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# Targeting HIV pre-exposure prophylaxis to adolescent sexual minority males in higher prevalence areas of the United States: a modeling study

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## Abstract

**Purpose—**Pre-exposure prophylaxis (PrEP) is an effective and safe intervention to prevent HIV transmission in men who have sex with men; current CDC guidelines indicate its use among high-risk adults. Adolescent sexual minority males (ASMM) also have significant HIV risk, but implementation strategies are likely to differ for this population. We aimed to estimate impact and efficiency of PrEP for ASMM in higher-prevalence US settings, using a variety of implementation strategies and assumptions about coverage, adherence, and background prevalence.

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**CONFLICTS OF INTEREST**

The authors report no real or perceived conflicts of interest.

Disclaimer: The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Institutes of Health.

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**Methods—**We develop a stochastic, dynamic, network-based model, parametrized using numerous ASMM behavioral and clinical data sources. We simulate 10 years with and without PrEP, comparing percent of incident infections averted (impact) and number of person-years on PrEP per infection averted (efficiency).

**Results—**Our main scenario (PrEP for 16–18 year-old ASMM, initiating PrEP six months after first anal intercourse, 40% coverage, adherence profiles from the ATN 113 trial; 2.9% background HIV prevalence among ASMM) prevents 27.8% of infections, with 38 person-years on PrEP per infection averted. Expanding implementation to cover younger ages or earlier initiation has small effects on impact and efficiency. Targeting highest-risk ASMM increases efficiency, but requires querying sexual histories. Across levels examined, coverage and adherence do not have major impacts on efficiency, while background prevalence does.

**Conclusions—**PrEP can have a large impact on HIV incidence among ASMM in the United States, especially in settings with high prevalence. However, willingness of, and support for, providers will be central to achieving the coverage needed to make this a success.

### Keywords

Adolescent sexual minority males; homosexual males; bisexual males; HIV; pre-exposure prophylaxis; mathematical modeling

## IMPLICATIONS AND CONTRIBUTION

This study uses modeling and recent trial data to estimate impact and efficiency for HIV pre-exposure prophylaxis (PrEP) among adolescent sexual minority males in higher-prevalence US settings under different targeting strategies. We find that PrEP can have a large impact on HIV incidence in this population, with reasonable efficiency.

Pre-exposure prophylaxis (PrEP) with daily oral combined tenofovir/emtricitabine is an effective and safe intervention to prevent human immunodeficiency virus (HIV) infection in adult men who have sex with men (MSM)(1, 2). Current CDC guidelines indicate use for sexually-active adult MSM at substantial risk for HIV acquisition, based on recent patterns of anal sex, monogamy, condom use, partner HIV status, and STI diagnosis, or who have injected drugs and shared needles (3). PrEP initiation requires a prescription; current CDC guidelines for ongoing PrEP users promote quarterly HIV tests, 6-monthly sexually transmitted infection (STI) tests, and screening for various side effects at both intervals.

Adolescent sexual minority males (ASMM)—ie, males under 18 who identify as gay or bisexual, or are sexually active with other males—have significant HIV risk. For instance, sexually-debuted high-school ASMM report higher frequencies of multiple risk behaviors than do sexually-debuted high-school adolescent males with only female partners, including prevalence of 4+ lifetime partners (33.4% vs. 25.4%), condomless last sex (48.6% vs. 37.9%), and use of drugs/alcohol at last sex (32.2% vs. 24.1%) (4). Although surveillance-based HIV incidence measures are not available for ASMM (5), measures of new diagnoses illuminate the high HIV risk that ASMM experience nationally. The Centers for Disease Control and Prevention (CDC) estimated that in 2015, 13–24-year-old adolescents and young adults comprised 22% of all new US HIV diagnoses, and 81% of the adolescent/

young adult diagnoses were in ASMM, for a total of 7,159 of 39,920 diagnoses (6). Nineteen percent of ASMM diagnoses occurred by age 19 and it remains unknown what proportion of all ASMM diagnoses reflect infections that occurred before 18. Per total population-based rates for 13–24-year-old MSM illustrate this group to have consistently the second-highest diagnosis rates among MSM, but stable diagnosis rates since 2010 (7). In the absence of surveillance-based incidence estimates and ASMM-specific denominators for estimating most-relevant rates (8), research studies have provided critical insights into the HIV burden among ASMM. HIV incidence among 16–17-year-old Chicago ASMM has been estimated at 5.2/100 person-years, and prevalence among 16–20-year-olds at 7.6% (9). Studies of adult MSM find HIV in the youngest participants, implying substantial risk in adolescents; e.g., HIV prevalence estimates among 18–22 year-old MSM from three rounds of the National HIV Behavioral Surveillance system were 11–14% (10). The InvolveMENt cohort (Atlanta) estimated 7.0% HIV prevalence among 18–19 year-olds (11), and the P18 cohort (New York City) reported HIV incidence of 2.9/100 person-years in MSM of the same ages (12). These population-specific estimates of HIV incidence are over 200-fold those seen in the general US population (5).

Initial PrEP trials and demonstration projects for MSM included only adults aged 18+ (1, 2, 13). Given the lack of adolescent-specific efficacy and safety data, current FDA indications only include adults, and CDC's clinical practice guidelines currently recommend that the risks and benefits of PrEP for adolescents be weighed carefully "in the context of local laws and regulations about autonomy in health care decision-making by minors" (3). One safety and feasibility study of PrEP in ASMM in the US aged 15–17 (ATN 113) was recently completed. Averaged across measured time points, high adherence (≥4 doses/week) in ATN 113 (41.6%) was lower than in a recent demonstration project with adult MSM (61.9%) (13–15). ATN 113 showed a high incidence rate (6.41 infections/100 person-years), higher than the 3.29 infections/100 person-years observed in its 18–22 year old MSM counterpart ATN 110 (16), although all infections in ATN 113 were among those whose drug levels indicated poor-to-no adherence. These results highlight the need for targeted research in adolescents to understand the impact PrEP may have on HIV incidence, and the unique challenges for ASMM in uptake, adherence, and defining and accessing target populations. Since risk behaviors evolve rapidly during adolescence, this could be a uniquely valuable time to get ASMM on PrEP surrounding specific high-risk behaviors, establishing early a norm of sexual health protection.

