top (insertive partner), or always a top (insertive partner). All responses except always a bottom and always a top were categorized as versatile. In the MMP survey, sex role was calculated from reported engagement in receptive and insertive anal sex with each of the most recent 5 partners. Men who reported both receptive and insertive sex with their partners were classified as versatile.

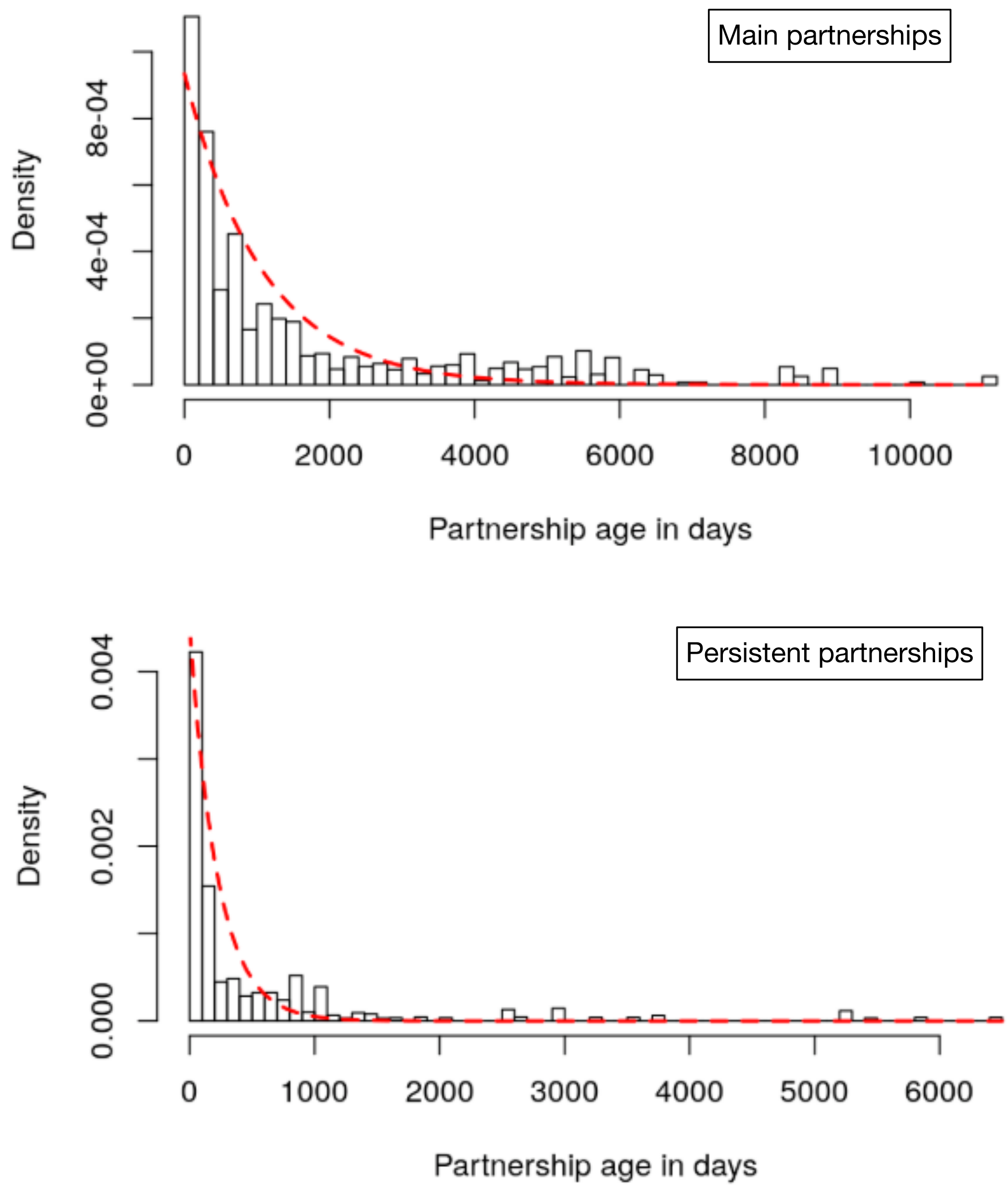
Table S2.8: Anal sex role	
Exclusively receptive	0.213
Exclusively insertive	0.149
Versatile	0.638

4.1.7 Duration

Main and persistent partnership dissolution was modeled as a memoryless process with a constant hazard of dissolution. With the assumption of an exponential distribution of durations for each partnership type, the mean age of active ties measured with cross-sectional data can be used as an unbiased estimator of the mean time from relationship onset to dissolution.[239] To estimate this, we used data from the WHPP and ARTnet datasets on the time since first sex (partnership age) in most recent main and persistent partnerships that were reported to be ongoing. We obtained the median partnership age from these data and calculated the corresponding mean duration assuming an exponential distribution. The expected durations were 1071 days (2.9 years) for main partnerships and 223 days (7.3 months) for persistent partnerships.

To test the assumption of an exponential distribution, the plots below show the observed distribution of partnership age in the reweighted samples, with an overlaid exponential distribution. Note the difference in the axes for the two plots. Although the exponential distribution does not provide a perfect fit to the observe data, particularly for main partnerships, we took it to be a reasonable fit. Future work to improve estimation and simulation of the process and determinants of partnership dissolution could improve model performance.

Figure S2.8: Observed partnership age with overlaid exponetial distribution



4.2 Statistical model

Exponential family random graph models (ERGMs) provide a statistically principled framework for estimation and simulation of sexual networks that reproduce features observed in empirical data.[222,223] These models estimate the probability of observing a set of relationships (y)

conditional on the network statistics ($g(y)$) and characteristics (x) of the n individuals in the network. For partnerships with duration across multiple time steps, separable temporal ERGMs additionally model partnership persistence, providing representation of the dynamic processes that generate an observed set of prevalent relationships.[111] Using an ERGM for estimation of instantaneous partnerships and STERGMs for main and persistent partnerships, our network models can be expressed as the conditional log odds of relationships existing, forming, and persisting:[94]

$$logit\left(P\left(Y_{ij,t} = 1 | Y_{ij,t-1} = 0, Y_{ij,t}^{c}\right)\right) = \theta_m^{+\prime}\partial\left(g_m^{+}(y)\right) \quad \text{Main partnership formation}$$

$$logit\left(P\left(Y_{ij,t} = 1 | Y_{ij,t-1} = 0, Y_{ij,t}^{c}\right)\right) = \theta_m^{-\prime}\partial\left(g_m^{-}(y)\right) \quad \text{Main partnership persistence}$$

$$logit\left(P\left(Y_{ij,t} = 1 | Y_{ij,t-1} = 0, Y_{ij,t}^{c}\right)\right) = \theta_p^{+\prime}\partial\left(g_p^{+}(y)\right) \quad \text{Persistent partnership formation}$$

$$logit\left(P\left(Y_{ij,t} = 1 | Y_{ij,t-1} = 0, Y_{ij,t}^{c}\right)\right) = \theta_p^{-\prime}\partial\left(g_p^{-}(y)\right) \quad \text{Persistent partnership persistence}$$

$$logit\left(P\left(Y_{ij,t} = 1 | Y_{ij,t}^{c}\right)\right) = \theta_i{}'\partial\left(g_i(y)\right) \quad \text{Instantaneous partnership existence}$$

where:

- $Y_{ij,t}$ = a binary indicator of the existence of a tie between persons i and j at time t
- $Y_{ij,t}^{c}$ = all other ties in the network at time t (the network complement of i, j)
- $g(y)$ = a vector of network statistics in each model.
- θ = a vectors of parameters in the formation (existence) model

The vectors $g(y)$ and θ are indexed by whether they correspond to the formation (+) or persistence (-) models for main (m), persistent (p), or instantaneous partnerships (i). The network statistics used to fit each of our models are indicated below. These correspond to the features of the network detailed in section 4.1. The target statistics provided to the model are given as counts, from which θ coefficents are estimated for simulation. Adjustments to these coefficients allow for preservation of the expected number of partnerships per person (degree) and patterns of mixing as network composition changes over the course of the simulation.[240]

Main partnership formation model statistics ($g_m^+(y)$):

1. Total number of active main partnerships
2. Number of men with 1 persistent partnership who are in a main partnership
3. Number of men with 2 persistent partnerships who are in a main partnership
4. Number of black men who are in a main partnership
5. Number of Hispanic men who are in a main partnership
6. Number of men in Eastern Washington who are in a main partnership
7. Number of men in Western Washington who are in a main partnership
8. Number of main partnerships that involve two black men
9. Number of main partnerships that involve two Hispanic men
10. Number of main partnerships that involve two men of other race/ethnicity
11. Sum of the absolute difference in the square root of the ages of partners across all main partnerships
12. Number of main partnerships between two exclusively receptive men
13. Number of main partnerships between two exclusively insertive men
14. Number of main partnerships between men residing in different regions

The latter three statistics were constrained to be 0, prohibiting partnerships of these types.

Main partnership persistence model statistic ($g_m^-(y)$):

1. Total number of active main partnerships

Persistent partnership formation model statistics ($g_p^+(y)$):

1. Total number of active persistent partnerships
2. Number of persistent partnerships involving men with 1 main partner
3. Number of persistent partnerships involving black men
4. Number of persistent partnerships involving Hispanic men
5. Number of persistent partnerships involving men in Eastern Washington
6. Number of persistent partnerships involving men in Western Washington
7. Number of men with 2 concurrent persistent partnerships
8. Number of persistent partnerships that involve two black men
9. Number of persistent partnerships that involve two Hispanic men
10. Number of persistent partnerships that involve two men of other race/ethnicity
11. Sum of the absolute difference in the square root of the ages of partners across all persistent partnerships
12. Number of persistent partnerships between two exclusively receptive men
13. Number of persistent partnerships between two exclusively insertive men
14. Number of persistent partnerships between men residing in different regions
15. Number of men with three or more persistent partnerships

For statistics 2-6, partnerships between two men with the same attribute were counted twice. As in the main partnership model, statistics 12-13 were constrained to be 0. Statistic 15 is also set to 0 to truncate persistent degree at 2.

Persistent partnership persistence model statistic ($g_p^-(y)$):

1. Total number of active persistent partnerships

Instantaneous partnership existence model statistics ($g_i(y)$):

1. Total number of instantaneous (inst.) partnerships in a given time step
2. Number of inst. partnerships involving men with 0 main and 1 persistent partner
3. Number of inst. partnerships involving men with 0 main and 2 persistent partners
4. Number of inst. partnerships involving men with 1 main and 0 persistent partner
5. Number of inst. partnerships involving men with 1 main and 1 persistent partner
6. Number of inst. partnerships involving men with 1 main and 2 persistent partners
7. Number of inst. partnerships involving men aged 18-49 in the first risk quartile
8. Number of inst. partnerships involving men aged 18-49 in the second risk quartile
9. Number of inst. partnerships involving men aged 18-49 in the third risk quartile
10. Number of inst. partnerships involving men aged 50-59 in the first risk quartile
11. Number of inst. partnerships involving men aged 50-59 in the second risk quartile
12. Number of inst. partnerships involving men aged 50-59 in the third risk quartile
13. Number of inst. partnerships involving men aged 50-59 in the fourth risk quartile
14. Number of inst. partnerships involving black men
15. Number of inst. partnerships involving Hispanic men
16. Number of inst. partnerships involving men in Eastern Washington
17. Number of inst. partnerships involving men in Western Washington
18. Number of inst. partnerships that involve two black men
19. Number of inst. partnerships that involve two Hispanic men
20. Number of inst. partnerships that involve two men of other race/ethnicity
21. Sum of the absolute difference in the square root of the ages of partners across all inst. partnerships
22. Number of inst. partnerships between two exclusively receptive men
23. Number of inst. partnerships between two exclusively insertive men

24. Number of inst. partnerships between men residing in different regions

For statistics 2-17, partnerships between two men with the same attribute were counted twice. As in the main and persistent partnership models, statistics 22-23 were constrained to be 0.

To simulate dynamic sexual networks using these models and statistics, we start with a network of 10,000 men with no partnerships, who are assigned attributes according to the distributions specified in sections 3 and 4. To initialize the network, individuals are assigned placeholder attributes for main and persistent degree to match the observed distributions in section 4.1.1. This attribute is updated as partnerships form and dissolve. We use the mean durations of main and persistent partnerships (section 4.1.7) to calculate persistence model parameters. Using the target statistics calculated from our data for each of the terms listed above, we use an MCMC algorithm to obtain maximum likelihood estimates of the corresponding parameters.[241] This step utilizes an approximation method for the main and persistent network STERGMs to improve computational efficiency.[242]

4.3 Network diagnostics

To ensure that the simulated networks reproduce the observed features of the sexual network, we ran diagnostics on the models for each of the three partnership types in the absence of epidemic and demographic dynamics. We achieved excellent fit with the main and instantaneous models, with mean simulated network statistics within 1-2% of the observed targets. For the persistent model, however, partnership duration was too short for the dynamic approximation method to work as expected.[242] To improve the fit, we adjusted the coefficients by sampling values from a range of ± 0.15 and taking the mean of the best-fitting 5 sets of coefficients from 10,000 simulations. This adjusted model resulted in mean simulated network statistics within 5% of the observed targets.

5. Behavior within sexual partnerships

In each time step, our model simulates four behaviors within active partnerships: HIV status disclosure, the number of anal sex acts, condom use in each act, and sex role in each act. These behaviors are modeled only in HIV serodiscordant partnerships, including those in which the positive partner is undiagnosed, to focus on events with transmission potential.

5.1 Disclosure

At the start of a serodiscordant partnership, we model whether or not the HIV-positive partner discloses his status, given that he's been diagnosed. Disclosure is assumed to influence the probability of condom use, as described in section 5.3. Using data from the Washington MMP sample, we estimated probabilities of disclosure by partner type. The MMP did not ask respondents to describe partners as main, so we defined main partners using a variable that measured respondents' level of commitment to each of their most recent 5 partners. Those whom respondents reported being "committed to above and beyond anyone else" were categorized as main. Partners with whom respondents reported having anal sex only once in the past 12 months were categorized as instantaneous, and all others were categorized as persistent. Disclosure was measured by asking respondents if their partners know their HIV status, and if so, if the partners were aware of their status every time they had sex in the past 12 months. In the 2014 dataset, 51 HIV-positive men reported on 102 partnerships with negative or unknown-status men. Of these, 13 were classified as main partners, 44 as persistent, and 45 as instantaneous. All men who reported disclosing their status to a discordant partner indicated that their partner was aware of their status every time they had sex in the past 12 months. Table S2.9 shows the proportion who reported disclosure with partners of each type.

Table S2.9: HIV status disclosure by partner type	
Main partners	1.000
Persistent partners	0.567
Instantaneous partners	0.492

Although the sample size for these data is small, particularly for main partners, we used these data to set the probability of disclosure in the model. We assumed that if disclosure does not occur at the outset of a relationship, it will not happen. We also assumed that all men disclose their status to main and persistent partners if they are diagnosed while in an ongoing partnership, consistent with previous models.[94,112]

5.2 Anal sex acts

In instantaneous partnerships, only one anal sex act is modeled by definition. In main and persistent partnerships, the number of anal sex acts per weekly time step is determined by a draw from a Poisson distribution, with mean values derived using data from the combined WHPP and ARTnet samples. Exploratory analyses did not indicate any meaningful differences in coital frequency by modeled attribute, so we calculated overall rates of coital frequency for each partnership type.

Table S2.10: Mean number of anal sex acts per week	
Main partnerships	1.30
Persistent partnerships	0.83

5.3 Condom use

The probability of condom use in a partnership is influenced by individual and dyad-level factors. For each partnership type, we specified base probabilities for dyads in which the positive partner has not yet been diagnosed. To estimate these probabilities, we used data on condom use with the most recent partner from the WHPP sample, restricted to partnerships where both partners were HIV negative or status-unknown. With the objective of estimating the baseline probability of condom use in a population with no PrEP use, we further restricted the sample for these analyses to respondents who had not used PrEP in the past 12 months and whose most recent partner was not known to be using PrEP. However, by excluding PrEP users, resulting estimates are likely to overestimate the probability of condom use, given that unprotected anal sex is an indication for starting on PrEP. For this reason, and in recognition of social desirability biases in self-reported data, we used condom use as a tuning parameter for calibration, as described in section 10.2.

