The PrEP Care Continuum and Racial Disparities in HIV Incidence among Men Who Have Sex with Men

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ABSTRACT

Background HIV preexposure prophylaxis (PrEP) could reduce the disparities in HIV incidence among black men who have sex with men (BMSM) compared to white MSM (WMSM), but this may depend on progression through the PrEP care continuum.

Methods We expanded our network-based mathematical model of HIV transmission for MSM, which simulates PrEP based on CDC's clinical practice guidelines, to include race-stratified transitions through the PrEP continuum steps of awareness, access, prescription, adherence, and retention. Continuum parameters were estimated based on published incidence cohorts and PrEP open-label studies. Counterfactuals included a no-PrEP reference scenario, and intervention scenarios in which the BMSM continuum step parameters were modified.

Results Implementing PrEP according to the observed BMSM continuum was projected to result in 8.4% of all BMSM on PrEP at year 10, yielding a 23% decline in incidence (HR = 0.77). On an absolute scale, the racial disparity in incidence in this scenario was 4.95 per 100 person-years at risk (PYAR), a 19% decline from the 6.08 per 100 PYAR disparity in the reference scenario. If BMSM continuum parameters were equal to WMSM values, 17.7% of BMSM would be on PrEP, yielding a 47% decline in incidence (HR = 0.53) and a disparity of 3.30 per 100 PYAR (a 46% decline in the disparity).

Conclusions PrEP could lower HIV incidence overall and reduce absolute racial disparities between BMSM and WMSM. Interventions addressing the racial gaps in the PrEP continuum will be needed to further decrease these HIV disparities.

KEY WORDS

Men who have sex with men; Racial disparities; Preexposure prophylaxis; Mathematical model; Sexual network

INTRODUCTION

HIV prevalence among black men who have sex with men (BMSM) is 3–6 times as high as white MSM (WMSM) across the United States [1,2]. The US Centers for Disease Control and Prevention (CDC) estimates that 1 in 2 BMSM will become infected over their lifetimes if current transmission trends continue [3]. The causes of these disparities have been challenging to quantify, as many measures of behavior associated with HIV acquisition often indicate lower risk for BMSM than WMSM [4,5]. Initiation and retention into HIV medical care, however, have been consistently worse metrics for BMSM [6], especially in the Southern US [7]. The US National HIV/AIDS Strategy has among its goals to reduce new HIV diagnoses by 25% overall and to reduce racial disparities in diagnoses on a relative scale by 15% [8]. To meet these goals, targeted and efficient scale-up of highly effective prevention tools like HIV preexposure prophylaxis (PrEP) are needed [9].

PrEP use by MSM has increased markedly since its approval by the FDA in 2012, but with substantial racial gaps. Pharmacy data suggest a 500% increase in PrEP prescriptions since 2014, yet black persons received only 10% of those despite accounting for nearly half of recent HIV cases [2,10]. Open-label PrEP studies and clinical cohorts have consistently highlighted specific challenges in reaching BMSM, supporting protective levels of PrEP adherence, and retaining them in PrEP care [11–21]. These racial gaps may limit the prevention benefits of PrEP for BMSM.

PrEP continuum models, following approaches used for HIV medical care [22], have helped to conceptually define these gaps by organizing PrEP implementation into distinct factors that may be potential targets for modification. Although several PrEP continuum models exist, they share many similarities. Kelley et al. defined the steps towards complete HIV prevention via PrEP: awareness of PrEP, access to PrEP-related healthcare services, obtaining a PrEP prescription, and adherence after initiation [23]. Race-stratified probabilities for each step were estimated based on an HIV incidence cohort in Atlanta [24]; BMSM had equal or worse outcomes on all four steps, consistent with other PrEP utilization data. Nunn et al. added a fifth step in this continuum, retention in PrEP care after initiation and effective adherence [25], also a persistent and challenging target for the HIV medical care continuum [26].

In this study, we used mathematical modeling to investigate the population-level implications of these racial gaps in the PrEP continuum for BMSM over the next decade of PrEP implementation. Reducing racial disparities in HIV incidence could be achieved with PrEP as part of a comprehensive HIV prevention approach [27], but whether that is possible given current estimates of lower PrEP initiation and retention in PrEP care for BMSM is a critical unanswered question. Our two major research aims were to project: 1) the PrEP-related reduction in HIV incidence for BMSM versus WMSM given recently observed race-specific PrEP continuum estimates; and 2) the impact of changes for each continuum step (awareness, access, prescription, adherence, and retention), individually and jointly, on disparities. We quantified disparities on both relative and absolute scales, and then evaluated the best metric for

understanding disparities in a dynamic, interventional context.

METHODS

We previously developed a robust mathematical model for HIV/STI transmission dynamics for US MSM using the *EpiModel* software platform (www.epimodel.org) [28], a generalized toolkit for simulating epidemics over complex sexual networks under the statistical framework of temporal exponential random graph models (TERGMs) [29]. Our prior applications investigated the sources of HIV racial disparities among MSM in Atlanta and the potential impact of PrEP for MSM in the US [30,31]. For this study, we integrated these two research streams to develop the model structure, parameterization, and analyses for simulating PrEP in a race-stratified approach to understand the implications of the PrEP continuum.

HIV Transmission and Progression. Our model simulates the dynamics of main, casual, and one-time MSM sexual partnerships for non-Hispanic BMSM and WMSM [30,31]. Predictors of partnership formation included partnership type, number of ongoing partnerships (degree), race and age mixing, and sorting by receptive versus insertive sexual position. For main and casual partnerships, we modeled relational dissolution as a constant hazard reflecting their median durations. Network model terms were stratified by race, with parameterization mainly from two large HIV incidence studies in Atlanta [24,32].