A broad definition of ASMM includes adolescents who either identify as gay/bisexual or have a history of sex with males; one key decision for future PrEP guidelines among ASMM, then, is whether to target adolescent populations based on sexual identity or reported risk behaviors. Overall impact (ie, cases averted) and efficiency (ie, number needed to treat) may depend on targeting strategy and the existing distribution of sexual risk. However, methods for identifying ASMM must recognize that they may be in early stages of sexual identity formation and may not self-identify as ASMM, nor disclose identity or risk behaviors to clinicians or counselors; moreover, not all providers for adolescents are prepared to elucidate this information.

In this study, we developed an agent-based network model of HIV transmission among ASMM to inform future guidelines and studies of PrEP interventions in adolescents. We modeled an open cohort of 13–18-year-old ASMM, and considered different targeting strategies, adherence and coverage levels, and baseline prevalence levels. We estimated the impact and efficiency of each strategy, and we interpret these results in the context of each strategy's feasibility within different settings.

## METHODS

We developed a stochastic, dynamic model built in the EpiModel software platform (www.epimodel.org) based on separable-temporal exponential-family random graph models (17). This general statistical model class specifies the probability each pair forms or breaks a relationship at each timestep in ways that allow users to preserve arbitrarily complex data-derived features of network structure. As with our previous adult MSM model (14), we modeled relationship formation and dissolution; sexual behavior within relationships (anal sex acts, condom use, role selection); HIV testing; HIV treatment initiation, adherence and cessation; PrEP initiation and adherence; transmission; intra-host viral dynamics; and agent demographic change. We restructured some components, and re-parametrized most, to fit ASMM; full details are in the online supplement. Code is available at https://github.com/statnet/ASMMPrep.

Briefly, males could enter our population at any age 13–18, with entry defined as either developing gay or bisexual identity or initiating willingness for sexual activity with another male. Those in the latter category immediately became eligible to enter into sexual relationships; those in the former had a constant probability of doing so thereafter. Actual sexual initiation occurred stochastically some time thereafter. We modeled relationships between two ASMM as a function of individual relational propensities and sexual role preferences, conditional on both having achieved eligibility. Relational propensities were calculated to capture observed variation in partner count, using both explicit (age) and latent categories. We included 18-year-olds given programmatic interest in reaching the school-aged population.

We included an additional constant hazard of infection from MSM above the modeled age range. This probability increased with age and varied with individual relational propensity. We derived an *initial* estimate (subsequently altered; see below) for the infection risk per week from older MSM for 18-year-olds based on partner age data reported by 19–25 year-olds (18).

Sexual behavior parameters were drawn from multiple sources (19–21) and new analyses of the American Men's Internet Survey (22), InvolveMENt Study (23), and MAN Project (24), with cross-validation when possible. Because this involved only secondary use of existing de-identified data sets, it was deemed exempt from review by the University of Washington Institutional Review Board. We calibrated our model to 7% HIV prevalence among 18-year-old ASMM, based on one Atlanta study (11); we then compared resulting incidence estimates against others from New York and Chicago (9, 12). We chose the first of these as our calibration measure since prevalence is a more stable metric than incidence in the short

term, and because some of our behavioral parameters were derived from Atlanta data. We varied two inputs—frequency of anal intercourse (AI) within ongoing relationships between two ASMM, and weekly probability of HIV infection from non-ASMM partners—for which source data were particularly old or subject to desirability bias. Following recent practice in epidemic modeling (25), we used approximate Bayesian computation (26) to accept a subset of estimates and calculate final parameter values. The final set of parameters that is fixed across all scenarios is compiled into two tables in Section 3 of the supplement.

## PrEP Scenarios

Our first intervention model (*16+/6 mos.*; see Table 1) considered PrEP for ASMM aged 16–18 who had initiated AI, with an average 6-month delay between having indications and initiating PrEP, reflecting the average interval expected when sexual debut occurs between annual healthcare visits. We considered this a reasonably feasible strategy, as it focused on older ASMM, did not require provider elucidation of extensive sexual behavior, and included initiation delay. In this, and all modeled scenarios, individuals could terminate PrEP while still indicated, given the high discontinuation rate in ATN 113 preliminary data (15). We then modeled more expansive strategies allowing for immediate initiation (*16+/immed.*), inclusion of younger ASMM (*13+/6 mos.*), or both (*13+/immed.*). The *13+/pre-AI* scenario modeled PrEP initiation occurring prior to AI initiation, when ASMM first begin seeking sexual partnerships.

We next considered strategies to focus PrEP among those reporting the greatest risk, measured as frequency of condomless AI (CAI) with other ASMM (≥5 or ≥10 CAI acts in last 6 months), each for the age groups 16–18 (*16+/CAI5* and *16+/CAI10*) and 13–18 (*13+/CAI5* and *13+/CAI10*). This requires greater provider elucidation of sexual history, but was expected to increase intervention efficiency.

For all nine base scenarios, we modeled 40% coverage to match our published adult model: at any time, 40% of those meeting relevant criteria were enrolled in PrEP. Our baseline cohort adherence profile reflects the means across all measured time points (4–48 weeks) in preliminary ATN 113 data (15); 20.9% had no measureable adherence, 24.4% had low (corresponding to < 2 pills per week), 13.1% had medium (2–3 pills), and, 41.6% had high (4+ pills). Relative risk reduction values for transmission by adherence level were 0%, 31%, 81%, and 95%, respectively (14, 27). The weighted average of effectiveness across levels implies that the average ASMM currently prescribed PrEP would receive a direct 58% reduction in per-act acquisition risk. We modeled PrEP termination such that 50% of initiators had terminated by 48 weeks (15); these could re-initiate if still indicated.

We conducted sensitivity analyses on coverage and adherence, varying both individually and jointly on the *16+/6 mos.* scenario. We considered coverage values of 20–60%, and optimistic and pessimistic adherence patterns derived from the first and last follow-up visits in ATN 113. We conducted a separate sensitivity analysis on background HIV prevalence, lowering it by approximately one-half and two-thirds with two scenarios (*16+/6 mos.* and *16+/CAI10*).