Exploratory analyses suggested age differences in the probability of condom use with main partners, with higher condom use in partnerships involving younger men. To represent this in the model, we defined separate probabilities of condom use with main partners for partnerships between two men aged 18-34 and for all other age combinations (Table S2.11). For persistent and instantaneous partnerships, we assigned attributes to indicate men who always use condoms in these partnerships. Using data from the WHPP survey, we defined the proportion of men who always use condoms with persistent partners as the proportion who reported 2 or more persistent partners in the past 12 months and reported no condomless anal sex with any non-main partners. We took a similar approach to define the proportion of men who always use condoms with instantaneous partners. To allocate these attributes in the network, we calculated the correlation between consistent condom use with persistent and instantaneous partners using a phi coefficient.

Table S2.11: Baseline condom use parameters for undiagnosed serodiscordant partnerships in the absence of PrEP: initial estimates before calibration	
Main partnerships	
Mean probability of condom use in dyads involving two men aged 18-34	0.339
Mean probability of condom use for all other age combinations	0.140
Persistent partnerships	
Proportion of men who always use condoms	0.092
Probability of condom use for inconsistent users	0.393
Instantaneous partnerships	
Proportion of men who always use condoms	0.198
Probability of condom use for inconsistent users	0.414
Correlation between consistent condom use with persistent and instantaneous partners	0.601

For calibration, we applied a general scalar to the baseline probability of condom use across partnership types and the proportion of men who always use condoms with persistent and instantaneous partnerships. We defined a prior distribution for this scalar with the lower bound corresponding to the relative reduction in the overall probability of condom use in our data if we assumed that none of the PrEP users used condoms before going on PrEP: 0.64. We set the upper bound to 1. The selected posterior value for this scalar was 0.73 (section 10.2).

To account for changes in condom use with diagnosis and disclosure, these baseline condom use probabilities were first transformed into log odds. Because we lacked data on the impact of diagnosis and disclosure on the probability of condom use with discordant partners among Washington MSM, we used estimated logistic regression coefficients from an analysis of data from Atlanta-area cohort studies.[94,112] These coefficients were added to the baseline log odds to modify condom use following disclosure or diagnosis, and were assumed to be the same across partnership types.

Table S2.12: Logit coefficients for the change in condom use with HIV diagnosis and disclosure	
Disclosure	0.670
Diagnosis	0.850

These logit values were then converted back to probabilities, and condom use was simulated stochastically for each act by sampling from a binomial distribution. After calibration, the mean proportion of acts that were protected by condoms was 17% in main partnerships, 41% in persistent partnerships, and 51% in instantaneous partnerships. As described in section 9, PrEP use was also assumed to modify the probability of condom use in scenarios with risk compensation.

5.4 Anal sex role

Sexual position is determined by a fixed attribute assigning men to be exclusively receptive, exclusively insertive, or versatile (section 4.6). For partnerships involving two versatile men, we define a probability that they will both take the receptive and the insertive role in a single anal intercourse event (intraevent versatility). Using data on the frequency of intraevent versatility with the up to the most recent 5 partners from the ARTnet survey, we estimated this probability at 27.9%. If intraevent versatility does not occur in a given sex act, sex role is determined by an attribute indicating each partner's preference for being the insertive partner, which is assigned by drawing from a uniform distribution between 0 and 1. The probability of being the insertive partner is given by each man's preference for insertativity divided by the sum of the insertativity preference values for both members of the partnership.

6. HIV natural history

Disease progression is modeled through changes in HIV viral load with each stage of infection. As in previous network-based MSM models,[94,112,239] viral load rises in the absence of treatment from a starting value of 0 to a peak value in acute infection after 45 days. Subsequently, viral load falls over 45 days to a chronic phase set point and remains at this value for 9.7 years until onset of AIDS (at 10 years post seroconversion), which is marked by an increase in viral load.[243] Our model deviates from previous models[94,112,239] in that we do not explicitly model AIDS mortality. As described in section 3.2, we instead represent HIV/AIDS-associated mortality by applying age-specific scalars to background mortality. For individuals who progress to AIDS, viral load is assumed to rise to a peak of 7 $\log_{10}$ within 2 years, after which point viral load stabilizes. Since we assume universal treatment with ART (see section 7), very few men are expected to reach this point. Because HIV/AIDS symptoms often appear before clinical AIDs,[116] we define an interval of 7.5 years from seroconversion to symptom onset, which is assumed to prompt diagnostic testing. Table S2.13 lists the relevant model parameters.

Table S2.13: HIV natural history parameters		
Parameter	Value	Source
Time from seroconversion to peak acute-stage viremia	45	[243,244]
Peak viral load in acute stage	6.866 $\log_{10}$	[244]
Time from peak acute-stage viremia to set point viral load	45	[243,244]
Level of set point viral load	4.5 $\log_{10}$	[245]
Time from seroconversion to symptom onset	2738 days	[116,117]
Duration of chronic stage infection	3550 days	[246,247]
Time to peak AIDS-stage viremia	728 days	[246]
Peak viral load in AIDS stage	7 $\log_{10}$	Estimated[94]

7. Clinical epidemiology

We model the processes of diagnosis, ART initiation, cycling on and off ART, and resulting changes in viral load. A fixed attribute determines men's probability of HIV testing and adherence to ART. For HIV testing, men are assigned to either screen at regular intervals or only with symptom onset. After diagnosis, all men are assumed to initiate ART and either treat with high adherence, resulting in full viral suppression, or treat with suboptimal adherence, resulting in partial viral suppression. As described in detail below, we derived values for these clinical parameters to match Washington State surveillance data on the proportion of MSM/MSM-IDU cases diagnosed with AIDS within one year of an HIV diagnosis and the proportions engaged in care, virally suppressed, and durably suppressed.

7.1 *HIV testing*

The screening interval for regular testers was estimated from WHPP survey data on days since the last HIV test among respondents not currently taking PrEP. Because the survey was not administered in connection with any testing event, we assume the survey date was randomly distributed within men's testing intervals, such that on average it fell halfway between testing events. We calculated the intertest interval as twice the reported days since the last test, which yielded an estimated median interval of 436 days. This interval did not appear to vary by race/ethnicity or region, so we used a single parameter for the entire network. We assume that tests that occur within a 21-day window period after infection will yield false-negative results,[248] and all other tests are 100% sensitive. Men using PrEP are assumed to test for HIV every 3 months.

We estimated the proportion of men who test only with symptom onset by race/ethnicity and region using Washington State surveillance data on the proportion of MSM/MSM-IDU cases that were diagnosed with AIDS within 1 year of their HIV diagnosis from 2013-2017. Because CD4+ cell count declines rapidly for some individuals[117], we adjusted this estimate to account for the fact that some proportion of late diagnoses will occur among men who test regularly. Since the average intertest interval for regular testers is 436 days, we assume that men in this group are diagnosed on average 218 days after seroconversion, such that regular testers would be considered late diagnoses if they progressed to AIDS within 583 days (~1.6 years) of seroconversion. From Lodi,[117] if 8.8% of men progress to AIDS within a year and 3.4% progress in the second year, approximately 10.8% of regular testers will be late diagnoses. The proportion of men who test only upon progression to symptoms can be expressed as $p = (obs - 0.108)/(1 - 0.108)$, where obs indicates the observed proportion of all diagnoses that are defined as late. Table S2.14 presents the estimated values from solving this equation using data on the observed proportion of diagnoses defined as late for each racial/ethnic group and region.

Table S2.14: Proportion of men who don't test for HIV until symptom onset		
Region	Race/ethnicity	Estimate
King County	Black	0.080
	Hispanic	0.064
	Other	0.104
Western WA	Black	0.120
	Hispanic	0.102
	Other	0.148
Eastern WA	Black	0.161
	Hispanic	0.140
	Other	0.192

7.2 Antiretroviral therapy (ART) initiation

We estimated the time from diagnosis to treatment initiation using data on the median time from diagnosis to viral suppression for each racial/ethnic group and region. Based on the typical timing of labs and expert consultation, we assumed that treatment was initiated an average of 8 weeks before the first recorded date of viral suppression. The resulting parameters for the time to ART initiation are listed in table S2.15. Lacking empirical data on the distribution of time to ART initiation, for simplicity we assume that all men start treatment after the specified intervals.

Table S2.15: Estimated weeks from diagnosis to ART initiation		
Region	Race/ethnicity	Estimate
King County	Black	6.6
	Hispanic	6.2
	Other	6.7
Western WA	Black	8.0
	Hispanic	7.6
	Other	8.1
Eastern WA	Black	7.6
	Hispanic	7.1
	Other	7.6

7.3 Antiretroviral therapy (ART) adherence, viral suppression, and retention in care

With initiation of ART, we modeled a decrease in viral load to either full or partial suppression according to men's assigned adherence profile. For men who treat with full suppression, viral load declines linearly over 28 days to an on-treatment level of 1.5 log10. The time to viral suppression was defined using data from randomized trials of dolutegravir to reflect the effects of contemporary regimens including integrates inhibitors.[249,250] For men who treat with partial suppression, we model a decline in viral load over 28 days to an on-treatment level of 3.5 log10, consistent with previous models.[94,112] With treatment cessation, viral load is assumed to increase back to set point viral load.[251–253] We assume that the slope of viral rebound for both groups mirrors the slope of viral suppression in full suppressors.

Rates of treatment cessation were derived from data on the durability of viral suppression. We obtained data on the proportion of MSM/MSM-IDU cases in Washington who were virally suppressed at their first lab visit in 2016 that remained virally suppressed at their next visit 5-7 months later. Because the typical timing of labs may differ for men who have demonstrated stable adherence, we also calculated the proportion of that remained virally suppressed at a subsequent visit within 11-13 months of their initial suppressed viral load in 2016. By including data only from men who had a follow-up viral load in the defined intervals, these proportions will over-estimate durable suppression since men who fall out of care are not included in the denominator. To adjust for this, we defined the probability of durable suppression through x months (corresponding to 6- or 12-month intervals) as the probability of remaining in care times the probability of remaining suppressed given that an individual is in care: $P(D_x) = P(IC) \times P(S_x \mid IC)$. The probability of remaining in care was estimated as 1 minus the proportion of men who were suppressed at their first visit in 2016 that had no viral load labs for the subsequent 18 months and were not on record as having died or moved to another jurisdiction.

Assuming that the process of treatment cessation follows a geometric distribution, we calculated the parameter p that has a cumulative distribution of Y at time x, where $Y = 1 - P(D_x)$, based on the geometric distribution cumulative distribution function, $p = 1 - (1 - Y)^{1/x}$. We solved this equation using data on durable suppression over both the 6- and 12-month intervals and took the weighted average of the estimated rates, which were very similar at 0.0022 and 0.0023 per weekly time step, respectively. The resulting value was used to define the rate of treatment cessation for men who treat with full suppression. We assume that men who treat with partial suppression fall out of care at twice this rate. Because of the constraints of this analysis, we did not stratify these parameters by race/ethnicity or region. However, as described in the next paragraph, we calculated differential rates of treatment reinitiation such that the proportion of men on treatment in the cross-section aligns with observed patterns.

Table S2.16: Rates of treatment cessation per weekly time step	
Full suppressors	0.002
Partial suppressors	0.004

Using the calculated rate of treatment cessation and observed cross-sectional proportions of diagnosed MSM who were engaged in care and virally suppressed in 2017, we solved for a) rates of treatment reinitiation and b) the proportions of men who treat with full suppression by race/ethnicity and region. Engagement in care is defined as having evidence of one or more HIV labs in the past year, as was used as a proxy indicator for the proportion on treatment. In solving for the rates of treatment reinitiation that are consistent with observed data, we assumed that partial suppressors reinitiate at half the rate for full suppressors.

Table S2.17: Rates of treatment reinitiation per weekly time step

Region	Race/ethnicity	Full suppressors	Partial suppressors
King County	Black	0.024	0.012
	Hispanic	0.024	0.012
	Other	0.028	0.014
Western WA	Black	0.020	0.010
	Hispanic	0.020	0.010
	Other	0.022	0.011
Eastern WA	Black	0.022	0.011
	Hispanic	0.021	0.011
	Other	0.024	0.012

Table S2.18: Estimated proportion of diagnosed men who treat with full suppression		
Region	Race/ethnicity	Proportion
King County	Black	0.839
	Hispanic	0.902
	Other	0.920
Western WA	Black	0.811
	Hispanic	0.885
	Other	0.905
Eastern WA	Black	0.759
	Hispanic	0.847
	Other	0.874

8. Transmission

HIV transmission is modeled stochastically for each anal sex act within active serodiscordant partnerships as a function of behavior and relevant attributes of each member of the dyad. We defined baseline probabilities of transmission for sex acts in which the susceptible partner takes the receptive role and acts in which the susceptible partner takes the insertive role. Published estimates of these probabilities reflect substantial uncertainty,[135–138,254] so, as described in section 10, we calibrated the model using baseline transmission probability as a tuning parameter. Our initial estimates are presented in Table S2.19, and we bounded our prior distribution such that the calibrated parameters fell within the range of estimates in the literature.

These baseline transmission probabilities are modified by the HIV viral load of the infected partner, acute stage infection, CCR5-Δ32 genotype and circumcision status of the susceptible partner, and condom use (Table S2.19). Transmission is simulated with a draw from a binomial distribution with the adjusted probability defined as a function of these factors. As described in section 9.2, PrEP use also modifies transmission risk, with varying efficacy as a function of adherence.

Table S2.19: Determinants of per-act HIV transmission probability		
Predictor	Parameter	References
Baseline probabilities[a]		
Susceptible partner is receptive	0.008938 when the HIV+ partner is at set point viral load (4.5 $\log_{10}$)	138
Susceptible partner is insertive	0.003379 when the HIV+ partner is at set point viral load (4.5 $\log_{10}$)	138
HIV viral load (VL)	Multiplier of $2.45^{(VL-4.5)}$	255
Acute stage infection	Multiplier of 6	256,257
Susceptible partner CCR5-Δ32 genotype		
Homozygous	Multiplier of 0	238
Heterozygous	Multiplier of 0.3	238
Susceptible partner circumcision status	Multiplier of 0.40 (for insertive sex)	258
Condom use	Multiplier of 0.25	259,260
[a]These baseline probabilities were adjusted in calibration (see section 10)		

9. PrEP

We defined a range of scenarios for PrEP use by jointly varying coverage, adherence, change in condom use (risk compensation), and the persistence of changes in condom use following discontinuation.

9.1 PrEP eligibility and coverage

Coverage was varied by setting the maximum proportion of eligible men who could be using PrEP, with eligibility defined based on Washington State guidelines.[35] These guidelines define indications for PrEP to be recommended and a lower tier of indications for PrEP to be discussed. Based on analyses of local data that identified factors associated with HIV acquisition, these indications include being in an ongoing serodiscordant relationship, use of meth or poppers, nonprescription injection drug use, diagnosis with a bacterial STI, use of non-occupational post-exposure prophylaxis (PEP), and condomless anal sex outside of the context of a long-term mutually monogamous relationship with an HIV-negative partner.

Because our model does not represent drug use, use of PEP, or STI diagnosis, we were not able to implement the full set of criteria to define eligibility. However, these indications are defined to serve as proxy measures of HIV exposure risk, which our model represents explicitly. We categorized men as eligible for PrEP in a given time step if they are in an active main or persistent partnership with a diagnosed HIV-positive partner or had condomless anal sex in the past 12 months with any persistent or instantaneous partners, in main partnerships where either member of the dyad had a concurrent partner, or with a main partner who had never been tested for HIV.[†] Men initiate PrEP at the time of HIV screening if they are eligible and current coverage in that time step is below the defined threshold. Because PrEP uptake is linked to HIV screening, individuals assumed not to test until symptom onset cannot initiate PrEP.

Data from the re-weighted WHPP survey indicate that 33.3% of men who meet guidelines for PrEP being recommended or discussed were using PrEP in 2017. Data form a range of sources in King County, Washington have found similar levels of use among high risk men.[33] In one scenario, we assume coverage stays at this level for the duration of the simulated 10-year period. In a second scenario, PrEP uptake increases linearly to a maximum of 50% coverage by 2020, meeting state goals.[33] In a third scenario, we allow coverage to continue to increase linearly up a maximum of 66%, based on the proportion of WHPP respondents who reported use of or interest in starting PrEP. Lastly, we consider a scenario with stable 25% coverage, allowing for the possibility that data from the WHPP survey overestimated PrEP use.