### Simulations and Analysis

Scenarios were conducted on populations of size 10,000 for 10 years. Although no individuals remained in the modeled population for this duration, sexual contacts between successive cohorts allowed incidence to potentially continue changing over this period. We calculated five outcomes for each scenario: HIV incidence; HIV prevalence; the number of infections averted (NIA) and percent of infections averted (PIA) relative to no PrEP; and the number of person-years on PrEP per infection averted (NNT, number needed to treat). We present two prevalence metrics: prevalence among 18-year olds (the metric to which we calibrated our model, as described in the Methods, and also an approximation for cumulative incidence through age 18 given low adolescent mortality), and across all 13–18 year-old ASMM.

Incidence is measured across the final year of the simulation, while NIA and PIA account for cumulative incidence across the 10-year time-series. NNT equals person-time on PrEP divided by NIA. We present means and 95% credible intervals (CI; middle 95% of simulated data) for each outcome across 100 simulations.

## RESULTS

Table 2 lists results for all scenarios, and Figure 1 highlights two key metrics (PIA and NNT) for our nine main scenarios. Our base scenario (ages 16–18, PrEP initiation 6 months after AI initiation, 40% coverage, moderate adherence profile) reduced prevalence among 18-year-olds from 7.5% to 5.5% (Figure 2a) over 10 years, and prevented 27.8% of infections (95% CI 22.3–33.3%). This required 38 person-years on PrEP per infection averted. The incidence reduction equilibrated quickly (Figure 2b), beginning at 15% and reaching nearly 25% in less than 2 years. This accumulation suggests strong indirect effects (ie, secondary cases averted), even when measured across a relatively short portion of the lifespan.

Moving PrEP initiation forward to immediately after first AI (*16+/immed.*) has only a minor effect on both PIA and NNT. Reducing the lower limit for indication to age 13 (*13+/6 mos.*, *13+/immed.*) increases PIA more substantially (37.8% for initiation 6 months after AI, 42.1% for immediate initiation) but at the cost of higher NNT (40 and 41, respectively). Enrolling adolescents prior to their first AI experience rather than after had a marginal effect on PIA (42.1% to 42.8%).

Scenarios in which PrEP was concentrated among the highest-risk ASMM were all more efficient than their more generalized counterparts. For instance, in comparing *16+/immed.* to *16+/CAI10* (ie with ≥10 CAI acts in the last 6 months), PIA declines from 30.1% to 28.1%, but NNT also declines (efficiency increases), from 38 to 35. The two scenarios focusing on 16–18 year-olds with high numbers of recent CAI (5 or 10) achieve the maximum efficiency observed. Dropping indication age but continuing to focus on CAI counts increases both PIA (to 39.4% and 40.4%) and NNT (36 and 37) again.

PIA increases almost linearly with coverage over the range observed, although with slight diminishing marginal returns at upper levels (Table 1, Figure 3). Efficiency is flat across

lower levels of coverage but decreases slightly at higher levels. The more optimistic adherence pattern is able to increase PIA by roughly 3–9 percentage points across adherence levels, and reduce NNT by 6–8. Lower adherence operates in the opposite direction, but with a larger effect (on average 4–11 percentage points fewer infections averted relative to moderate adherence, increase in NNT always >12). The most optimistic scenario of all—high (60%) coverage and high adherence—prevents just under half (47.2%) of new infections among ASMM.

In settings where background prevalence is lower than our main model, PIA declines slightly to moderately. Measured in absolute numbers of infections averted (NIA), effectiveness declines much more. NNT increases dramatically, to 85 and 75 (in moderate-prevalence settings with broad targeting and risk-based targeting, respectively), or 141 and 125 (for the same scenarios in lower-prevalence settings).

## DISCUSSION

Our models suggest that PrEP has the potential to reduce HIV incidence significantly among adolescent sexual minority males (ASMM), with intervention efficiency for a generalized ASMM targeting strategy in higher-prevalence settings being less than twice that for highly targeted adult MSM interventions (14). Coverage strongly affects impact over the range examined, but has little effect on efficiency. Focusing on ASMM with the highest sexual risk behaviors decreases NNT, with the added challenge of ascertaining elements of sexual history beyond sexual identity. Targeting 16–18 year-olds has more efficiency than 13–18, and likely has higher feasibility and acceptability, especially in jurisdictions with an age of consent of 16 or with close-in-age exemptions that cover this age range (28, 29). A mean 6-month delay in initiating PrEP after debut affects results marginally relative to immediate initiation, so a system of annual evaluations should represent a good balance of effectiveness and feasibility.

The impact and efficiency of our modeled interventions are directly dependent on current HIV burden, which varies across communities; higher burden makes PrEP much more efficient, and more effective in terms of absolute number of infections averted. Our main model was calibrated to 7% prevalence among 18-year-olds, an estimate derived from one Atlanta study and supported by additional studies of young adults in other large urban settings. In these calibrated simulations, the HIV prevalence seen among ASMM overall (13–18 years old) was 3.2%, with an incidence of 2.3/100 person-years among sexually-initiated ASMM. The latter figure is lower than studies in Chicago and New York (9, 12); settings like these might experience higher efficiency than we estimate. In contrast, the many communities with ASMM incidence or prevalence lower than our model would see less impact and efficiency. Although we did not conduct a cost-effectiveness analysis, we can expect that cost-effectiveness will generally parallel efficiency. Our results provide a guide for jurisdictions to weigh their own estimates of ASMM HIV incidence or prevalence with their tolerance for levels of intervention impact and efficiency, in determining the value of ASMM PrEP scale-up, ideally within a cost-effectiveness analysis. Our results may also add further impetus for the FDA to evaluate PrEP indication for adolescents, a vital step in

achieving levels of coverage that could, like those modeled in this paper, make a significant impact on the epidemic.

The little data on potential PrEP adherence among ASMM comes from the ATN 113 trial, where it was lower than among adults, tapering off after 12 weeks when the study switched from monthly to quarterly visits (15). Our results suggest that lower adherence profiles may still yield considerable impact, so that if monthly visits are infeasible, ASMM PrEP may still be worth pursuing. However, these do not represent the full range over which adherence might vary in clinical practice, and may be high since the trial involved extensive counseling. More studies of adherence among ASMM will be needed, as will close monitoring in any ASMM demonstration trial. Increasing adherence among adolescent ASMM will help improve the efficiency and effectiveness of PrEP, and a large literature reveals the unique challenges of doing so in this population (30–32). Potential approaches include adapting strategies common to adherence efforts in general, including pill boxes, automated reminders, and case management. In addition, NIH is currently supporting the evaluation of several youth-specific PrEP adherence interventions, including a theoretically-based mobile app and an adaptation of the LifeSteps intervention (33), both being evaluated through the Adolescent Trials Network (30–32). In the longer term, the adherence landscape may change dramatically if long-lasting injectable PrEP advances through trials to market (34).