[†] Because our model assumes a fixed interval of 436 days between HIV tests for all men who test, men who have ever tested will have done so a maximum of 436 days ago.

9.2 PrEP adherence and efficacy

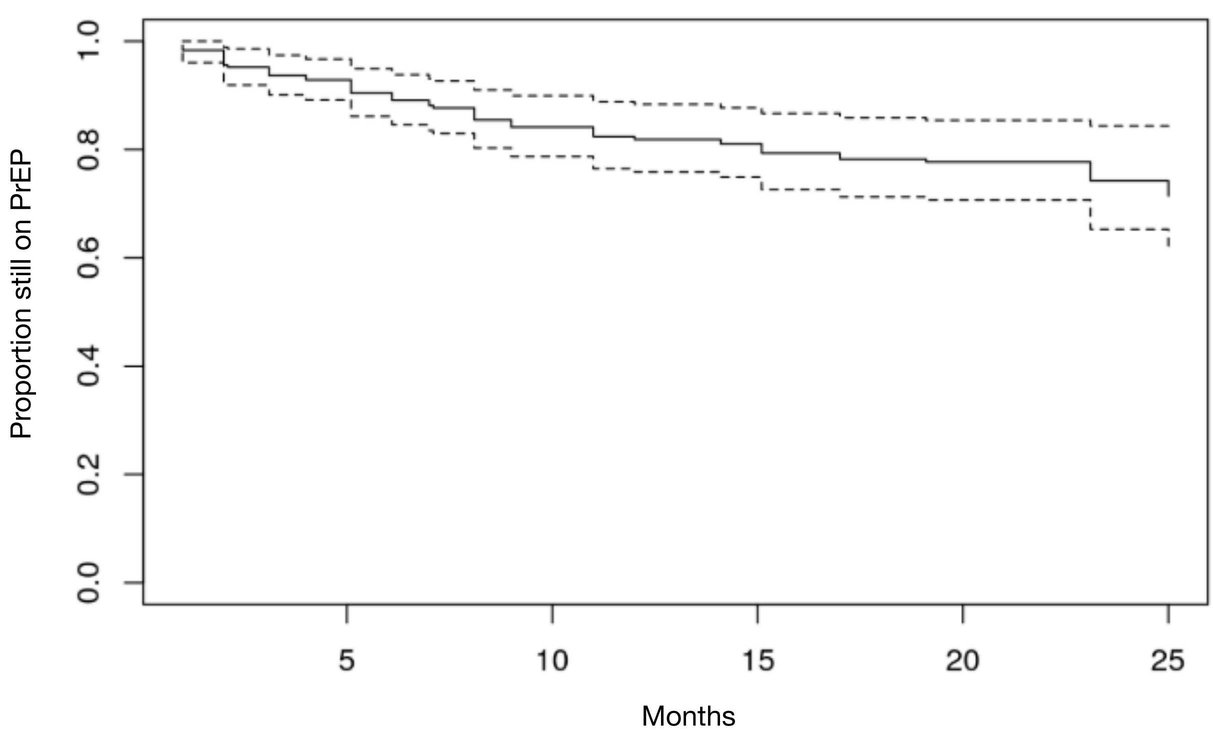
Adherence to PrEP is determined by a fixed attribute with three levels: low adherence (<2 doses/week), moderate adherence (2-3 doses/week), and high adherence (≥4 doses per week). Data from observational studies have suggested that adherence is high among MSM, however the proportion of men maintaining high adherence has been found to decrease over time.[118,119,122] We defined two adherence profiles, with lower levels based on data from studies that measured tenofovir diphosphate concentrations over time using dried blood spots,[118,119] and optimistic higher levels based on self-reported data, medication possession ratios, and cross-sectional dried blood spot samples taken closer to the time of PrEP initiation.[114,118–123] The proportions of men in the low, moderate, and high adherence classes for these two scenarios were 5%, 30%, and 65% and 3%, 7%, and 90%, respectively.

The percent reduction in the per-act probability of HIV transmission was 31% with low adherence, 81% with moderate adherence, and 96% with high adherence.[14,15] We assume the protective effects of PrEP apply immediately upon initiation and cover all exposures up to the date of discontinuation. This may overestimate the impact of PrEP, as pharmacokinetic analyses suggest that TFV-DP reaches protective levels after approximately 7 days of dosing and MSM are recommended to continue PrEP for 4 weeks after the last potential exposure.[261] However, we do not expect this to have a meaningful impact on our findings. While on PrEP, men are assumed to test for HIV every 3 months.

9.3 PrEP discontinuation

Men discontinue PREP in three ways: with diagnosis of HIV, following changes in sexual partnerships and condom use that result in PrEP no longer being indicated, or spontaneously. Discontinuation is assumed to occur in the time step at which men cease to be eligible. To inform parameters for spontaneous discontinuation, Figure S2.9 shows data from a Kaplan-Meier analysis of time to discontinuation among WHPP survey respondents. This analysis is based on reported dates of first and last PrEP use among 229 respondents who had ever used PrEP, reweighted to the demographics of Washington MSM, as reported in section 2.3. Current users' time on PrEP was censored at the date of survey completion. Although it is difficult to draw conclusions about patterns of discontinuation beyond ~18 months from these data, we assumed that up to 30% of men will discontinue PrEP spontaneously. Upon initiating PrEP, men are assigned to either stay on PrEP until they are no longer eligible (at 70%) or experience a constant hazard of discontinuation (30%). To calculate the rate of discontinuation among these 30%, we will fit an exponential distribution to the survival curve up to 70%, with the median corresponding to the 85th survival quantile. From this, we estimated a mean 13-month duration of PrEP use, for a weekly rate of discontinuation of 0.0177.

Figure S2.9: Kaplan-Meier plot of time to PrEP discontinuation



9.3 Risk compensation

To assess the impact of changes in risk behavior with PrEP use, we model scenarios with the probability of condom use reduced by 0%, 20%, 40%, 60%, 80%, and 100% in partnerships where the susceptible partner is using PrEP. These reductions are assumed to apply uniformly across partnership types and PrEP adherence classes. Based on data showing no change or decreases in the number of sex partners with PrEP use,[15,15,121,124–126,129,132,149] we model decreased condom use as the only form of risk compensation. To explore the implications of persistent changes in condom use following discontinuation,[133] we model scenarios in which men who discontinue PrEP spontaneously maintain on-PrEP levels of condom use. These men may reinitiate PrEP at their next HIV test if current coverage is below the defined threshold.

10. Calibration and simulation

10.1 Calibration

To calibrate our model, we compared the simulated prevalence of diagnosed infection to the observed prevalence in 2017, which was defined using surveillance data on the number of MSM/MSM-IDU cases aged 18-59 in residing in Washington divided by the estimated MSM population size, described in section 2.3. As explained by Goodreau,[239] our methods seek to represent the current epidemiologic profile, rather than replicating historical trends in the epidemic. While the latter approach would more accurately represent the dynamic determinants of transmission and the implied epidemic trajectory, the lack of longitudinal data on changes network structure, behavior, and demographics make this unfeasible.

We initiated the model with a population of 10,000 MSM and seed infection in a random sample of 7% of the population. We then ran burn-in simulations for a period of 40 years to allow the network, demographic, and epidemiologic processes to evolve and stabilize. With our initial parameter estimates, our model projected sustained decreases in prevalence. To fit the model to the target prevalence of 8.18%, we used approximate Bayesian computation with sequential Monte Carlo sampling[139] to calibrate the model.

As described in sections 5.3. and 8, we used condom use and baseline per-contact transmission probability as tuning parameters. Informed by the magnitude and likely direction of uncertainty in these parameters, we defined prior distributions for multiplicative scalars to adjust the initial values. For condom use, we sampled from a uniform prior distribution from 0.65 to 1, with the lower bound corresponding to the relative reduction in condom use estimates from the WHPP survey if none of the men on PrEP used condoms in the absence of PrEP (see section 5.3). This scalar was applied to the proportion of men who use always use condoms with persistent and instantaneous partners and to the probability of condom use per act in dyads of inconsistent condom users. For the baseline transmission probability, we defined from a uniform prior distribution from 1 to 1.25 for the relative increase in the per-act probability of transmission. This range was consistent with the range of estimates in the literature.[135–138,254]

We used the EpiABC package in R, which extends the functionality of the EasyABC package to run calibration simulations. We ran 30 sequential waves of the ABC-SMC algorithm, and selected the set of parameters from the posterior distribution that produced an equilibrium prevalence of diagnosed infection within 0.1% of the target of 8.18%. The resulting scalars were 0.73 for condom use and 1.19 for the per-act transmission probability.

10.1 Intervention simulations

Using the calibrated model, we simulated a baseline scenario and all combinations of the PrEP use scenarios, each 500 times. After 40 years of burn-in simulations to allow the model to equilibrate, we evaluated scenarios over 10 years, representing the calendar period from 2017 to 2027. Simulations were conducted on the Hyak supercomputer system at the University of Washington.

SUPPLEMENTAL APPENDIX 3: Technical details on the Chapter 3 mathematical model

Model structure and assumptions

The model represents a cohort of 100,000 individuals from age 16 to 64. The population is stratified into four groups with varying HIV risk and testing practices: low- and high-risk men who have sex with men (MSM), men who have sex with women only (MSW) and women. Figure S3.1 presents a simplified model schematic. Individuals in each of the four population groups enter the model at age 16 and progress in yearly time-steps through age 64, exiting at age 65 or with HIV diagnosis. All persons start in the susceptible state, and age- and risk group-specific HIV incidence rates are applied to determine the number who become infected at each age. HIV-positive individuals are stratified by year of infection, and HIV diagnosis occurs in one of five ways: through risk-based screening of MSM, prenatal screening of pregnant women, upon progression to symptomatic HIV/AIDS, as a result of partner notification, or with routine screening. Those who remain undiagnosed at the end of the year progress to the next year of infection up through year 16, at which point all are assumed to experience symptoms leading to diagnostic testing. The model was built using Microsoft Excel (Version 16.9).

As a static linear model, it does not represent transmission dynamics or account for the impact of screening and diagnosis on downstream infection. We assume an implicit ordering of events, with HIV infections occurring at the beginning of each year, diagnoses through risk-based, prenatal, and routine screening at the mid-point of the year, and diagnoses prompted by symptom onset or partner notification at the end of the year. The rate of symptom development was estimated from data on time from HIV seroconversion to CD4+ cell count <200 cells/mm^3,[117] which suggest an 8.8% probability of reaching this threshold after 1 year and an approximately linear increase up through a cumulative 32% probability by year 5. Consistent with Golden et al.,[163] we model a 6.08% risk of progression in each subsequent year, with all individuals progressing to CD4+ <200 cells/mm^3 after 16 years. We assume that HIV/AIDS associated symptoms present upon reaching

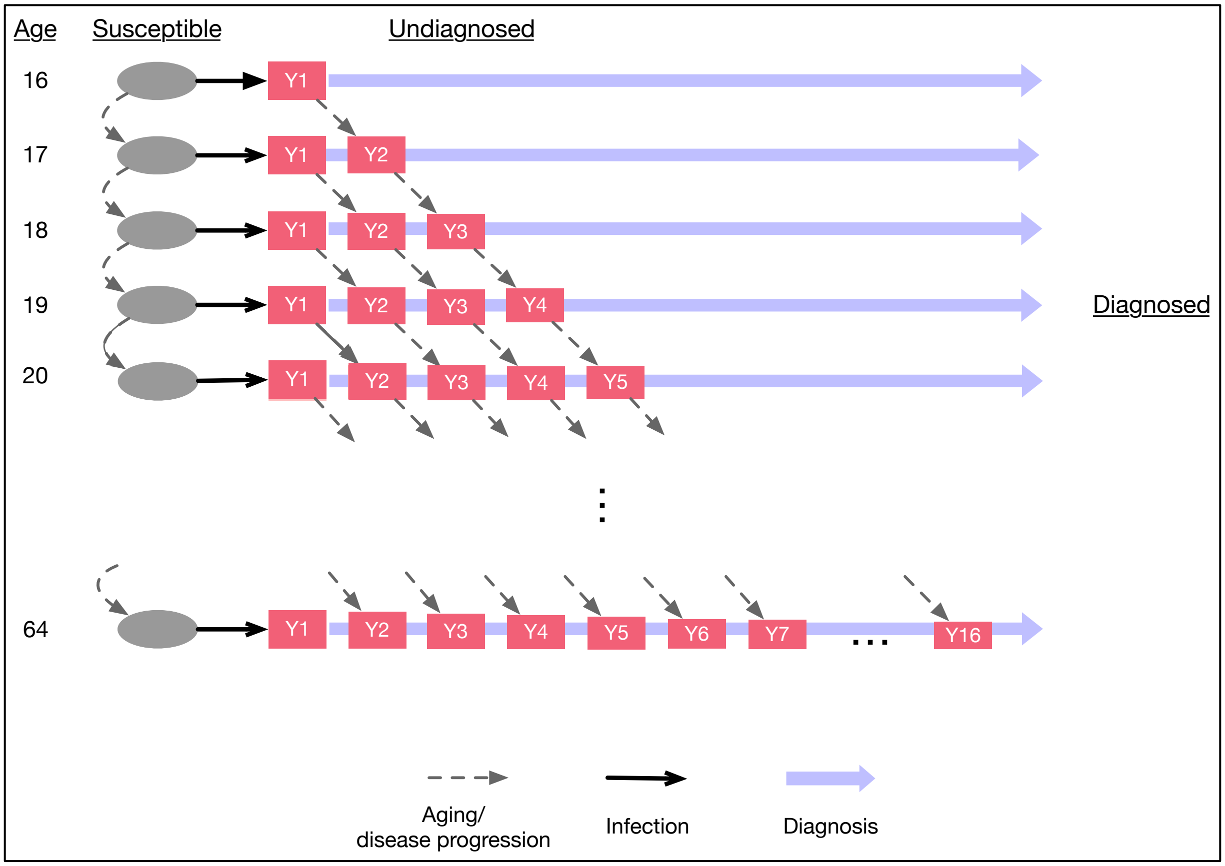


Figure S3.1: Model schematic showing the processes of infection, aging, disease progression, and diagnosis for one of the four modeled population groups.

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this threshold and prompt diagnosis. While some people develop HIV/AIDS-associated symptoms before CD4+ cell depletion, others may experience symptoms later. Our model suggests a median time to symptom onset of 8 years, aligning with estimates from cohort studies.[116,204]

Risk-based, prenatal, and routine screening occur at the midpoint of the year, such that individuals diagnosed through these strategies contribute half a year of undiagnosed infection in the year they are diagnosed. Persons not screened for HIV remain undiagnosed until they develop symptoms or are notified of potential exposure to an infected partner. For partner notification, we assume no bridging of the MSM and heterosexual populations: the number of diagnoses resulting from partner notification among MSW and women depend on the number of diagnoses from other modes of testing among females and MSW, respectively, and partner notification diagnoses among

MSM are calculated based on the number of other diagnoses among MSM in both risk groups. In allocating these diagnoses by age, we make a simplifying assumption of perfect age matching in partnerships. All HIV tests are assumed to be 100 sensitive and specific, and individuals exit the model once they become diagnosed.

Monte Carlo simulation: uncertainty distributions

To account for uncertainty in model inputs, we conducted Monte Carlo simulation using @RISK software (version 7.6, Palisade Company, Ithaca, NY). For parameter estimates for which a 95% confidence interval was available in the literature, we sampled from normal distributions with standard deviations equal to the range of the confidence interval divided by 2×1.96. Where estimates from different sources were inconsistent, we defined normal distributions with standard deviations equal to the range of estimates divided by 2×1.96.

For the King County and Philadelphia County models, we lacked confidence interval data on the size of the MSM population or the number of incident cases. We applied a range of $\pm$20% to both sets of parameters, as this range encompassed an alternate estimate of the size of the MSM population in King County and was larger than the margin of error in incidence estimates at the national level, accounting for greater uncertainty with smaller counts. We used this range to define normal distributions around point estimates of incidence as described above. However, because we did not have reason to believe that either estimate for the size of the MSM population in King County was closer to the truth,[33,134] we sampled values for this parameter from a uniform distribution. As data were not available on the relative probability of risk-based screening for high- and low-risk men, we defined uniform uncertainty intervals with ranges informed by expert opinion.

To account for dependence in parameters defining the proportion of MSM who are high-risk, the incidence rate ratio for high- to low-risk MSM, and the relative risk-based screening frequencies, we defined a correlation matrix to ensure that sampled values for these parameters preserved expected relationships between these variables. We assumed that as the size of the high-risk population decreased, the differences in incidence rates and HIV testing relative to low-risk MSM would become more extreme. We also assumed that, as the relative likelihood of screening annually for high-risk MSM increased, the relative likelihood of not screening would decrease. For each of these associations, we defined moderate correlations, shown in Table S3.1.

Table S3.1: Correlation coefficients for Monte Carlo Simulation

	Proportion high risk	Incidence rate ratio (high:low risk)	Relative risk of annual screening	Relative risk of no screening
Proportion high risk	1			
Incidence rate ratio (high:low risk)	-0.6	1		
Relative risk of annual screening	-0.5	0.5	1	
Relative risk of no screening	0.5	-0.5	-0.6	1

Model processes and formulae

Table S3.2 defines model parameters, and the sections that follow detail the formulae and assumptions used to construct and execute the model.

Table S3.2: Parameter definitions

Parameter/ variable	Definition
a	Age
y	Year of infection (1-16)
r	Risk group (high-risk MSM, msm_h; low-risk MSM, msm_l; non-MSM males, msw; females, fem)
p_r	Proportion of the population in risk group r

f_a	Fertility rate for women of age a
x	Targeted screening group. Among MSM, groups are never, annual, and non-annual risk-based screeners ($ann, nann$, and nev). Among females, groups define pregnant and non-pregnant women ($preg$ and $npreg$). MSW are not stratified by targeted screening group.
n	Non-annual risk-based screening interval (years)
$px_x^{r,a}$	Proportion of low- and high-risk MSM of age a in each risk-based testing group x (never, annual, and non-annual)
$prtest$	Proportion of pregnant women screened for HIV in the pre- or perinatal periods
$dxpn$	Number of new diagnoses from partner services resulting from one index case
δ	Age of routine screening
$rtcov$	Routine screening acceptance rate
α	Proportion of HIV-infected persons who develop symptoms in years 2-16 of infection
β	Proportion of HIV-infected persons who develop symptoms in year 1 of infection
$S_{x,a}^r$	Number of susceptible individuals in risk group r, targeted screening group x, and age a
$I_{x,a}^r$	Incident infections in risk group r and targeted screening group x occurring at age a
IR_a^r	Incidence rate among persons of risk group r and age a
$U_{x,a,y}^r$	Number of undiagnosed infections in risk group r, screening group x, and age a at the start of year of infection y
$RB_{x,a,y}^r$	Number of diagnoses due to risk-based screening among MSM in high- or low-risk group r, screening group x, and age a in year of infection y
$PR_{a,y}$	Number of new diagnoses due to prenatal screening among females at age a in year of infection y
$RT_{x,a,y}^r$	Number of new diagnoses due to routine screening among persons in risk group r, screening group x, and age a in year of infection y
$SX_{x,a,y}^r$	Number of new diagnoses due to symptomatic testing among persons in risk group r, screening group x, and age a in year of infection y
$PN_{x,a,y}^r$	Number of new diagnoses due to partner notification testing among persons in risk group r, screening group x, and age a in year of infection y
$U_{x,a,y}^r$	Number of persons in risk group r, screening group x, and age a who are HIV-infected and undiagnosed at the start of year of infection y
SY	Total number of undiagnosed cases that develop symptoms
YU	Cumulative population-level years of undiagnosed infection

1. Initial population size for each risk group r and screening group x

$$for\ r \in \{msm_l, msm_h\},\ S^{r}_{x,16} = N \times p_r \times px^{r,a}_{x}$$
$$S^{fem}_{preg,16} = N \times p_r \times f_{16}$$

$$S^{fem}_{npreg,16} = N \times p_r \times (1 - f_{16})$$

$$S^{msw}_{x,16} = N \times p_r$$

Assumptions: All persons enter the model at age 16 in the susceptible state.

2. Number susceptible in risk group $r$and screening group x at age a>16

$$for\ r \in \{msm_l, msm_h\}, \qquad S^{r}_{x,a>16} = \sum_{x}\left(S^{r}_{x,a>(16-1)} - I^{r}_{x,a>(16-1)}\right) \times px^{r,a}_{x}$$
$$S^{fem}_{preg,a>16} = \sum_{x}\left(S^{fem}_{x,a>(16-1)} - I^{fem}_{x,a>(16-1)}\right) \times f_a$$
$$S^{fem}_{npreg,a>16} = \sum_{x}\left(S^{fem}_{x,a>(16-1)} - I^{fem}_{x,a>(16-1)}\right) \times (1 - f_a)$$
$$S^{msw}_{x,a>16} = S^{msw}_{x,a>(16-1)} - I^{msw}_{x,a>(16-1)}$$

Assumptions: No mortality and no new entries to the population.

3. Incident infections in risk group $r$and screening group x at age a

$$I^{r}_{x,a} = S^{r}_{x,a} \times IR^{r}_{a}$$

4. Undiagnosed infections in risk group r, screening group x, and age a at the start of year of infection y

$$for\ r \in \{msm_l, msm_h\},$$
$$U^{r}_{x,a,y} = U^{r}_{x,a-1,y-1} - RB^{r}_{x,a-1,y-1} - RT^{r}_{x,a-1,y-1} - SX^{r}_{x,a-1,y-1} - PN^{r}_{x,a-1,y-1}$$

$$U^{fem}_{preg,a,y} = f_a \times \left(U^{fem}_{npreg,a-1,y-1} - RT^{fem}_{npreg,a-1,y-1} - SX^{fem}_{npreg,a-1,y-1} - PN^{fem}_{npreg,a-1,y-1}\right)$$
$$U^{fem}_{npreg,a,y} = (1 - f_a) \times \left(\left(U^{fem}_{npreg,a-1,y-1} - RT^{fem}_{npreg,a-1,y-1} - SX^{fem}_{npreg,a-1,y-1} - PN^{fem}_{npreg,a-1,y-1}\right) + \left(U^{fem}_{preg,a-1,y-1} - RT^{fem}_{preg,a-1,y-1} - SX^{fem}_{preg,a-1,y-1} - PN^{fem}_{preg,a-1,y-1}\right)\right)$$

$$U^{msw}_{x,a,y} = U^{msw}_{x,a-1,y-1} - RT^{msw}_{x,a-1,y-1} - SX^{msw}_{x,a-1,y-1} - PN^{msw}_{x,a-1,y-1}$$

5. Number of MSM in high- or low-risk group r, screening group x, age a, and year of infection y diagnosed through risk-based screening

$$RB^{r}_{ann,a,1} = I^{r}_{ann,a}$$

$$RB^{r}_{nann,a,1} = \left(\frac{1}{n}\right) \times I^{r}_{nann,a}$$

$$for\ y \in \{2, \ldots, 16\},$$

$$RB^{r}_{nann,a,y} = \left(\frac{1}{n-(y-1)}\right) \times U^{r}_{nann,a,y}$$

Assumptions: Risk-based screening is modeled for MSM only. Of MSM who test every n years, $1/n$ *of those not yet diagnosed are assumed to test in years 1:n.*

6. Number in risk group r, screening group x, age a and year of infection y diagnosed through routine screening

$$RT^{r}_{x,\delta,y} = \left(U^{r}_{x,\delta,y} - RB^{r}_{x,\delta,y} - PR_{\delta,y}\right) \times rtcov$$

Assumptions: Routine screening is implemented only for those in the specified age who were not already screened through prenatal or risk-based testing in that year.

7. Number of women at age a and year of infection y diagnosed through prenatal screening

$$PR_{a,y} = U^{fem}_{preg,a,y} \times prtest$$

Assumptions: Pregnancy occurs at the start of the year. Women cannot be pregnant two years in a row, such that all women pregnant at age a *were not pregnant at age* $a-1$.

8. Number in risk group r, screening group x, age a and year of infection y diagnosed through symptom-based testing

$$SX^{r}_{x,a,1} = \left(U^{r}_{x,a,1} - RB^{r}_{x,a,1} - RT^{r}_{x,a,1} - PR_{a,1}\right) \times \beta$$

$$for\ y \in \{2, \ldots, 16\}, \qquad SX^{r}_{x,a,y} = \left(U^{r}_{x,a,y} - RB^{r}_{x,a,y} - RT^{r}_{x,a,y} - PR_{a,y}\right) \times \left(\frac{\alpha}{(1-\alpha(y-2)-\beta)}\right)$$

Assumptions: The proportion of individuals who progress to symptomatic HIV/AIDS is assumed to be constant for years 2-16 of infection at 0.608. All persons who develop symptoms are diagnosed, and all persons living with undiagnosed HIV/AIDS are assumed to develop symptoms resulting in diagnosis by year 16.

9. Number in risk group r, screening group x, age a and year of infection y diagnosed through partner notification

$$\begin{aligned} &for\ r \in \{msm_{high}, msm_{low}\},\\ &\quad PN^{r}_{x,a,y} = dxpn \times U^{r}_{x,a,y}\\ &\qquad \times \sum_{r' \in \{msm_h, msm_l\}} \sum_{x'} \sum_{y'} \left(\frac{\left(RB^{r'}_{x,a,y} + RT^{r'}_{x,a,y} + SX^{r'}_{x,a,y}\right)}{\left(U^{r'}_{x',a,y'} - RB^{r'}_{x',a,y'} - RT^{r'}_{x',a,y'} - SX^{r'}_{x',a,y'}\right)} \right) \end{aligned}$$

$$\begin{aligned} PN^{msw}_{x,a,y} = dxpn \times &\left(\frac{U^{msw}_{x,a,y}}{\sum_{x'} \sum_{y'} U^{msw}_{x',a,y'} - RT^{msw}_{x',a,y'} - SX^{msw}_{x',a,y'}} \right)\\ &\times \sum_{x'} \sum_{y'} \left(PR^{fem}_{a,y'} + RT^{fem}_{x'a,y'} + SX^{fem}_{x',a,y'} \right) \end{aligned}$$

$$PN^{fem}_{x,a,y} = dxpn \times \left(\frac{U^{fem}_{x,a,y}}{\sum_{x'} \sum_{y'} U^{fem}_{x',a,y'} - RT^{fem}_{x',a,y'} - SX^{fem}_{x',a,y'}} \right) \times \sum_{x'} \sum_{y'} \left(RT^{msw}_{x'a,y'} + SX^{msw}_{x',a,y'} \right)$$

Assumptions: MSM are assumed to only partner with other MSM, non-MSM males partner exclusively with females, and females partner exclusively with non-MSM males. Notified partners are of the same age as index cases, reflecting an assumption of perfect age matching in sexual partnerships. For persons in risk group r and age a, the number of new diagnoses resulting from partner notification is a function of the number of diagnoses from risk-based, prenatal, routine, or symptomatic testing among members of the group with whom they partner who are in the same age a, multiplied by the diagnostic yield from partner notification (dxpn). These partner notification diagnoses are distributed across year of infection and screening group according to the proportion of cases that remain undiagnosed at the end of the year in risk group r and age a that are in each year of infection and screening group.

10. Total number of cases that progress to symptomatic HIV/AIDS prior to diagnosis

$$SY = \sum_{r} \sum_{x} \sum_{a} \sum_{y} SX^{r}_{x.a,y}$$

Assumptions: All symptomatic HIV/AIDS cases are diagnosed at the time of symptom onset. Persons diagnosed before symptoms arise exit the model and do not contribute to the count of symptomatic cases.

11. Cumulative population-level years of undiagnosed infection

$$YU = \sum_{r} \sum_{a} \left(U^{r}_{x,a,y} - RB^{r}_{x,a,y} - PR_{a,y} - RT^{r}_{x,a,y} \right) + \left(\frac{1}{2}\right) \times \left(RB^{r}_{x,a,y} + PR_{a,y} + RT^{r}_{x,a,y} \right)$$

Assumptions: Persons diagnosed through risk-based, prenatal, and routine screening contribute half a year of undiagnosed infection in the year of diagnosis. Persons diagnosed through symptomatic testing or partner notification contribute 1 year of undiagnosed infection, as do those who remain undiagnosed at the end of the year

REFERENCES

1 Song R, Hall HI, Green TA, Szwarcwald CL, Pantazis N. Using CD4 Data to Estimate HIV Incidence, Prevalence, and Percent of Undiagnosed Infections in the United States. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2017;**74**:3–9. https://doi.org/10.1097/qai.0000000000001151.

2 Centers for Disease Control and Prevention. *HIV Prevention in the United States: New opportunities, new expectations*. Atlanta, GA: Centers for Disease Control and Prevention; 2015.

3 Centers for Disease Control and Prevention. *HIV Surveillance Report, 2017*. 2018.

4 Singh S, Song R, Johnson A, McCray E, Hall H. HIV incidence, HIV prevalence, and undiagnosed HIV infections in men who have sex with men, United States. *Annals of Internal Medicine* 2018. https://doi.org/10.7326/M17-2082.

5 Beyrer C, Sullivan P, Sanchez J, Baral SD, Collins C, Wirtz AL, *et al.* The increase in global HIV epidemics in MSM. *AIDS (London, England)* 2013;**27**:2665–78. https://doi.org/10.1097/01.aids.0000432449.30239.fe.

6 Hall HI, An Q, Tang T, Song R, Chen M, Green T, *et al.* Prevalence of Diagnosed and Undiagnosed HIV Infection - United States, 2008-2012. *MMWR Morb Mortal Wkly Rep* 2015;**64**:657–62.

7 Centers for Disease Control and Prevention. *Estimated HIV incidence and prevalence in the United States, 2010-2016*. 2019.

8 Azar A. *Ending the HIV Epidemic: A Plan for America*. HHS.Gov. 2019. URL: https://www.hhs.gov/blog/2019/02/05/ending-the-hiv-epidemic-a-plan-for-america.html (Accessed 10 April 2019).

9 Fauci AS, Redfield RR, Sigounas G, Weahkee MD, Giroir BP. Ending the HIV Epidemic: A Plan for the United States 2019. https://doi.org/10.1001/jama.2019.1343.

10 Smith DK, Van Handel M, Grey J. Estimates of adults with indications for HIV pre-exposure prophylaxis by jurisdiction, transmission risk group, and race/ethnicity, United States, 2015. *Annals of Epidemiology* 2018. https://doi.org/10.1016/j.annepidem.2018.05.003.

11 Centers for Disease Control and Prevention. *Monitoring selected national HIV prevention and care objectives by using HIV surveillance data -- United States and 6 dependent areas, 2016*. 2018.

12 Vallabhaneni S, Li X, Vittinghoff E, Donnell D, Pilcher CD, Buchbinder SP. Seroadaptive Practices: Association with HIV Acquisition among HIV-Negative Men Who Have Sex with Men. *PLoS ONE* 2012;**7**:e45718. https://doi.org/10.1371/journal.pone.0045718.

13 Smith DK, Herbst JH, Zhang X, Rose CE. Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the United States. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2015;**68**:337–44. https://doi.org/10.1097/qai.0000000000000461.

14 Anderson PL, Glidden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, *et al.* Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Science Translational Medicine* 2012;**4**:151ra125. https://doi.org/10.1126/scitranslmed.3004006.

15 Grant RM, Anderson PL, McMahan V, Liu A, Amico KR, Mehrotra M, *et al.* Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *The Lancet Infectious Diseases* 2014;**14**:820–9. https://doi.org/10.1016/s1473-3099(14)70847-3.

16 Cohen SE, Vittinghoff E, Bacon O, Doblecki-Lewis S, Postle BS, Feaster DJ, *et al.* High interest in preexposure prophylaxis among men who have sex with men at risk for HIV infection: baseline data from the US PrEP demonstration project. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2015;**68**:439–48. https://doi.org/10.1097/qai.0000000000000479.