Our study includes numerous limitations, including the fact that some parameters were based on relatively uncertain estimates. Two in particular (AI frequency within relationships and risk of HIV acquisition from older partners) were based on data that were either old or subject to strong desirability bias. Because our baseline model yielded low prevalence, we used these as uncertainty parameters. However, the mismatch between the observed HIV prevalence to which we calibrated (11) and that first predicted by our model may result from other forms of misspecification.

Our model assumed no risk compensation after PrEP initiation, since early reports from adult MSM found little evidence (13, 27). While preliminary ATN 113 results do not mention risk compensation directly, STI incidence declined over the study, suggesting little evidence of risk compensation (15). However, recent reports find risk compensation in adults (35–37), and any PrEP roll-out among adolescents would need to monitor closely for similar evidence.

Our model does not disaggregate risk or impact by race, despite large racial disparities in HIV among young MSM in the US. Targeting of PrEP within ASMM communities with the highest HIV burden may help reduce these large disparities; work on this extension is in progress. We also did not track ASMM beyond age 18, and thus miss multiple later-life effects of PrEP, meaning we cannot assess the impact of adolescent PrEP on the overall epidemic. Considering the full lifecourse could increase PrEP's estimated impact and efficiency in two ways. First, it allows reduced HIV prevalence among men recently aged out of the ASMM population to reduce risk to ASMM through reductions in prevalence among partners. Second, adolescent engagement with PrEP may set a lifelong norm for MSM, leading to both higher lifelong retention and adherence. On the other hand,

considering the full lifecourse could reduce our estimates of impact and efficacy, since it might reveal that adolescent PrEP does not avert infections so much as postpone them. Such postponement, however, has the potential to avert additional secondary infections. Measuring the complete impact of PrEP for ASMM on HIV burden, whether for ASMM or for all MSM, thus requires a combined model for both communities that tracks ASMM across the lifecourse. We are currently conducting this work.

A growing body of evidence, including this model, indicates that over a range of coverage levels and with anticipated adherence and appropriate targeting, PrEP has the potential to substantially decrease HIV burden among adolescent sexual minority males, an underserved and at-risk population. Our work suggests optimal settings for PrEP outreach and delivery for ASMM. In higher-prevalence settings, an approach in which adolescent males are asked by a provider about their sexual identity on three occasions (once a year from ages 16–18) would provide information necessary for PrEP targeting that yields reasonable efficiency. One additional question about recent sexual activity could increase efficiency further, especially in lower-prevalence settings. In all cases, achieving reasonable uptake and retention will be key to intervention success. Making ASMM PrEP scalable will require strong buy-in from pediatricians or other providers, accompanied by strong training and support, as well as structural changes to expressly allow for minors to consent to PrEP. These will all likely be easier to achieve in higher-prevalence settings (28). More information on HIV burden among ASMM by jurisdiction, and more dissemination of that information, may increase PrEP willingness among both providers and ASMM (38, 39). All of these represent logistical challenges, although experiences from parallel endeavors (e.g. contraception for adolescents) will likely assist (40). Tackling these challenges could make a substantial impact in the large and often underappreciated HIV burden among US adolescent sexual minority males.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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As part of the cooperative agreement model, research scientists affiliated with the funder (the US Centers for Disease Control and Prevention) contributed to the design of the study through a series of collaborative meetings. They also approved the decision to submit the manuscript for publication, and CDC staff scientists reviewed and approved the final manuscript. Those individuals who played significant roles in the scientific development of the project are listed as co-authors. The coresponding author (Steven M Goodreau) wrote the first draft of the manuscript.

## ABBREVIATIONS

| | |
|---|---|
| **HIV** | human immunodeficiency virus |
| **PrEP** | pre-exposure prophylaxis |
| **ASMM** | adolescent sexual minority male |
| **MSM** | men who have sex with men |
| **NIA** | number of infections averted |
| **PIA** | Percent of infections averted |
| **NNT** | number needed to treat |
| **CDC** | Centers for Disease Control and Prevention |
| **STI** | sexually transmitted infections |
| **AI** | anal intercourse |
| **CAI** | condomless anal intercourse |

## References


1. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. New England Journal of Medicine. 2010; 363:2587–2599. [PubMed: 21091279]
2. Grohskopf LA, Chillag KL, Gvetadze R, et al. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. J Acquir Immune Defic Syndr. 2013; 64:79–86. [PubMed: 23466649]
3. Centers for Disease Control Prevention. Preexposure prophylaxis for the prevention of HIV infection in the United States-2014: a clinical practice guideline. Atlanta: U.S. Public Health Service; 2014. http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf
4. Kann L, Olsen EO, McManus T, et al. Sexual Identity, Sex of Sexual Contacts, and Health-Related Behaviors Among Students in Grades 9–12 — United States and Selected Sites, 2015. MMWR Surveill Summ. 2016; 65:1–202.
5. Hall HI, Song R, Tang T, et al. HIV Trends in the United States: Diagnoses and Estimated Incidence. JMIR Public Health Surveill. 2017; 3:e8. [PubMed: 28159730]
6. Division of HIV/AIDS Prevention. Diagnoses of HIV Infection in the United States and Dependent Areas. Atlanta: Centers for Disease Control;; 2016. p. 2015
7. Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, Sexual Transmitted Diseases and Tuberculosis Prevention, Centers for Disease Control and Prevention. HIV Surveillance—Men Who Have Sex with Men (MSM) (through 2015). Atlanta: 2015. https://www.cdc.gov/hiv/pdf/library/slidesets/cdc-hiv-surveillance-slides-msm.pdf
8. Grey JA, Bernstein KT, Sullivan PS, 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 Surveill. 2016; 2:e14. [PubMed: 27227149]
9. Garofalo R, Hotton AL, Kuhns LM, et al. Incidence of HIV infection and Sexually Transmitted Infections and Related Risk Factors among Very Young Men Who Have Sex with Men. Journal of acquired immune deficiency syndromes. 1999:2016.
10. Wejnert C, Hess KL, Rose CE, et al. Age-Specific Race and Ethnicity Disparities in HIV Infection and Awareness Among Men Who Have Sex With Men–20 US Cities, 2008–2014. J Infect Dis. 2016; 213:776–783. [PubMed: 26486637]

11. Sullivan PS, Peterson J, Rosenberg ES, et al. Understanding racial HIV/STI disparities in black and white men who have sex with men: a multilevel approach. PLoS One. 2014; 9:e90514. [PubMed: 24608176]
12. Halkitis P, Kapadia F, Ompad D. Incidence of HIV Infection in Young Gay, Bisexual, and Other YMSM: The P18 Cohort Study. J Acquir Immune Defic Syndr. 2015; 69:466–473. [PubMed: 26115438]
13. Liu AY, Cohen SE, Vittinghoff E, et al. Preexposure Prophylaxis for HIV Infection Integrated With Municipal- and Community-Based Sexual Health Services. JAMA Intern Med. 2016; 176:75–84. [PubMed: 26571482]
14. Jenness SM, Goodreau SM, Rosenberg E, 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. J Infect Dis. 2016
15. Hosek, S., Landovitz, R., Rudy, B., et al. An HIV Pre-Exposure Prophylaxis Demonstration Project and Safety Study for Adolescent MSM ages 15–17 in the US (ATN 113); AIDS 2016: 21st International AIDS Conference; Durban.
16. Hosek S, Rudy D, Landovitz R, et al. An HIV Preexposure Prophylaxis Demonstration Project and Safety Study for Young MSM. Journal of Acquired Immune Deficiency Syndrome. 2017; 74:21–29.
17. Krivitsky PN, Handcock MS. A separable model for dynamic networks. Journal of the Royal Statistical Society Series B-Statistical Methodology. 2014; 76:29–46.
18. Grey JA, Rothenberg RB, Sullivan PS, et al. Disassortative Age-Mixing Does Not Explain Differences in HIV Prevalence between Young White and Black MSM: Findings from Four Studies. PLoS One. 2015; 10:e0129877. [PubMed: 26090814]
19. Rotheram-Borus MJ, Reid H, Rosario M. Factors mediating changes in sexual HIV risk behaviors among gay and bisexual male adolescents. Am J Public Health. 1994; 84:1938–1946. [PubMed: 7998634]
20. Halkitis PN, Kapadia F, Siconolfi DE, et al. Individual, psychosocial, and social correlates of unprotected anal intercourse in a new generation of young men who have sex with men in New York City. Am J Public Health. 2013; 103:889–895. [PubMed: 23488487]
21. Hidalgo MA, Kuhns LM, Hotton AL, et al. The MyPEEPS randomized controlled trial: a pilot of preliminary efficacy, feasibility, and acceptability of a group-level, HIV risk reduction intervention for young men who have sex with men. Arch Sex Behav. 2015; 44:475–485. [PubMed: 25135064]
22. Sanchez T, Zlotorzynska M, Sineath C, et al. 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 Surveill. 2016; 2:e23. [PubMed: 27244770]
23. Sullivan PS, Rosenberg ES, Sanchez TH, et al. Explaining racial disparities in HIV incidence in black and white men who have sex with men in Atlanta, GA: a prospective observational cohort study. Ann Epidemiol. 2015; 25:445–454. [PubMed: 25911980]
24. Hernandez-Romieu AC, Sullivan PS, Rothenberg R, et al. Heterogeneity of HIV Prevalence Among the Sexual Networks of Black and White Men Who Have Sex With Men in Atlanta: Illuminating a Mechanism for Increased HIV Risk for Young Black Men Who Have Sex With Men. Sex Transm Dis. 2015; 42:505–512. [PubMed: 26267877]
25. Bellan SE, Dushoff J, Galvani AP, et al. Reassessment of HIV-1 acute phase infectivity: accounting for heterogeneity and study design with simulated cohorts. PLoS Med. 2015; 12:e1001801. [PubMed: 25781323]
26. Sunnaker M, Busetto AG, Numminen E, et al. Approximate Bayesian Computation. Plos Comput Biol. 2013; 9
27. Grant RM, Anderson PL, McMahan V, 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. Lancet Infect Dis. 2014; 14:820–829. [PubMed: 25065857]
28. Makadon, HJ., Mayer, KH., Potter, J., et al. The Fenway guide to lesbian, gay, bisexual, and transgender health. Second edition. Philadelphia: American College of Physicians; 2015.

29. Mustanski B. Ethical and regulatory issues with conducting sexuality research with LGBT adolescents: a call to action for a scientifically informed approach. Arch Sex Behav. 2011; 40:673–686. [PubMed: 21528402]

30. Adeyemi AO, Rascati KL, Lawson KA, et al. Adherence to oral antidiabetic medications in the pediatric population with type 2 diabetes: a retrospective database analysis. Clin Ther. 2012; 34:712–719. [PubMed: 22381712]

31. Greenley RN, Gumidyala AP, Nguyen E, et al. Can You Teach a Teen New Tricks? Problem Solving Skills Training Improves Oral Medication Adherence in Pediatric Patients with Inflammatory Bowel Disease Participating in a Randomized Trial. Inflamm Bowel Dis. 2015; 21:2649–2657. [PubMed: 26218142]

32. Ingerski LM, Baldassano RN, Denson LA, et al. Barriers to oral medication adherence for adolescents with inflammatory bowel disease. J Pediatr Psychol. 2010; 35:683–691. [PubMed: 19776229]

33. Psaros C, Haberer JE, Katabira E, et al. An intervention to support HIV preexposure prophylaxis adherence in HIV-serodiscordant couples in Uganda. J Acquir Immune Defic Syndr. 2014; 66:522–529. [PubMed: 24853311]

34. Landovitz R, Li S, Grinsztejn B, et al. Safety, tolerability and pharmacokinetics of long-acting injectable cabotegravir in low-risk HIV-uninfected women and men: HPTN 077. International AIDS Society Paris. 2017

35. de Wit J, Murphy D, Lal L, et al. Pre-exposure prophylaxis and risk compensation: evidence of decreased condom use at three-month follow-up among predominantly gay male participants in the vicprep study. Sex Transm Infect. 2015; 91:A68.