17 Strauss BB, Greene GJ, Phillips G 2nd, Bhatia R, Madkins K, Parsons JT, *et al.* Exploring Patterns of Awareness and Use of HIV Pre-Exposure Prophylaxis Among Young Men Who Have Sex with Men. *AIDS and Behavior* 2016;**21**:1288–98. https://doi.org/10.1007/s10461-016-1480-0.

18 Goedel WC, Halkitis PN, Greene RE, Duncan DT. Correlates of Awareness of and Willingness to Use Pre-exposure Prophylaxis (PrEP) in Gay, Bisexual, and Other Men Who Have Sex with Men Who Use Geosocial-Networking Smartphone Applications in New York City. *AIDS and Behavior* 2016;**20**:1435–42. https://doi.org/10.1007/s10461-016-1353-6.

19 Patrick R, Forrest D, Cardenas G, Opoku J, Magnus M, Phillips G, *et al.* Awareness, Willingness, and Use of Pre-exposure Prophylaxis Among Men Who Have Sex With Men in Washington, DC and Miami-Dade County, FL: National HIV Behavioral Surveillance, 2011 and 2014. *J Acquir Immune Defic Syndr* 2017;**75 Suppl 3**:S375–82. https://doi.org/10.1097/QAI.0000000000001414.

20 Dailey AF, Hoots BE, Hall HI, Song R, Hayes D, Fulton P Jr, *et al.* Vital Signs: Human Immunodeficiency Virus Testing and Diagnosis Delays - United States. *MMWR Morbidity and Mortality Weekly Report* 2017;**66**:1300–6. https://doi.org/10.15585/mmwr.mm6647e1.

21 INSIGHT START Study Group, Lundgren JD, Babiker AG, Gordin F, Emery S, Grund B, *et al.* Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *N Engl J Med* 2015;**373**:795–807. https://doi.org/10.1056/NEJMoa1506816.

22 Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al.* Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *New England Journal of Medicine* 2016;**375**:830–9. https://doi.org/10.1056/NEJMoa1600693.

23 Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. *AIDS (London, England)* 2006;**20**:1447–50. https://doi.org/10.1097/01.aids.0000233579.79714.8d.

24 Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, *et al.* Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recommendations and Reports : Morbidity and Mortality Weekly Report Recommendations and Reports / Centers for Disease Control* 2006;**55**:1–17; quiz CE1-4.

25 Moyer VA. Screening for HIV: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine* 2013;**159**:51–60. https://doi.org/10.7326/0003-4819-159-1-201307020-00645.

26 Haukoos JS, Hopkins E, Bucossi MM. Routine opt-out HIV screening: more evidence in support of alternative approaches? *Sexually Transmitted Diseases* 2014;**41**:403–6. https://doi.org/10.1097/olq.0000000000000139.

27 Klein PW, Messer LC, Myers ER, Weber DJ, Leone PA, Miller WC. Impact of a routine, opt-out HIV testing program on HIV testing and case detection in North Carolina sexually transmitted disease clinics. *Sexually Transmitted Diseases* 2014;**41**:395–402. https://doi.org/10.1097/olq.0000000000000141.

28 Weissman S, Kintziger K, Albrecth H, Stephens T, Edun B, Duffus W. Late HIV Diagnosis and Missed Opportunities for HIV Testing in South Carolina. Presented at the Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts.

29 Hall HI, Song R, Tang T, An Q, Prejean J, Dietz P, *et al.* HIV Trends in the United States: Diagnoses and Estimated Incidence. *JMIR Public Health and Surveillance* 2017;**3**:e8. https://doi.org/10.2196/publichealth.7051.

30 Cassels S, Goodreau SM. Interaction of mathematical modeling and social and behavioral HIV/AIDS research. *Current Opinion in HIV and AIDS* 2011;**6**:119–23. https://doi.org/10.1097/COH.0b013e328343acad.

31 Baggaley RF, Fraser C. Modelling sexual transmission of HIV: testing the assumptions, validating the predictions. *Current Opinion in HIV and AIDS* 2010;**5**:269–76. https://doi.org/10.1097/COH.0b013e32833a51b2.

32 Garnett GP. An introduction to mathematical models in sexually transmitted disease epidemiology. *Sexually Transmitted Infections* 2002;**78**:7–12.

33 HIV/AIDS Epidemiology Unit, Public Health – Seattle & King County, Infectious Disease Assessment Unit, Washington State Department of Health. *HIV/AIDS Epidemiology Report 2018*. 2018.

34 Washington State Department of Health. *End AIDS Washington*. Washington State Department of Health; 2016.

35 Golden MR, Lindquist S, Dombrowski JC. Public Health-Seattle & King County and Washington State Department of Health Preexposure Prophylaxis Implementation Guidelines, 2015. *Sexually Transmitted Diseases* 2016;**43**:264–5. https://doi.org/10.1097/olq.0000000000000427.

36 White House Office of National AIDS Policy. *National HIV/AIDS Strategy for the United States: Updated to 2020*. Washington, DC: The White House; 2015.

37 Riddell J, Iv, Amico K, Mayer KH. HIV preexposure prophylaxis: A review. *JAMA* 2018;**319**:1261–8. https://doi.org/10.1001/jama.2018.1917.

38 Centers for Disease Control and Prevention. *HIV Surveillance Report, 2016*. 2017.

39 US Public Health Service. *Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2014: A Clinical Practice Guideline*. Department of Health and Human Services and Centers for Disease Control and Prevention; 2014.

40 Parsons JT, Rendina HJ, Lassiter JM, Whitfield TH, Starks TJ, Grov C. Uptake of HIV Pre-Exposure Prophylaxis (PrEP) in a National Cohort of Gay and Bisexual Men in the United States. *Journal of Acquired Immune Deficiency Syndromes* 2017;**74**:285–92. https://doi.org/10.1097/QAI.0000000000001251.

41 Hoots BE, Finlayson T, Nerlander L, Paz-Bailey G. Willingness to Take, Use of, and Indications for Pre-Exposure Prophylaxis among Men Who Have Sex with Men - 20 U.S. Cities, 2014. *Clinical Infectious Diseases* 2016. https://doi.org/10.1093/cid/ciw367.

42 Chan PA, Glynn TR, Oldenburg CE, Montgomery MC, Robinette AE, Almonte A, *et al.* Implementation of Preexposure Prophylaxis for Human Immunodeficiency Virus Prevention Among Men Who Have Sex With Men at a New England Sexually Transmitted Diseases Clinic. *Sexually Transmitted Diseases* 2016;**43**:717–23. https://doi.org/10.1097/olq.0000000000000514.

43 Helms DJ, Weinstock HS, Mahle KC, Bernstein KT, Furness BW, Kent CK, *et al.* HIV testing frequency among men who have sex with men attending sexually transmitted disease clinics: implications for HIV prevention and surveillance. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2009;**50**:320–6. https://doi.org/10.1097/QAI.0b013e3181945f03.

44 Wejnert C, Raymond HF, Robbins T, Prejean J, Hall HI, McCray E, *et al.* Achieving Greater HIV Prevention Impact Through CDC’s National HIV Behavioral Surveillance System.

Journal of Acquired Immune Deficiency Syndromes (1999) 2017;**75 Suppl 3**:S249-s252. https://doi.org/10.1097/qai.0000000000001430.

45 Hood JE, Buskin SE, Dombrowski JC, Kern DA, Barash EA, Katzi DA, *et al.* Dramatic increase in preexposure prophylaxis use among MSM in Washington state. *AIDS (London, England)* 2016;**30**:515–9. https://doi.org/10.1097/qad.0000000000000937.

46 Grov C, Breslow AS, Newcomb ME, Rosenberger JG, Bauermeister JA. Gay and bisexual men's use of the Internet: research from the 1990s through 2013. *Journal of Sex Research* 2014;**51**:390–409. https://doi.org/10.1080/00224499.2013.871626.

47 Sanchez T, Smith A, Denson D, DiNenno E, Lansky A. Developing a Web-Based HIV Behavioral Surveillance Pilot Project Among Men Who Have Sex with Men. *The Open AIDS Journal* 2012;**6**:224–31. https://doi.org/10.2174/1874613601206010224.

48 Stack C, Oldenburg C, Mimiaga M, Elsesser SA, Krakower D, Novak DS, *et al.* Sexual Behavior Patterns and PrEP Dosing Preferences in a large sample of North American Men who have Sex with Men. *Journal of Acquired Immune Deficiency Syndromes* 2015. https://doi.org/10.1097/qai.0000000000000816.

49 Holloway I, Dougherty R, Gildner J, Beougher SC, Pulsipher C, Montoya JA, *et al.* PrEP Uptake, Adherence, and Discontinuation among California YMSM Using Geosocial Networking Applications. *Journal of Acquired Immune Deficiency Syndromes* 2017. https://doi.org/10.1097/qai.0000000000001164.

50 Sanchez TH, Zlotorzynska M, Sineath RC, Kahle E, Tregear S, Sullivan PS. National Trends in Sexual Behavior, Substance Use and HIV Testing Among United States Men Who have Sex with Men Recruited Online, 2013 Through 2017. *AIDS and Behavior* 2018. https://doi.org/10.1007/s10461-018-2168-4.

51 HIV/AIDS Epidemiology Unit PH– S& KC, Infectious Disease Assessment Unit WSD of H. *HIV/AIDS Epidemiology Report 2017*. 2017.

52 Marrazzo JM, del Rio C, Holtgrave DR, et al. HIV prevention in clinical care settings: 2014 recommendations of the International Antiviral Society–USA panel. *JAMA* 2014;**312**:390–409. https://doi.org/10.1001/jama.2014.7999.

53 World Health Organization. *Guildeline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV*. Geneva, Switzerland: World Health Organization; 2015.

54 Grey JA, Konstan J, Iantaffi A, Wilkerson JM, Galos D, Rosser BR. An updated protocol to detect invalid entries in an online survey of men who have sex with men (MSM): how do valid and invalid submissions compare? *AIDS and Behavior* 2015;**19**:1928–37. https://doi.org/10.1007/s10461-015-1033-y.

55 Hoots BE, Wejnert C, Martin A, Haaland R, Masciotra S, Sionean C, *et al.* Undisclosed HIV infection among men who have sex with men in National HIV Behavioral Surveillance, 2014. *AIDS (London, England)* 2019. https://doi.org/10.1097/QAD.0000000000002147.

56 Chen YH, Snowden JM, McFarland W, Raymond HF. Pre-exposure Prophylaxis (PrEP) Use, Seroadaptation, and Sexual Behavior Among Men Who Have Sex with Men, San Francisco, 2004-2014. *AIDS and Behavior* 2016. https://doi.org/10.1007/s10461-016-1357-2.

57 Mayer KH, Biello KB, Novak D, Krakower D, Mimiaga M. PrEP Uptake Disparities in a Diverse On-Line Sample of US Men Who Have Sex with Men. Presented at the Conference on Retroviruses and Opportunistic Infections.

58 Parsons JT, Rendina HJ, Lassiter JM, Whitfield TH, Starks TJ, Grov C. Uptake of HIV Pre-Exposure Prophylaxis (PrEP) in a National Cohort of Gay and Bisexual Men in the United States. *Journal of Acquired Immune Deficiency Syndromes* 2017;**74**:285–92. https://doi.org/10.1097/QAI.0000000000001251.

59 Katz DA, Dombrowski JC, Barry M, Spellman D, Bell TR, Golden MR. STD Partner Services to Monitor and Promote HIV Pre-Exposure Prophylaxis Use Among Men Who Have Sex with Men. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2019. https://doi.org/10.1097/qai.0000000000001952.

60 Marcus JL, Hurley LB, Hare CB, Nguyen DP, Phengrasamy T, Silverberg MJ, *et al.* Preexposure prophylaxis for HIV prevention in a large integrated healthcare system: adherence, renal safety, and discontinuation. *J Acquir Immune Defic Syndr* 2016;**73**:540–6. https://doi.org/10.1097/QAI.0000000000001129.

61 Chan PA, Mena L, Patel R, Oldenburg CE, Beauchamps L, Perez-Brumer AG, *et al.* Retention in care outcomes for HIV pre-exposure prophylaxis implementation programmes among men who have sex with men in three US cities. *Journal of the International AIDS Society* 2016;**19**:20903. https://doi.org/10.7448/ias.19.1.20903.

62 Dombrowski JC, Golden MR, Barbee LA, Khosropour CM. Patient Disengagement from an HIV Pre-Exposure Prophylaxis Program in a Sexually Transmitted Disease Clinic. *Sexually Transmitted Diseases* 2018. https://doi.org/10.1097/olq.0000000000000823.

63 Sanchez T, Smith A, Denson D, Dinenno E, Lansky A. Internet-based methods may reach higher-risk men who have sex with men not reached through venue-based sampling. *The Open AIDS Journal* 2012;**6**:83–9. https://doi.org/10.2174/1874613601206010083.

64 Grey J. *MSM Estimation State Profiles*. n.d. URL: http://www.emorycamp.org/item.php?i=50 (Accessed 26 December 2017).

65 Washington State Department of Health IDAU. HIV surveillance data, based on case information reported through 11/30/17 March 18, 1.

66 Becker RA, Wilks AR, Brownrigg R, Minka TP, Deckmyn A. *maps: Draw Geographical Maps*. 2018.

67 Wickam H. *ggplot2: Elegant Graphics for Data Analysis*. New York: Springer-Verlag; 2016.

68 R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2017.

69 Saag MS, Benson CA, Gandhi RT, Hoy JF, Landovitz RJ, Mugavero MJ, *et al.* Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2018 Recommendations of the International Antiviral Society–USA Panel. *JAMA* 2018;**320**:379–96. https://doi.org/10.1001/jama.2018.8431.

70 Katz I, Jha AK. HIV in the United States: Getting to Zero Transmissions by 2030. *JAMA* 2019. https://doi.org/10.1001/jama.2019.1817.

71 Hernandez-Romieu AC, Siegler AJ, Sullivan PS, Crosby R, Rosenberg ES. How often do condoms fail? A cross-sectional study exploring incomplete use of condoms, condom failures and other condom problems among black and white MSM in southern U.S.A. *Sexually Transmitted Infections* 2014;**90**:602–7. https://doi.org/10.1136/sextrans-2014-051581.

72 Mustanski B, Ryan DT, Garofalo R. Associations of sexually transmitted infections with condom problems among young men who have sex with men. *Sex Transm Dis* 2014;**41**:427–32. https://doi.org/10.1097/OLQ.0000000000000150.

73 Paz-Bailey G, Mendoza M, Finlayson T, Wejnert C, Le B, Rose C, *et al.* Trends in condom use among men who have sex with men in the united states: the role of antiretroviral therapy and sero-adaptive strategies. *AIDS (London, England)* 2016. https://doi.org/10.1097/qad.0000000000001139.

74 Hess KL, Hu X, Lansky A, Mermin J, Hall HI. Lifetime Risk of a Diagnosis of HIV Infection in the United States. *Annals of Epidemiology* 2017. https://doi.org/10.1016/j.annepidem.2017.02.003.

75 Johnson AS, Heitgerd J, Koenig LJ, VanHandel M, Branson BM, Connelly E, *et al.* Vital signs: HIV testing and diagnosis among adults--United States, 2001-2009. *MMWR Morbidity and Mortality Weekly Report* 2010;**59**:1550–5.

76 Millett GA, Peterson JL, Flores SA, Hart TA, Jeffries WL, Wilson PA, *et al.* Comparisons of disparities and risks of HIV infection in black and other men who have sex with men in Canada, UK, and USA: a meta-analysis. *Lancet* 2012;**380**:341–8. https://doi.org/10.1016/s0140-6736(12)60899-x.

77 Rosenberg ES, Grey JA, Sanchez TH, Sullivan PS. Rates of Prevalent HIV Infection, Prevalent Diagnoses, and New Diagnoses Among Men Who Have Sex With Men in US States, Metropolitan Statistical Areas, and Counties, 2012-2013. *JMIR Public Health Surveill* 2016;**2**:e22. https://doi.org/10.2196/publichealth.5684.

78 Vaughan Sarrazin MS, Ohl ME, Richardson KK, Asch SM, Gifford AL, Bokhour BG. Patient and Facility Correlates of Racial Differences in Viral Control for Black and White Veterans with HIV Infection in the Veterans Administration. *AIDS Patient Care STDS* 2018;**32**:84–91. https://doi.org/10.1089/apc.2017.0213.