36. McCormack S, Dunn DT, Desai M, 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. 2016; 387:53–60. [PubMed: 26364263]

37. Volk JE, Marcus JL, Phengrasamy T, et al. No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting. Clin Infect Dis. 2015; 61:1601–1603. [PubMed: 26334052]

38. Castel AD, Feaster DJ, Tang W, et al. Understanding HIV Care Provider Attitudes Regarding Intentions to Prescribe PrEP. J Acquir Immune Defic Syndr. 2015; 70:520–528. [PubMed: 26247895]

39. Silapaswan A, Krakower D, Mayer KH. Pre-Exposure Prophylaxis: A Narrative Review of Provider Behavior and Interventions to Increase PrEP Implementation in Primary Care. J Gen Intern Med. 2017; 32:192–198. [PubMed: 27761767]

40. Hartman LB, Monasterio E, Hwang LY. Adolescent contraception: review and guidance for pediatric clinicians. Curr Probl Pediatr Adolesc Health Care. 2012; 42:221–263. [PubMed: 22959636]

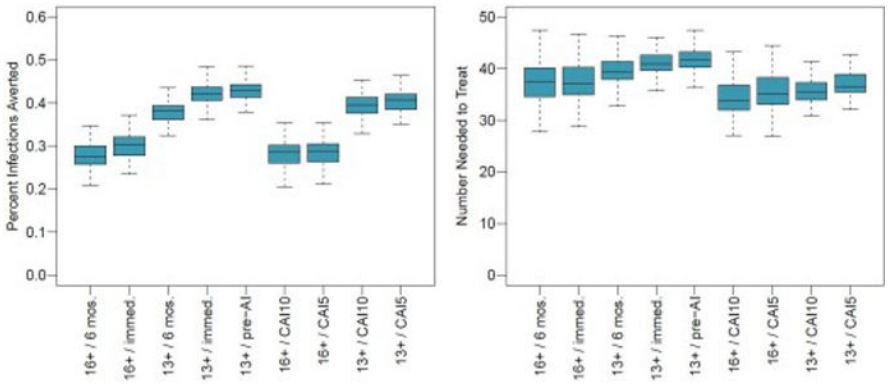


**Figure 1. Intervention impact for nine base PrEP implementation scenarios**

Boxplots show the median (center line), interquartile range (outer box) and 95% credible interval (whiskers) for each scenario. Scenario descriptions are found in Table 1. (a) Percent of infections averted (PIA); (b) number needed to treat (NNT).

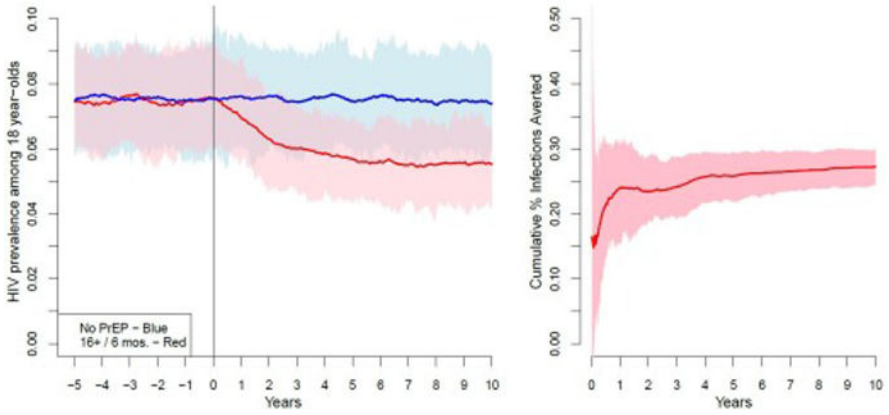


**Figure 2. Time series of intervention impact, 16+ / 6 mos. base scenario**

PrEP indications for this scenario are age 16–18 and having initiated anal intercourse; mean time until PrEP initiation is 6 months after indicated; coverage is 40%; adherence profile is drawn from the ATN 113 trial (see text). This corresponds to the first of the "base scenarios" listed in both Tables 1 and 2. Dark lines = means of 100 simulations from a given set of parameters; lighter areas = 95% credible interval across 100 simulations. (a) HIV prevalence among 18 year-old ASMM in the absence (blue) and presence (red) of PrEP over the 10 years after rollout. Time scale on the *x*-axis reflects time relative to PrEP rollout; scenarios before this are identical and differ only through stochastic variation. (b) Cumulative percentage of infections averted (PIA) by the same PrEP indication scenario as in (a). The increase in PIA after the initial simulation is primarily due to the accumulation of indirect effects (see text).

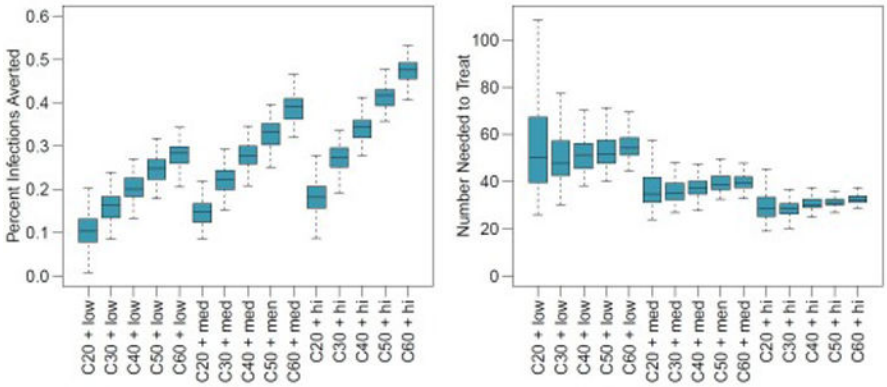


**Figure 3. Intervention impact for sensitivity analyses**

Boxplots show the median (center line), interquartile range (outer box) and 95% credible interval (whiskers) for each scenario. Scenario descriptions are found in Table 1. (a) Percent of infections averted (PIA); (b) number needed to treat (NNT). Note that the large difference in the median NNT for the C20+low scenario (50, shown here) and the mean (64, reported in Table 2) is due to individual simulation runs with very high NNT.