79 El-Sadr WM, Mayer KH, Hodder SL. AIDS in America — Forgotten but Not Gone. *N Engl J Med* 2010;**362**:967–70. https://doi.org/10.1056/NEJMp1000069.

80 Carnegie NB, Morris M. Size matters: concurrency and the epidemic potential of HIV in small networks. *PloS One* 2012;**7**:e43048. https://doi.org/10.1371/journal.pone.0043048.

81 Eaton JW, Hallett TB, Garnett GP. Concurrent sexual partnerships and primary HIV infection: a critical interaction. *AIDS and Behavior* 2011;**15**:687–92. https://doi.org/10.1007/s10461-010-9787-8.

82 Goodreau SM. A decade of modelling research yields considerable evidence for the importance of concurrency: a response to Sawers and Stillwaggon. *Journal of the International AIDS Society* 2011;**14**:12. https://doi.org/10.1186/1758-2652-14-12.

83 Jenness SM, Goodreau SM, Morris M, Cassels S. Effectiveness of combination packages for HIV-1 prevention in sub-Saharan Africa depends on partnership network structure: a mathematical modelling study. *Sexually Transmitted Infections* 2016. https://doi.org/10.1136/sextrans-2015-052476.

84 Moody J, Benton RA. Interdependent effects of cohesion and concurrency for epidemic potential. *Annals of Epidemiology* 2016;**26**:241–8. https://doi.org/10.1016/j.annepidem.2016.02.011.

85 Morris M, Epstein H, Wawer M. Timing is everything: international variations in historical sexual partnership concurrency and HIV prevalence. *PloS One* 2010;**5**:e14092. https://doi.org/10.1371/journal.pone.0014092.

86 Pines HA, Wertheim JO, Liu L, Garfein RS, Little SJ, Karris MY. Concurrency and HIV transmission network characteristics among men who have sex with men with recent HIV infection. *AIDS (London, England)* 2016. https://doi.org/10.1097/qad.0000000000001256.

87 Potterat JJ, Zimmerman-Rogers H, Muth SQ, Rothenberg RB, Green DL, Taylor JE, *et al.* Chlamydia transmission: concurrency, reproduction number, and the epidemic trajectory. *American Journal of Epidemiology* 1999;**150**:1331–9.

88 Cassels S, Clark SJ, Morris M. Mathematical models for HIV transmission dynamics: tools for social and behavioral science research. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2008;**47 Suppl 1**:S34-9. https://doi.org/10.1097/QAI.0b013e3181605da3.

89 Morris M, Kurth AE, Hamilton DT, Moody J, Wakefield S. Concurrent partnerships and HIV prevalence disparities by race: linking science and public health practice. *American Journal of Public Health* 2009;**99**:1023–31. https://doi.org/10.2105/ajph.2008.147835.

90 Carnegie NB, Goodreau SM, Liu A, Vittinghoff E, Sanchez J, Lama JR, *et al.* Targeting pre-exposure prophylaxis among men who have sex with men in the United States and peru: partnership types, contact rates, and sexual role. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2015;**69**:119–25. https://doi.org/10.1097/qai.0000000000000555.

91 Chaillon A, Hoenigl M, Mehta SR, Weibel N, Little SJ, Smith DM. A practical online tool to estimate antiretroviral coverage for HIV infected and susceptible populations needed to reduce local HIV epidemics. *Scientific Reports* 2016;**6**:28707. https://doi.org/10.1038/srep28707.

92 Chen A, Dowdy DW. Clinical Effectiveness and Cost-Effectiveness of HIV Pre-Exposure Prophylaxis in Men Who Have Sex with Men: Risk Calculators for Real-World Decision-Making. *PLoS ONE* 2014;**9**:e108742. https://doi.org/10.1371/journal.pone.0108742.

93 Drabo EF, Hay JW, Vardavas R, Wagner ZR, Sood N. A Cost-Effectiveness Analysis Of Pre-Exposure Prophylaxis For The Prevention Of HIV Among Los Angeles County Men Who Have Sex With Men. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2016. https://doi.org/10.1093/cid/ciw578.

94 Jenness SM, Goodreau SM, Rosenberg E, Beylerian EN, Hoover KW, Smith DK, *et al.* Impact of the Centers for Disease Control's HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States. *The Journal of Infectious Diseases* 2016. https://doi.org/10.1093/infdis/jiw223.

95 Jenness SM, Maloney KM, Smith DK, Hoover KW, Goodreau SM, Rosenberg ES, *et al.* Addressing Gaps in HIV Preexposure Prophylaxis Care to Reduce Racial Disparities in HIV

Incidence in the United States. *American Journal of Epidemiology* 2018. https://doi.org/10.1093/aje/kwy230.

96 Jenness SM, Weiss KM, Goodreau SM, Gift T, Chesson H, Hoover KW, *et al.* Incidence of Gonorrhea and Chlamydia Following HIV Preexposure Prophylaxis among Men Who Have Sex with Men: A Modeling Study. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2017. https://doi.org/10.1093/cid/cix439.

97 Jenness SM, Sharma A, Goodreau SM, Rosenberg ES, Weiss KM, Hoover KW, *et al.* Individual HIV Risk versus Population Impact of Risk Compensation after HIV Preexposure Prophylaxis Initiation among Men Who Have Sex with Men. *PLOS ONE* 2017;**12**:e0169484. https://doi.org/10.1371/journal.pone.0169484.

98 Juusola JL, Brandeau ML, Owens DK, Bendavid E. The cost-effectiveness of preexposure prophylaxis for HIV prevention in the United States in men who have sex with men. *Annals of Internal Medicine* 2012;**156**:541–50. https://doi.org/10.7326/0003-4819-156-8-201204170-00001.

99 Kasaie P, Pennington J, Shah MS, Berry SA, German D, Flynn CP, *et al.* The Impact of Pre-Exposure Prophylaxis Among Men Who Have Sex With Men: An Individual-Based Model. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2017. https://doi.org/10.1097/qai.0000000000001354.

100 Kessler J, Myers JE, Nucifora KA, Mensah N, Toohey C, Khademi A, *et al.* Evaluating the impact of prioritization of antiretroviral pre-exposure prophylaxis in New York City. *AIDS (London, England)* 2014. https://doi.org/10.1097/qad.0000000000000460.

101 Khurana N, Yaylali E, Farnham PG, Hicks KA, Allaire BT, Jacobson E, *et al.* Impact of Improved HIV Care and Treatment on PrEP Effectivenesss in the United States, 2016-2020.

Journal of Acquired Immune Deficiency Syndromes (1999) 2018. https://doi.org/10.1097/qai.0000000000001707.

102 MacFadden DR, Tan DH, Mishra S. Optimizing HIV pre-exposure prophylaxis implementation among men who have sex with men in a large urban centre: a dynamic modelling study. *Journal of the International AIDS Society* 2016;**19**:20791. https://doi.org/10.7448/ias.19.1.20791.

103 Marshall BDL, Goedel WC, King MRF, Singleton A, Durham DP, Chan PA, *et al.* Potential effectiveness of long-acting injectable pre-exposure prophylaxis for HIV prevention in men who have sex with men: a modelling study. *The Lancet HIV* 2018. https://doi.org/10.1016/s2352-3018(18)30097-3.

104 Punyacharoensin N, Edmunds WJ, De Angelis D, Delpech V, Hart G, Elford J, *et al.* Effect of pre-exposure prophylaxis and combination HIV prevention for men who have sex with men in the UK: a mathematical modelling study. *The Lancet HIV* 2016;**3**:e94–104. https://doi.org/10.1016/S2352-3018(15)00056-9.

105 Ross EL, Cinti SK, Hutton DW. A cost-effective, clinically actionable strategy for targeting HIV preexposure prophylaxis to high-risk men who have sex with men. *JAIDS Journal of Acquired Immune Deficiency Syndromes* 2016;**Publish Ahead of Print**: https://doi.org/10.1097/qai.0000000000000987.

106 Schneider K, Gray RT, Wilson DP. A cost-effectiveness analysis of HIV preexposure prophylaxis for men who have sex with men in Australia. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2014;**58**:1027–34. https://doi.org/10.1093/cid/cit946.

107 Shen M, Xiao Y, Rong L, Meyers LA, Bellan SE. The cost-effectiveness of oral HIV pre-exposure prophylaxis and early antiretroviral therapy in the presence of drug resistance

among men who have sex with men in San Francisco. *BMC Medicine* 2018;**16**:58. https://doi.org/10.1186/s12916-018-1047-1.

108 Smith DK, Herbst JH, Rose CE. Estimating HIV protective effects of method adherence with combinations of preexposure prophylaxis and condom use among African American men who have sex with men. *Sexually Transmitted Diseases* 2015;**42**:88–92. https://doi.org/10.1097/olq.0000000000000238.

109 Jenness SM, Goodreau SM, Morris M. EpiModel: An R Package for Mathematical Modeling of Infectious Disease over Networks. *Journal of Statistical Software* 2017;**84**:. https://doi.org/10.18637/jss.v084.i08.

110 Liljeros F, Edling CR, Nunes Amaral LA. Sexual networks: implications for the transmission of sexually transmitted infections. *Microbes and Infection / Institut Pasteur* 2003;**5**:189–96.

111 Krivitsky PN, Handcock MS. A Separable Model for Dynamic Networks. *Journal of the Royal Statistical Society Series B, Statistical Methodology* 2014;**76**:29–46. https://doi.org/10.1111/rssb.12014.

112 Goodreau SM, Rosenberg ES, Jenness SM, Luisi N, Stansfield SE, Millett GA, *et al.* Sources of racial disparities in HIV prevalence in men who have sex with men in Atlanta, GA, USA: a modelling study. *The Lancet HIV* 2017;**4**:e311–20. https://doi.org/10.1016/s2352-3018(17)30067-x.

113 Krivitsky PN, Morris M. INFERENCE FOR SOCIAL NETWORK MODELS FROM EGOCENTRICALLY SAMPLED DATA, WITH APPLICATION TO UNDERSTANDING PERSISTENT RACIAL DISPARITIES IN HIV PREVALENCE IN THE US. *Ann Appl Stat* 2017;**11**:427–55. https://doi.org/10.1214/16-AOAS1010.

114 Rao DW, Carr J, Naismith K, Hood JE, Hughes JP, Morris M, *et al.* Monitoring HIV Preexposure Prophylaxis Use Among Men Who Have Sex With Men in Washington State:

Findings From an Internet-Based Survey. *Sex Transm Dis* 2019;**46**:221–8. https://doi.org/10.1097/OLQ.0000000000000965.

115 Centers for Disease Control and Prevention. *Behavioral and Clinical Characteristics of Persons Receiving Medical Care for HIV Infection: Medical Monitoring Project, United States, 2014 Cycle (June 2014-May 2015)*. Centers for Disease Control and Prevention; 2016.

116 Lee CA, Phillips AN, Elford J, Janossy G, Griffiths P, Kernoff P. Progression of HIV disease in a haemophilic cohort followed for 11 years and the effect of treatment. *BMJ (Clinical Research Ed)* 1991;**303**:1093–6.

117 Lodi S, Phillips A, Touloumi G, Geskus R, Meyer L, Thiebaut R, *et al.* Time from human immunodeficiency virus seroconversion to reaching CD4+ cell count thresholds <200, <350, and <500 Cells/mm(3): assessment of need following changes in treatment guidelines. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2011;**53**:817–25. https://doi.org/10.1093/cid/cir494.

118 Landovitz RJ, Beymer M, Kofron R, Amico KR, Psaros C, Bushman L, *et al.* Plasma Tenofovir-levels to Support Adherence to TDF/FTC Pre-exposure Prophylaxis for HIV Prevention in MSM in Los Angeles, California. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2017. https://doi.org/10.1097/qai.0000000000001538.

119 Liu AY, Cohen SE, Vittinghoff E, Anderson PL, Doblecki-Lewis S, Bacon O, *et al.* Preexposure Prophylaxis for HIV Infection Integrated With Municipal- and Community-Based Sexual Health Services. *JAMA Internal Medicine* 2016;**176**:75–84. https://doi.org/10.1001/jamainternmed.2015.4683.

120 Grant RM, Liu A, Hecht J, Buchbinder SP, Crouch P-C, Gibson S, *et al.* Scale-Up of Preexposure Prophylaxis in San Francisco to Impact HIV Incidence. Presented at the Coference on Retroviruses and Opportunistic Infections (CROI) 2015.

121 Lal L, Audsley J, Murphy DA, Fairley CK, Stoove M, Roth N, *et al.* Medication adherence, condom use and sexually transmitted infections in Australian preexposure prophylaxis users. *AIDS (London, England)* 2017;**31**:1709–14. https://doi.org/10.1097/qad.0000000000001519.

122 Myers JJ, Kang Dufour M-S, Koester KA, Udoh I, Frazier R, Packard R, *et al.* Adherence to PrEP among young men who have sex with men participating in a sexual health services demonstration project in Alameda County, California. *J Acquir Immune Defic Syndr* 2019. https://doi.org/10.1097/QAI.0000000000002051.

123 Zablotska IB. Likely impact of pre-exposure prophylaxis on HIV epidemics among men who have sex with men. *Sexual Health* 2016. https://doi.org/10.1071/sh16153.

124 Hoornenborg E, Coyer L, van Laarhoven A, Achterbergh R, de Vries H, Prins M, *et al.* Change in sexual risk behaviour after six months of pre-exposure prophylaxis use: results from the Amsterdam PrEP demonstration project. *AIDS (London, England)* 2018. https://doi.org/10.1097/qad.0000000000001874.

125 McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, *et al.* Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet (London, England)* 2016;**387**:53–60. https://doi.org/10.1016/s0140-6736(15)00056-2.

126 Milam J, Jain S, Dube MP, Daar ES, Sun X, Corado K, *et al.* Sexual Risk Compensation in a Pre-exposure Prophylaxis Demonstration Study among Individuals at Risk for HIV. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2018. https://doi.org/10.1097/qai.0000000000001885.

127 Molina JM, Charreau I, Spire B, Cotte L, Chas J, Capitant C, *et al.* Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *The Lancet HIV* 2017. https://doi.org/10.1016/s2352-3018(17)30089-9.

128 Nguyen VK, Greenwald ZR, Trottier H, Cadieux M, Goyette A, Beauchemin M, *et al.* Incidence of sexually transmitted infections before and after Pre-Exposure Prophylaxis for HIV: a cohort study. *AIDS (London, England)* 2017. https://doi.org/10.1097/qad.0000000000001718.

129 Oldenburg CE, Nunn AS, Montgomery M, Almonte A, Mena L, Patel RR, *et al.* Behavioral Changes Following Uptake of HIV Pre-exposure Prophylaxis Among Men Who Have Sex with Men in a Clinical Setting. *AIDS and Behavior* 2017. https://doi.org/10.1007/s10461-017-1701-1.

130 Traeger MW, Schroeder SE, Wright EJ, Hellard ME, Cornelisse VJ, Doyle JS, *et al.* Effects of Pre-exposure Prophylaxis for the Prevention of HIV Infection on Sexual Risk Behavior in Men Who Have Sex with Men: A Systematic Review and Meta-analysis. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2018. https://doi.org/10.1093/cid/ciy182.

131 Volk JE, Nguyen DP, Hare CB, Marcus JL. HIV Infection and Drug Resistance with Unsupervised Use of HIV Preexposure Prophylaxis. *AIDS Research and Human Retroviruses* 2017. https://doi.org/10.1089/aid.2017.0285.

132 Volk JE, Marcus JL, Phengrasamy T, Blechinger D, Nguyen DP, Follansbee S, *et al.* No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2015;**61**:1601–3. https://doi.org/10.1093/cid/civ778.

133 Jonas KJ, Yaemim N. HIV Prevention After Discontinuing Pre-Exposure Prophylaxis: Conclusions From a Case Study. *Front Public Health* 2018;**6**:. https://doi.org/10.3389/fpubh.2018.00137.

134 Grey JA, Bernstein KT, Sullivan PS, Purcell DW, Chesson HW, Gift TL, *et al.* Estimating the Population Sizes of Men Who Have Sex With Men in US States and Counties Using Data From the American Community Survey. *JMIR Public Health and Surveillance* 2016;**2**:e14. https://doi.org/10.2196/publichealth.5365.

135 Baggaley RF, White RG, Boily M-C. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *Int J Epidemiol* 2010;**39**:1048–63. https://doi.org/10.1093/ije/dyq057.

136 Jin F, Jansson J, Law M, Prestage GP, Zablotska I, Imrie JC. Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART. *Aids* 2010;**24**:. https://doi.org/10.1097/QAD.0b013e3283372d90.

137 Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. *AIDS* 2014;**28**:1509–19. https://doi.org/10.1097/QAD.0000000000000298.

138 Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *Am J Epidemiol* 1999;**150**:306–11.

139 Toni T, Welch D, Strelkowa N, Ipsen A, Stumpf MP. Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. *Journal of the Royal Society, Interface* 2009;**6**:187–202.

140 Zablotska IB, Vaccher SJ, Bloch M, Carr A, Foster R, Grulich AE, *et al.* High Adherence to HIV Pre-exposure Prophylaxis and No HIV Seroconversions Despite High Levels of Risk

Behaviour and STIs: The Australian Demonstration Study PrELUDE. *AIDS and Behavior* 2018. https://doi.org/10.1007/s10461-018-2290-3.

141 Gantenberg JR, King M, Montgomery MC, Galárraga O, Prosperi M, Chan PA, *et al.* Improving the impact of HIV pre-exposure prophylaxis implementation in small urban centers among men who have sex with men: An agent-based modelling study. *PLOS ONE* 2018;**13**:e0199915. https://doi.org/10.1371/journal.pone.0199915.

142 Kasaie P, Berry SA, Shah MS, Rosenberg ES, Hoover KW, Gift TL, *et al.* Impact of providing pre-exposure prophylaxis for HIV at clinics for sexually transmitted infections in Baltimore City: an agent-based model. *Sexually Transmitted Diseases* 2018. https://doi.org/10.1097/olq.0000000000000882.

143 Grulich AE, Guy R, Amin J, Jin F, Selvey C, Holden J, *et al.* Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. *The Lancet HIV* 2018. https://doi.org/10.1016/s2352-3018(18)30215-7.

144 Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, *et al.* Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *The New England Journal of Medicine* 2010;**363**:2587–99. https://doi.org/10.1056/NEJMoa1011205.

145 Molina J-M, Capitant C, Charreau I, Meyer L, Spire B, Pialoux G, *et al.* On Demand PrEP With Oral TDF-FTC in MSM: Results of the ANRS Ipergay Trial. Presented at the Conference on Retroviruses and Opportunistic Infections (CROI).

146 Marcus JL, Volk JE, Pinder J, Liu AY, Bacon O, Hare CB, *et al.* Successful Implementation of HIV Preexposure Prophylaxis: Lessons Learned From Three Clinical Settings. *Current HIV/AIDS Reports* 2016:1–9. https://doi.org/10.1007/s11904-016-0308-x.

147 Mayer KH, Hosek S, Cohen S, Liu A, Pickett J, Warren M, *et al.* Antiretroviral pre-exposure prophylaxis implementation in the United States: a work in progress. *Journal of the International AIDS Society* 2015;**18**:19980. https://doi.org/10.7448/ias.18.4.19980.

148 Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for human immunodeficiency virus and sexually transmitted infection acquisition among men who have sex with men. *AIDS (London, England)* 2016. https://doi.org/10.1097/qad.0000000000001185.

149 Montano MA, Dombrowski JC, Dasgupta S, Golden MR, Duerr A, Manhart LE, *et al.* Changes in Sexual Behavior and STI Diagnoses Among MSM Initiating PrEP in a Clinic Setting. *AIDS and Behavior* 2018. https://doi.org/10.1007/s10461-018-2252-9.

150 Traeger MW, Cornelisse VJ, Asselin J, Price B, Roth NJ, Willcox J, *et al.* Association of HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infections Among Individuals at High Risk of HIV Infection. *JAMA* 2019;**321**:1380–90. https://doi.org/10.1001/jama.2019.2947.

151 Parsons JT, John SA, Whitfield THF, Cienfuegos-Szalay J, Grov C. Human Immunodeficiency Virus/Sexually Transmitted Infection Counseling and Testing Services Received by Gay and Bisexual Men Using Preexposure Prophylaxis at Their Last PrEP Care Visit. *Sexually Transmitted Diseases* 2018;**45**:798–802. https://doi.org/10.1097/olq.0000000000000880.

152 Spinelli MA, Scott HM, Vittinghoff E, Liu AY, Morehead-Gee A, Gonzalez R, *et al.* Provider Adherence to Pre-exposure Prophylaxis Monitoring Guidelines in a Large Primary Care Network. *Open Forum Infectious Diseases* 2018;**5**:ofy099. https://doi.org/10.1093/ofid/ofy099.

153 Holt M, Murphy DA. Individual Versus Community-Level Risk Compensation Following Preexposure Prophylaxis of HIV. *American Journal of Public Health* 2017:e1–4. https://doi.org/10.2105/ajph.2017.303930.

154 Rozhnova G, van der Loeff MF, Heijne JC, Kretzschmar ME. Impact of Heterogeneity in Sexual Behavior on Effectiveness in Reducing HIV Transmission with Test-and-Treat Strategy. *PLoS Computational Biology* 2016;**12**:e1005012. https://doi.org/10.1371/journal.pcbi.1005012.

155 Khosropour CM, Dombrowski JC, Kerani RP, Katz DA, Barbee LA, Golden MR. Changes in Condomless Sex and Serosorting Among Men Who Have Sex With Men After HIV Diagnosis. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2016;**73**:475–81. https://doi.org/10.1097/qai.0000000000001128.

156 Rodger AJ, Cambiano V, Bruun T, Vernazza P, Collins S, Degen O, *et al.* Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. *The Lancet* 2019:S0140673619304180. https://doi.org/10.1016/S0140-6736(19)30418-0.

157 Bavinton BR, Pinto AN, Phanuphak N, Grinsztejn B, Prestage GP, Zablotska-Manos IB, *et al.* Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *The Lancet HIV* 2018. https://doi.org/10.1016/s2352-3018(18)30132-2.

158 Paltiel AD, Walensky RP, Schackman BR, Seage GR 3rd, Mercincavage LM, Weinstein MC, *et al.* Expanded HIV screening in the United States: effect on clinical outcomes, HIV transmission, and costs. *Annals of Internal Medicine* 2006;**145**:797–806.

159 Sanders GD, Bayoumi AM, Sundaram V, Bilir SP, Neukermans CP, Rydzak CE, *et al.* Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. *The New England Journal of Medicine* 2005;**352**:570–85. https://doi.org/10.1056/NEJMsa042657.

160 Lyons MS, Lindsell CJ, Ruffner AH, Wayne DB, Hart KW, Sperling MI, *et al.* Randomized comparison of universal and targeted HIV screening in the emergency department. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2013;**64**:315–23. https://doi.org/10.1097/QAI.0b013e3182a21611.

161 Rodriguez V, Lester D, Connelly-Flores A, Barsanti FA, Hernandez P. Integrating Routine HIV Screening in the New York City Community Health Center Collaborative. *Public Health Reports (Washington, DC : 1974)* 2016;**131 Suppl 1**:11–20.

162 Osorio G, Hoenigl M, Quartarolo J, Barger K, Morris SR, REED SL, *et al.* Evaluation of Opt-out Inpatient HIV Screening at an Urban Teaching Hospital. *AIDS Care* 2017;**29**:1014–8. https://doi.org/10.1080/09540121.2017.1282106.

163 Golden MR, Hughes JP, Dombrowski JC. Optimizing the Timing of HIV Screening as Part of Routine Medical Care. *AIDS Patient Care and STDs* 2017;**31**:27–32. https://doi.org/10.1089/apc.2016.0185.

164 Pitasi MA, Delaney KP, Oraka E, Bradley H, DiNenno EA, Brooks JT, *et al.* Interval Since Last HIV Test for Men and Women with Recent Risk for HIV Infection - United States, 2006-2016. *MMWR Morbidity and Mortality Weekly Report* 2018;**67**:677–81. https://doi.org/10.15585/mmwr.mm6724a2.

165 U.S. Census Bureau PD. Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States: April 1, 2010 to July 1, 2015 2016.

166 U.S. Census Bureau, Population Division. Annual Estimates of the Resident Population for Selected Age Groups by Sex for the United States, States, Counties, and Puerto Rico Commonwealth and Municipios: April 1, 2010 to July 1, 2017 2018.

167 Purcell DW, Johnson CH, Lansky A, Prejean J, Stein R, Denning P, *et al.* Estimating the population size of men who have sex with men in the United States to obtain HIV and syphilis rates. *The Open AIDS Journal* 2012;**6**:98–107. https://doi.org/10.2174/1874613601206010098.

168 Fellows IE, Morris M, Birnbaum JK, Dombrowski JC, Buskin S, Bennett A, *et al.* A New Method for Estimating the Number of Undiagnosed HIV Infected Based on HIV Testing History, with an Application to Men Who Have Sex with Men in Seattle/King County, WA. *PLOS ONE* 2015;**10**:e0129551. https://doi.org/10.1371/journal.pone.0129551.

169 Philadelphia Department of Public Health. *AIDS Activities Coordinating Office Surveillance Report, 2017*. Philadelphia, PA: City of Philadelphia; 2018.

170 Menza TW, Hughes JP, Celum CL, Golden MR. Prediction of HIV acquisition among men who have sex with men. *Sex Transm Dis* 2009;**36**:. https://doi.org/10.1097/OLQ.0b013e3181a9cc41.

171 Finlayson TJ, Le B, Smith A, Bowles K, Cribbin M, Miles I, *et al.* HIV risk, prevention, and testing behaviors among men who have sex with men--National HIV Behavioral Surveillance System, 21 U.S. cities, United States, 2008. *Morbidity and Mortality Weekly Report Surveillance Summaries (Washington, DC : 2002)* 2011;**60**:1–34.

172 Centers for Disease Control and Prevention. *A web-based survey of HIV testing and risk behaviors among gay, bisexual, and other men who have sex with men--United States, 2012.* Atlanta, GA: Centers for Disease Control and Prevention; 2016.

173 Sanchez T, Zlotorzynska M, Sineath C, Kahle E, Sullivan P. The Annual American Men's Internet Survey of Behaviors of Men Who have Sex with Men in the United States: 2014 Key Indicators Report. *JMIR Public Health and Surveillance* 2016;**2**:e23. https://doi.org/10.2196/publichealth.5476.

174 Hammack PL, Meyer IH, Krueger EA, Lightfoot M, Frost DM. HIV testing and pre-exposure prophylaxis (PrEP) use, familiarity, and attitudes among gay and bisexual men in the United States: A national probability sample of three birth cohorts. *PloS One* 2018;**13**:e0202806. https://doi.org/10.1371/journal.pone.0202806.

175 Hoenigl M, Anderson CM, Green N, Mehta SR, Smith DM, Little SJ. Repeat HIV-testing is associated with an increase in behavioral risk among men who have sex with men: a cohort study. *BMC Medicine* 2015;**13**:218. https://doi.org/10.1186/s12916-015-0458-5.

176 Commonwealth of Pennsylvania - Department of Health, Division of Health Informatics. Resident Live Births by Age of Mother: Counties and Pennsylvania, 2016 2019.

177 Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final Data for 2016. *Natl Vital Stat Rep* 2018;**67**:1–55.

178 Washington State Department of Health. *Birth Tables by Year: 2016*. 2016. URL: https://www.doh.wa.gov/DataandStatisticalReports/HealthStatistics/Birth/BirthTablesbyYear (Accessed 11 March 2019).

179 Centers for Disease Control and Prevention. PRAMStat 2016.

180 Centers for Disease Control and Prevention (CDC). HIV testing among pregnant women--United States and Canada, 1998-2001. *MMWR Morb Mortal Wkly Rep* 2002;**51**:1013–6.

181 Lawrence JM, Liu IL, Towner WJ. Trends and correlates of HIV testing during pregnancy in racially/ethnically diverse insured population, 1997-2006. *Maternal and Child Health Journal* 2009;**13**:633–40. https://doi.org/10.1007/s10995-008-0403-8.

182 Ross CE, Tao G, Patton M, Hoover KW. Screening for human immunodeficiency virus and other sexually transmitted diseases among U.S. women with prenatal care. *Obstetrics and Gynecology* 2015;**125**:1211–6. https://doi.org/10.1097/aog.0000000000000756.

183 Golden MR, Stekler J, Kent JB, Hughes JP, Wood RW. An evaluation of HIV partner counseling and referral services using new disposition codes. *Sexually Transmitted Diseases* 2009;**36**:95–101. https://doi.org/10.1097/OLQ.0b013e31818d3ddb.

184 Brewer DD. Case-finding effectiveness of partner notification and cluster investigation for sexually transmitted diseases/HIV. *Sexually Transmitted Diseases* 2005;**32**:78–83.

185 Centers for Disease Control and Prevention PEB. *Partner Services Annual Report 2014*. Atlanta, GA: Centers for Disease Control and Prevention; 2015.

186 Golden MR, Hogben M, Potterat JJ, Handsfield HH. HIV partner notification in the United States: a national survey of program coverage and outcomes. *Sexually Transmitted Diseases* 2004;**31**:709–12.

187 Paltiel AD, Weinstein MC, Kimmel AD, Seage GRI, Losina E, Zhang H, *et al.* Expanded Screening for HIV in the United States — An Analysis of Cost-Effectiveness. *New England Journal of Medicine* 2005;**352**:586–95. https://doi.org/10.1056/NEJMsa042088.

188 Sanders GD, Anaya HD, Asch S, Hoang T, Golden JF, Bayoumi AM, *et al.* Cost-effectiveness of strategies to improve HIV testing and receipt of results: economic analysis of a randomized controlled trial. *Journal of General Internal Medicine* 2010;**25**:556–63. https://doi.org/10.1007/s11606-010-1265-5.

189 Neilan AM, Dunville R, Ocfemia MCB, Salomon JA, Francke JA, Bulteel AJB, *et al.* The Optimal Age for Screening Adolescents and Young Adults Without Identified Risk Factors for HIV. *The Journal of Adolescent Health : Official Publication of the Society for Adolescent Medicine* 2018;**62**:22–8. https://doi.org/10.1016/j.jadohealth.2017.08.028.

190 Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV*. Department of Health and Human Services; n.d.

191 Lucas A, Armbruster B. The cost-effectiveness of expanded HIV screening in the United States. *AIDS* 2013;**27**:795–801. https://doi.org/10.1097/QAD.0b013e32835c54f9.

192 Shah M, Risher K, Berry SA, Dowdy DW. The Epidemiologic and Economic Impact of Improving HIV Testing, Linkage, and Retention in Care in the United States. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2016;**62**:220–9. https://doi.org/10.1093/cid/civ801.

193 Bernstein KT, Liu K-L, Begier EM, Koblin B, Karpati A, Murrill C. Same-sex attraction disclosure to health care providers among New York City men who have sex with men: implications for HIV testing approaches. *Arch Intern Med* 2008;**168**:1458–64. https://doi.org/10.1001/archinte.168.13.1458.

194 Rao DW, Carr J, Naismith K, Golden MR. *Washington HIV Prevention Project: Key findings, 2017*. Washington State Department of Health; 2017.

195 Frasca K, Nassau T, McLaughlin C, Brady KA. Factors Associated with Recent HIV Testing among Men Who Have Sex with Men in Philadelphia: a Cross-Sectional Analysis of the National Behavioral Surveillance System Survey. *AIDS Care* 2018:1–8. https://doi.org/10.1080/09540121.2018.1533228.

196 Liddicoat RV, Horton NJ, Urban R, Maier E, Christiansen D, Samet JH. Assessing missed opportunities for HIV testing in medical settings. *J Gen Intern Med* 2004;**19**:349–56. https://doi.org/10.1111/j.1525-1497.2004.21251.x.

197 Shirreffs A, Lee DP, Henry J, Golden MR, Stekler JD. Understanding barriers to routine HIV screening: knowledge, attitudes, and practices of healthcare providers in King County, Washington. *PloS One* 2012;**7**:e44417. https://doi.org/10.1371/journal.pone.0044417.

198 Brennan MB, Kolehmainen C, Barocas J, Isaac C, Crnich CJ, Sosman JM. Barriers and facilitators of universal HIV screening among internal medicine residents. *WMJ* 2013;**112**:199–205.