**TABLE 1**

Names and descriptions of scenarios modeled

| | Scenario name | Background ASMM HIV prev. | PrEP eligibility criteria | Timing of PrEP initiation | Coverage | Cohort distribution by adherence level (none, low, med., high) |
|---|---|---|---|---|---|---|
| High prev. base | No PrEP | 2.9% | N/A | N/A | N/A | N/A |
| Base scenarios | 16+ / 6 mos. | 2.9% | Aged 16–18 and AI experienced | 6 months after eligibility | 40% | 20.9%, 24.4%, 13.1%, 41.6% |
| | 16+ / immed. | | | at point of eligibility | | |
| | 13+ / 6 mos. | | Aged 13–18 and AI experienced | 6 months after eligibility | | |
| | 13+ / immed. | | | at point of eligibility | | |
| | 13+ / pre-AI | | Aged 13–18 | at point of seeking first sexual partnership | | |
| | 16+ / CAI10 | | Aged 16–18, ≥ 10 acts of CAI in the prior 6 mos. | at point of eligibility | | |
| | 16+ / CAI5 | | Aged 16–18, ≥ 5 acts of CAI in the prior 6 mos. | | | |
| | 13+ / CAI10 | | Aged 13–18, ≥ 10 acts of CAI in the prior 6 mos. | | | |
| | 13+ / CAI5 | | Aged 13–18, ≥ 5 acts of CAI in the prior 6 mos. | | | |
| Sensitivity analyses | C20 | 2.9% | Aged 16–18 and AI experienced | 6 months after eligibility | 20% | 20.9%, 24.4%, 13.1%, 41.6% |
| | C30 | | | | 30% | |
| | C40[a] | | | | 40% | |
| | C50 | | | | 50% | |
| | C60 | | | | 60% | |
| | C20 + Hi Adh | 2.9% | Aged 16–18 and AI experienced | 6 months after eligibility | 20% | 4.6%, 18.5%, 16.9%, 60.0% |
| | C30 + Hi Adh | | | | 30% | |
| | C40 + Hi Adh | | | | 40% | |
| | C50 + Hi Adh | | | | 50% | |
| | C60 + Hi Adh | | | | 60% | |
| | C20 + Low Adh | 2.9% | Aged 16–18 and AI experienced | 6 months after eligibility | 20% | 46.2%, 20.5%, 5.1%, 28.2% |
| | C30 + Low Adh | | | | 30% | |

| Scenario name | Background ASMM HIV prev. | PrEP eligibility criteria | Timing of PrEP initiation | Coverage | Cohort distribution by adherence level (none, low, med., high) |
|---|---|---|---|---|---|
| C40 + Low Adh | | | | 40% | |
| C50 + Low Adh | | | | 50% | |
| C60 + Low Adh | | | | 60% | |
| Med prev + no PrEP | | N/A | N/A | | |
| Med prev / 16+ / 6 mos. | 1.5%[b] | 16–18 and AI experienced | 6 months after eligibility | | |
| Med prev / 16+ / CAI10 | | 16–18, ≥ 10 acts of CAI in the prior 6 months | at point of eligibility | 40% | 20.9%, 24.4%, 13.1%, 41.6% |
| Low prev + no PrEP | | N/A | N/A | | |
| Low prev / 16+ / 6 mos. | 0.9%[b] | 16–18 and AI experienced | 6 months after eligibility | | |
| Low prev / 16+ / CAI10 | | 16–18, >10 acts of CAI in the prior 6 months | at point of eligibility | | |

AI = anal intercourse CAI = condomless anal intercourse

[a]This scenario matches the first base scenario, but is repeated here for easier comparison with sensitivity scenarios

[b]Medium and low prevalence were selected to be 1/2 and 1/3 of observed prevalence, respectively. 100 simulations were conducted, and those within 0.05% of the target prevalence were included in the final analysis.

**TABLE 2**

Model results

| | | Mean (95% Cred. Int.) | | | | | |
|---|---|---|---|---|---|---|---|
| | | **Prev. among 18 year-old ASMM** | **Prev. among ASMM** | **Inc. (per 100 py) among sexually initiated ASMM** | **NIA** | **PIA** | **NNT** |
| High prev. base | No PrEP | 7.54 (6.15–8.79) | 3.20 (2.66–3.74) | 2.34 (2.12–2.54) | | | |
| Base scenarios | 16+ / 6 mos. | 5.46 (4.31–6.62) | 2.43 (1.86–2.91) | 1.67 (1.53–1.79) | 643.3 (520.8–771.9) | 27.8 (22.3–33.3) | 38 (30–45) |
| | 16+ / immed. | 5.38 (4.29–6.61) | 2.40 (1.99–2.91) | 1.62 (1.47–1.73) | 697.4 (569.9–829.1) | 30.1 (24.6–35.9) | 38 (31–44) |
| | 13+ / 6 mos. | 4.62 (3.38–5.64) | 1.96 (1.60–2.26) | 1.43 (1.33–1.54) | 868.3 (743.5–964.0) | 37.8 (32.4–41.4) | 40 (36–46) |
| | 13+ / immed. | 4.30 (3.25–5.45) | 1.80 (1.47–2.11) | 1.33 (1.23–1.42) | 964.7 (864.5–1058.3) | 42.1 (37.8–46.0) | 41 (37–46) |
| | 13+ / pre-AI | 4.19 (2.99–5.15) | 1.75 (1.39–2.06) | 1.31 (1.22–1.41) | 981.3 (875.9–1071.9) | 42.8 (38.0–46.8) | 42 (38–46) |
| | 16+ / CAI10 | 5.40 (4.10–6.83) | 2.41 (1.89–3.03) | 1.67 (1.54–1.82) | 650.1 (482.8–765.7) | 28.1 (21.0–33.2) | 35 (29–46) |
| | 16+ / CAI5 | 5.36 (4.32–6.52) | 2.40 (1.99–2.81) | 1.65 (1.52–1.77) | 665.2 (533.9–790.9) | 28.8 (23.0–33.8) | 36 (29–43) |
| | 13+ / CAI10 | 4.37 (3.28–5.52) | 1.85 (1.38–2.28) | 1.39 (1.28–1.50) | 905.3 (792.1–1001.6) | 39.4 (34.4–43.6) | 36 (32–40) |
| | 13+ / CAI5 | 4.35 (3.47–5.35) | 1.83 (1.48–2.19) | 1.37 (1.24–1.48) | 928.5 (816.8–1041.2) | 40.4 (35.6–44.9) | 37 (32–42) |
| Sensitivity analyses | C20 | 6.44 (4.88–7.81) | 2.79 (2.24–3.30) | 1.99 (1.83–2.12) | 342.1 (201.7–469.0) | 14.7 (8.6–20.3) | 38 (25–57) |
| | C30 | 5.80 (4.41–7.12) | 2.54 (1.98–3.10) | 1.81 (1.65–1.96) | 509.9 (353.9–670.6) | 22.0 (15.2–28.8) | 37 (27–51) |
| | C40 * | 5.46 (4.31–6.62) | 2.43 (1.86–2.91) | 1.67 (1.53–1.79) | 643.3 (520.8–771.9) | 27.8 (22.3–33.3) | 38 (30–45) |
| | C50 | 5.14 (3.80–6.28) | 2.28 (1.80–2.68) | 1.55 (1.42–1.69) | 760.3 (604.6–891.5) | 32.9 (26.2–38.6) | 39 (33–48) |
| | C60 | 4.57 (3.40–6.14) | 2.08 (1.68–2.50) | 1.41 (1.26–1.54) | 894.1 (761.3–1041.1) | 38.8 (32.8–45.2) | 39 (34–46) |
| | C20 + Hi Adh | 6.18 (4.61–7.65) | 2.71 (2.17–3.19) | 1.90 (1.73–2.07) | 418.2 (225.8–581.9) | 18.0 (9.8–25.0) | 30 (21–49) |
| | C30 + Hi Adh | 5.49 (4.07–6.82) | 2.47 (1.97–3.02) | 1.69 (1.55–1.87) | 625.8 (444.5–759.4) | 27.0 (19.3–32.8) | 29 (24–40) |
| | C40 + Hi Adh | 5.02 (3.66–6.19) | 2.27 (1.83–2.78) | 1.52 (1.39–1.63) | 785.8 (673.8–902.8) | 34.0 (29.1–39.2) | 31 (26–35) |
| | C50 + Hi Adh | 4.50 (3.33–5.55) | 2.08 (1.71–2.45) | 1.35 (1.21–1.45) | 952.3 (847.3–1086.7) | 41.4 (36.7–46.9) | 31 (27–35) |
| | C60 + Hi Adh | 4.05 (3.10–5.04) | 1.92 (1.60–2.33) | 1.21 (1.10–1.33) | 1083.6 (950.9–1192.2) | 47.2 (41.2–51.8) | 33 (29–37) |
| | C20 + Low Adh | 6.74 (5.36–8.40) | 2.93 (2.21–3.47) | 2.09 (1.94–2.25) | 242.5 (74.8–383.7) | 10.4 (3.2–16.5) | 64 (30–144) |
| | C30 + Low Adh | 6.30 (4.89–7.73) | 2.72 (2.18–3.26) | 1.95 (1.79–2.10) | 372.5 (222.8–524.9) | 16.0 (9.6–22.8) | 51 (34–80) |
| | C40 + Low Adh | 5.90 (4.56–7.18) | 2.58 (2.10–2.93) | 1.84 (1.70–1.96) | 475.4 (348.0–613.0) | 20.5 (15.1–26.4) | 51 (39–67) |
| | C50 + Low Adh | 5.77 (4.36–6.77) | 2.52 (2.00–3.08) | 1.74 (1.60–1.88) | 572.4 (433.9–692.0) | 24.7 (18.9–29.7) | 53 (42–68) |
| | C60 + Low Adh | 5.45 (4.06–6.88) | 2.39 (1.88–2.90) | 1.67 (1.53–1.80) | 645.5 (510.3–764.5) | 27.9 (22.0–33.0) | 55 (45–69) |

| | Mean (95% Cred. Int.) | | | | | |
|---|---|---|---|---|---|---|
| | **Prev. among 18 year-old ASMM** | **Prev. among ASMM** | **Inc. (per 100 py) among sexually initiated ASMM** | **NIA** | **PIA** | **NNT** |
| Med prev + No PrEP | 3.43 (2.63–4.11) | 1.43 (1.18–1.67) | 1.01 (0.95–1.06) | | | |
| Med prev + scenario 1 | 3.44 (2.38–4.39) | 1.44 (1.17–1.76) | 1.02 (0.93–1.09) | 283.0 (222.6–343.2) | 21.9 (17.0–26.8) | 85 (60–90) |
| Med prev + scenario 6 | 2.65 (1.88–3.52) | 1.04 (0.81–1.26) | 0.79 (0.71–0.86) | 273.1 (192.7–336.9) | 21.1 (14.9–26.2) | 75 (47–80) |
| Low prev + No PrEP | 2.10 (1.48–2.80) | 0.85 (0.64–1.08) | 0.62 (0.56–0.67) | | | |
| Low prev + scenario 1 | 2.14 (1.57–2.76) | 0.89 (0.57–0.98) | 0.63 (0.58–0.67) | 176.0 (118.8–229.8) | 22.2 (15.0–39.0) | 141(103–197) |
| Low prev + scenario 6 | 7.54 (6.15–8.79) | 3.20 (2.66–3.74) | 2.34 (2.12–2.54) | 162.6 (119.8–205.2) | 20.5 (15.1–26.1) | 125 (95–164) |

ASMM = adolescent sexual minority males

Cred. Int = credible interval from the range of simulations

Prev. = prevalence (measured 10 years after PrEP rollout)

Inc. = incidence (per 100 person years, measured in 10th year after PrEP rollout)

NIA = number of infections averted, per 100k years of person-time at risk (measured across 10 years following PrEP rollout) PIA = percent of infections averted (measured across 10 years following PrEP rollout)

NNT = number needed to treat = person-years on PrEP per case averted (measured across 10 years following PrEP rollout)

* This scenario matches the first base scenario, but is repeated here for easier comparison with sensitivity scenarios

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