199 Blumenthal J, Jain S, Mulvihill E, Sun S, Hanashiro M, Ellorin E, *et al.* Perceived versus calculated HIV risk: Implications for Pre-exposure prophylaxis uptake in a randomized trial of men who have sex with men. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2018. https://doi.org/10.1097/qai.0000000000001888.

200 Wilton J, Mishra S, Tan DHS. Considerations for Using the HIRI-MSM Screening Tool to Identify MSM Who Would Benefit Most From PrEP. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2017;**76**:e58–61. https://doi.org/10.1097/qai.0000000000001472.

201 Haukoos JS, Hopkins E, Bucossi MM, Lyons MS, Rothman RE, White DA, *et al.* Brief report: Validation of a quantitative HIV risk prediction tool using a national HIV testing cohort. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2015;**68**:599–603. https://doi.org/10.1097/qai.0000000000000518.

202 Haukoos JS, Hopkins E, Bender B, Sasson C, Al-Tayyib AA, Thrun MW. Comparison of Enhanced Targeted Rapid HIV Screening Using the Denver HIV Risk Score to Nontargeted Rapid HIV Screening in the Emergency Department. *Ann Emerg Med* 2013;**61**:353–61. https://doi.org/10.1016/j.annemergmed.2012.10.031.

203 Xia Q, Braunstein SL, Wiewel EW, Eavey JJ, Shepard CW, Torian LV. Persons Living With HIV in the United States: Fewer Than We Thought. *J Acquir Immune Defic Syndr* 2016;**72**:552–7. https://doi.org/10.1097/QAI.0000000000001008.

204 Goedert JJ, Kessler CM, Aledort LM, Biggar RJ, Andes WA, White GC, *et al.* A prospective study of human immunodeficiency virus type 1 infection and the development of AIDS in subjects with hemophilia. *N Engl J Med* 1989;**321**:1141–8. https://doi.org/10.1056/NEJM198910263211701.

205 Broz D, Wejnert C, Pham HT, DiNenno E, Heffelfinger JD, Cribbin M, *et al.* HIV infection and risk, prevention, and testing behaviors among injecting drug users -- National HIV Behavioral Surveillance System, 20 U.S. cities, 2009. *MMWR Surveill Summ* 2014;**63**:1–51.

206 Heimer R, Grau LE, Curtin E, Khoshnood K, Singer M. Assessment of HIV Testing of Urban Injection Drug Users: Implications for Expansion of HIV Testing and Prevention Efforts. *Am J Public Health* 2007;**97**:110–6. https://doi.org/10.2105/AJPH.2005.078105.

207 Department of Health and Human Services, Centers for Disease Control and Prevention. *NCHHSTP AtlasPlus*. 2017. URL: https://www.cdc.gov/nchhstp/atlas/index.htm (Accessed 12 March 2019).

208 Centers for Disease Control and Prevention. *Estimated HIV incidence in the United States, 2010-2015*. 2018.

209 Centers for Disease Control and Prevention. *HIV Infection Risk, Prevention, and Testing Behaviors among Men Who Have Sex With Men—National HIV Behavioral Surveillance, 20 U.S. Cities, 2014*. Atlanta, GA: U.S. Department of Health and Human Services, Atlanta, Georgia.; 2016.

210 Zlotorzynska M, Sullivan P, Sanchez T. The Annual American Men’s Internet Survey of Behaviors of Men Who Have Sex With Men in the United States: 2015 Key Indicators

Report. *JMIR Public Health and Surveillance* 2017;**3**:e13. https://doi.org/10.2196/publichealth.7119.

211 Institute of Medicine (US) Committee on Lesbian G Bisexual, and Transgender Health Issues and Research Gaps and Opportunities. *The Health of Lesbian, Gay, Bisexual, and Transgender People: Building a Foundation for Better Understanding*. Washington (DC): National Academies Press (US); 2011.

212 Magnani R, Sabin K, Saidel T, Heckathorn D. Review of sampling hard-to-reach and hidden populations for HIV surveillance. *AIDS (London, England)* 2005;**19 Suppl 2**:S67-72.

213 Meyer IH, Wilson PA. Sampling lesbian, gay, and bisexual populations. *Journal of Counseling Psychology* 2009;**56**:23–31. https://doi.org/10.1037/a0014587.

214 Walensky RP, Freedberg KA, Weinstein MC, Paltiel AD. Cost-effectiveness of HIV testing and treatment in the United States. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2007;**45 Suppl 4**:S248-54. https://doi.org/10.1086/522546.

215 Grov C, Jonathan Rendina H, Patel VV, Kelvin E, Anastos K, Parsons JT. Prevalence of and Factors Associated with the Use of HIV Serosorting and Other Biomedical Prevention Strategies Among Men Who Have Sex with Men in a US Nationwide Survey. *AIDS and Behavior* 2018. https://doi.org/10.1007/s10461-018-2084-7.

216 Chan GA, Johnson KL, Mosca NG, Dobbs TE, Dombrowski JC, Bennett AB, *et al.* Emerging Regional and Racial Disparities in the Lifetime Risk of Human Immunodeficiency Virus Infection Among Men who Have Sex With Men: A Comparative Life Table Analysis in King County, WA and Mississippi. *Sexually Transmitted Diseases* 2017;**44**:227–32. https://doi.org/10.1097/olq.0000000000000589.

217 Hood JE. 2016 Seattle Pride Survey. In: Buskin SE, Glick SN, Jaenicke T, editors. *HIV/AIDS Epidemiology Report 2016*, vol. 85. 2016. p. 46–50.

218 Khosropour CM, Dombrowski JC, Swanson F, Kerani RP, Katz DA, Barbee LA, *et al.* Trends in Serosorting and the Association With HIV/STI Risk Over Time Among Men Who Have Sex With Men. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2016;**72**:189–97. https://doi.org/10.1097/qai.0000000000000947.

219 Golub SA, Gamarel KE, Rendina HJ, Surace A, Lelutiu-Weinberger CL. From efficacy to effectiveness: facilitators and barriers to PrEP acceptability and motivations for adherence among MSM and transgender women in New York City. *AIDS Patient Care and STDs* 2013;**27**:248–54. https://doi.org/10.1089/apc.2012.0419.

220 Rolle CP, Rosenberg ES, Siegler AJ, Sanchez TH, Luisi N, Weiss K, *et al.* Challenges in Translating PrEP Interest into Uptake in an Observational Study of Young Black MSM. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2017. https://doi.org/10.1097/qai.0000000000001497.

221 Centers for Disease Control and Prevention. National HIV Behavioral Surveillance (NHBS) Round 3 and MSM4 Questionnaire n.d.

222 Handcock MS, Gile KJ. Modeling social networks from sampled data. *The Annals of Applied Statistics* 2010;**4**:5–25. https://doi.org/10.1214/08-AOAS221.

223 Krivitsky PN, Goodreau SM, Morris M, Li K, Beylerian EN. *Fit, Simulate and Diagnose Exponential-Family Random Graph Models to Egocentrically Sampled Network Data*. 2016.

224 Jenness SM, Goodreau SM, Beylerian EN. *EpiModelHIV*. 2016.

225 Handcock MS, Hunter DR, Butts CT, Goodreau SM, Morris M. statnet: Software Tools for the Representation, Visualization, Analysis and Simulation of Network Data. *J Stat Softw* 2008;**24**:1548–7660.

226 Hamilton DT, Goodreau SM, Jenness SM, Sullivan PS, Wang LY, Dunville RL, *et al.* Potential Impact of HIV Preexposure Prophylaxis Among Black and White Adolescent Sexual Minority Males. *American Journal of Public Health* 2018;**108**:S284-s291. https://doi.org/10.2105/ajph.2018.304471.

227 Washington State Department of Health. *Death Data*. Washington State Department of Health. n.d. URL: https://www.doh.wa.gov/DataandStatisticalReports/HealthStatistics/Death.

228 U.S. Census Bureau. *2011-2015 American Community Survey Selected Population Tables*. American FactFinder. n.d. URL: https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_15_SPT_B01001&prodType=table (Accessed 1 November 2018).

229 Centers for Disease Control and Prevention. *Medical Monitoring Project (MMP)*. 2015. URL: http://www.cdc.gov/hiv/statistics/systems/mmp/ (Accessed 5 May 2016).

230 Gallagher KM, Sullivan PS, Lansky A, Onorato IM. Behavioral Surveillance Among People at Risk for HIV Infection in the U.S.: The National HIV Behavioral Surveillance System. *Public Health Rep* 2007;**122**:32–8.

231 Lumley T. *Analysis of Complex Survey Samples*. n.d.

232 May MT, Vehreschild JJ, Trickey A, Obel N, Reiss P, Bonnet F, *et al.* Mortality According to CD4 Count at Start of Combination Antiretroviral Therapy Among HIV-infected Patients Followed for up to 15 Years After Start of Treatment: Collaborative Cohort Study. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America* 2016;**62**:1571–7. https://doi.org/10.1093/cid/ciw183.

233 The Antiretroviral Therapy Cohort Collaboration. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. *The Lancet HIV* 2017;**4**:e349–56. https://doi.org/10.1016/s2352-3018(17)30066-8.

234 May MT, Gompels M, Delpech V, Porter K, Orkin C, Kegg S, *et al.* Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. *AIDS (London, England)* 2014;**28**:1193–202. https://doi.org/10.1097/qad.0000000000000243.

235 Patterson S, Cescon A, Samji H, Chan K, Zhang W, Raboud J, *et al.* Life expectancy of HIV-positive individuals on combination antiretroviral therapy in Canada. *BMC Infectious Diseases* 2015;**15**:274–274. https://doi.org/10.1186/s12879-015-0969-x.

236 Samji H, Cescon A, Hogg RS, Modur SP, Althoff KN, Buchacz K, *et al.* Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. *PloS One* 2013;**8**:e81355–e81355. https://doi.org/10.1371/journal.pone.0081355.

237 Office of Financial Management. *Estimates of April 1 population by age, sex, race and Hispanic origin*. 2016. URL: http://www.ofm.wa.gov/pop/asr/default.asp (Accessed 6 March 2017).

238 Marmor M, Sheppard HW, Donnell D, Bozeman S, Celum C, Buchbinder S, *et al.* Homozygous and heterozygous CCR5-Delta32 genotypes are associated with resistance to HIV infection. *Journal of Acquired Immune Deficiency Syndromes (1999)* 2001;**27**:472–81.

239 Goodreau SM, Carnegie NB, Vittinghoff E, Lama JR, Sanchez J, Grinsztejn B, *et al.* What drives the US and Peruvian HIV epidemics in men who have sex with men (MSM)? *PloS One* 2012;**7**:e50522. https://doi.org/10.1371/journal.pone.0050522.

240 Krivitsky PN, Handcock MS, Morris M. Adjusting for Network Size and Composition Effects in Exponential-Family Random Graph Models. *Stat Methodol* 2011;**8**:319–39. https://doi.org/10.1016/j.stamet.2011.01.005.

241 Snjiders TAB. Markov Chain Monte Carlo Estimation of Exponential Random Graph Models. *Journal of Social Structure* 2002;**3**:1–40.

242 Carnegie NB, Krivitsky PN, Hunter DR, Goodreau SM. An approximation method for improving dynamic network model fitting. *J Comput Graph Stat* 2015;**24**:502–19. https://doi.org/10.1080/10618600.2014.903087.

243 Fauci AS. Immunopathogenic Mechanisms of HIV Infection. *Annals of Internal Medicine* 1996;**124**:654. https://doi.org/10.7326/0003-4819-124-7-199604010-00006.

244 Little SJ, McLean AR, Spina CA, Richman DD, Havlir DV. Viral Dynamics of Acute HIV-1 Infection. *J Exp Med* 1999;**190**:841–50.

245 Herbeck JT, Gottlieb GS, Li X, Hu Z, Detels R, Phair J, *et al.* Lack of evidence for changing virulence of HIV-1 in North America. *PLoS ONE* 2008;**3**:e1525. https://doi.org/10.1371/journal.pone.0001525.

246 Buchbinder SP, Katz MH, Hessol NA, O’Malley PM, Holmberg SD. Long-term HIV-1 infection without immunologic progression. *AIDS* 1994;**8**:1123–8.

247 Katz MH, Hessol NA, Buchbinder SP, Hirozawa A, O’Malley P, Holmberg SD. Temporal trends of opportunistic infections and malignancies in homosexual men with AIDS. *J Infect Dis* 1994;**170**:198–202.

248 Fiebig EW, Wright DJ, Rawal BD, Garrett PE, Schumacher RT, Peddada L, *et al.* Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. *AIDS* 2003;**17**:1871–9. https://doi.org/10.1097/01.aids.0000076308.76477.b8.

249 Clotet B, Feinberg J, van Lunzen J, Khuong-Josses M-A, Antinori A, Dumitru I, *et al.* Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naive adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study. *Lancet* 2014;**383**:2222–31. https://doi.org/10.1016/S0140-6736(14)60084-2.

250 Walmsley SL, Antela A, Clumeck N, Duiculescu D, Eberhard A, Gutierrez F, *et al.* Dolutegravir plus abacavir-lamivudine for the treatment of HIV-1 infection. *The New England Journal of Medicine* 2013;**369**:1807–18. https://doi.org/10.1056/NEJMoa1215541.

251 Neumann AU, Tubiana R, Calvez V, Robert C, Li TS, Agut H, *et al.* HIV-1 rebound during interruption of highly active antiretroviral therapy has no deleterious effect on reinitiated treatment. Comet Study Group. *AIDS* 1999;**13**:677–83.

252 Steingrover R, Pogány K, Fernandez Garcia E, Jurriaans S, Brinkman K, Schuitemaker H, *et al.* HIV-1 viral rebound dynamics after a single treatment interruption depends on time of initiation of highly active antiretroviral therapy: *AIDS* 2008;**22**:1583–8. https://doi.org/10.1097/QAD.0b013e328305bd77.

253 Treasure GC, Aga E, Bosch RJ, Mellors JW, Kuritzkes DR, Para M, *et al.* Relationship Among Viral Load Outcomes in HIV Treatment Interruption Trials. *J Acquir Immune Defic Syndr* 2016;**72**:310–3. https://doi.org/10.1097/QAI.0000000000000964.

254 Scott HM, Vittinghoff E, Irvin R, Sachdev D, Liu A, Gurwith M, *et al.* Age, Race/Ethnicity, and Behavioral Risk Factors Associated with Per-Contact Risk of HIV Infection Among Men Who Have Sex with Men in the United States. *J Acquir Immune Defic Syndr* 2014;**65**:115–21. https://doi.org/10.1097/QAI.0b013e3182a98bae.

255 Wilson DP, Law MG, Grulich AE, Cooper DA, Kaldor JM. Relation between HIV viral load and infectiousness: a model-based analysis. *Lancet* 2008;**372**:314–20. https://doi.org/10.1016/S0140-6736(08)61115-0.

256 Bellan SE, Dushoff J, Galvani AP, Meyers LA. Reassessment of HIV-1 Acute Phase Infectivity: Accounting for Heterogeneity and Study Design with Simulated Cohorts. *PLoS Med* 2015;**12**:e1001801. https://doi.org/10.1371/journal.pmed.1001801.

257 Leynaert B, Downs AM, de Vincenzi I. Heterosexual Transmission of Human Immunodeficiency VirusVariability of Infectivity throughout the Course of Infection. *Am J Epidemiol* 1998;**148**:88–96. https://doi.org/10.1093/oxfordjournals.aje.a009564.

258 Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* 2007;**369**:. https://doi.org/10.1016/s0140-6736(07)60313-4.

259 Varghese B, Maher JE, Peterman TA, Branson BM, Steketee RW. Reducing the risk of sexual HIV transmission: quantifying the per-act risk for HIV on the basis of choice of partner, sex act and condom use. *Sex Transm Dis* 2002;**29**:. https://doi.org/10.1097/00007435-200201000-00007.

260 Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2002:CD003255. https://doi.org/10.1002/14651858.CD003255.

261 Seifert SM, Glidden DV, Meditz AL, Castillo-Mancilla JR, Gardner EM, Predhomme JA, *et al.* Dose Response for Starting and Stopping HIV Preexposure Prophylaxis for Men Who Have Sex With Men. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America* 2015;**60**:804–10. https://doi.org/10.1093/cid/ciu916.

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