Men progressed through HIV disease stages in the absence of antiretroviral therapy (ART) with evolving HIV viral loads that modified the rate of HIV transmission in discordant pairs [33]. After infection, men were assigned into clinical care trajectories controlling rates of HIV diagnosis, ART initiation, and HIV viral suppression, matching empirical estimates [34,35]. ART was associated with decreased mortality and lower HIV transmissibility [36]. Other factors modifying the HIV acquisition probability included current infection with other sexually transmitted infections [37], condom use [38], sexual position [39], and circumcision of the insertive partner [40].

PrEP Continuum. We represented PrEP use based on a step-down continuum: awareness of PrEP, access to healthcare, likelihood of receiving a PrEP prescription, and effective (4+ doses per week) adherence to PrEP. Race-stratified probabilities were drawn from two PrEP demonstration projects [21,23]: 50% awareness for both races; 76% and 95% access for BMSM and WMSM, respectively; 63% and 73% receipt of a prescription; and 60% and 93% effective adherence. Awareness and access were modeled as fixed attributes assigned at entry into the network.

PrEP prescription was simulated as a Bernoulli random draw at the point of clinical evaluation for PrEP. Consistent with previous models [37], we simulated the four bio-behavioral indications defined in the CDC guidelines [41]: higher-risk sexual behavior in various partnership configurations or an STI diagnosis within the prior 6 months. Because indications were time-varying, the full probability of a PrEP prescription was a joint function of the race-specific probability of receiving a prescription plus current

indications at clinical evaluation. Given the small sample sizes of active PrEP users in Kelley et al. [23] and to maintain consistency with prior models, we based adherence step probabilities on the PrEP Demo Project, which measured men taking <2 doses, 2–3 doses, and 4–7 doses per week across 48 weeks of follow-up [21]. The estimated distribution at week 48 (conditional on prescription) for BMSM was 16.7%, 23.5%, and 59.8%; for WMSM it was 2.8%, 4.4%, and 92.8%. Taking PrEP at these weekly dosages was associated with a 31%, 81%, and 98% relative reduction in HIV acquisition risk per sexual act, following Grant et al [42] and our prior models. We simulated spontaneous discontinuation from PrEP based on drop-off rates from the PrEP Demo Project. The observed proportions who had discontinued at week 48 (43.8% for BMSM and 18.3% for WMSM) were transformed into a median time to discontinuation (1.1 years and 3.2 years, respectively) assuming a hypergeometric distribution, then transformed into a per-week probability. In addition to spontaneous discontinuation, men stopped PrEP if they no longer exhibited CDC indications (evaluated annually for active PrEP users), consistent with the guidelines [41].

Counterfactual Scenarios. To test the impact of the PrEP continuum for BMSM, we varied the probabilities for each of the five steps individually and jointly. For individual steps, we set the parameters for BMSM to those observed for WMSM and higher levels, while holding other BMSM continuum parameters fixed at the observed levels. WMSM parameters were always held fixed at their observed values across all scenarios. For scenarios modifying parameters in combination, we varied the BMSM parameters on a relative scale. Scenarios in which BMSM parameters were set to 150% of observed values, for example, multiplied each of the empirical estimates by 1.5. For one analysis, we grouped the five continuum steps into two factor groups — initiation (awareness, access, and prescription) and engagement (adherence and retention) — and then projected outcomes across a spectrum of relative BMSM values in each group.

Calibration, Simulation, and Analysis. With a starting network size of 10,000 MSM (50% in each race), we calibrated our model to empirical race-specific HIV prevalence observed in the baseline Atlanta cohort: 43.4% for BMSM and 13.2% for WMSM [24]. Due to challenges in replicating these values in prior empirical models [30], we incorporated the full 95% confidence intervals of estimated rates of anal intercourse and probabilities of condom use for calibration. We also implemented two race-specific parameters governing the probability of condom failure (due to slippage or breakage), consistently higher in BMSM [43–45], and the rate of diagnostic screening for bacterial STIs (increasing the risk of HIV if untreated), often lower for BMSM [4]. Approximate Bayesian computation methods estimated the values of these parameters best fitting the observed prevalence data [37,46].

Intervention models simulated the different counterfactual scenarios over a 10-year time horizon. For each scenario, we simulated the model 250 times and summarized the distribution of results based on median values and 95% credible intervals (middle 95% of the simulated data). Outcomes included HIV

prevalence and incidence per 100 person years at risk (at year 10), the hazard ratio comparing incidence to the no-PrEP reference scenario, and the percent of infections averted (PIA) comparing the cumulative incidence in each intervention scenario to the reference scenario. The number needed to treat (NNT) was the number of person-years on PrEP required to avert one new HIV infection. Two disparity indices were calculated to compare the performance of PrEP for BMSM versus WMSM: the absolute disparity was the difference in incidence for BMSM and WMSM, and the relative disparity was the ratio of incidence rates. We also calculated a prevention index as the difference in hazard ratios associated with PrEP uptake for BMSM and WMSM.

RESULTS

Table 1 shows the impact of individual PrEP continuum steps for BMSM at observed and other values. In comparison with the reference scenario in which no one (of either race) received PrEP, the observed PrEP continuum scenario for BMSM projected 8.4% of BMSM to be on PrEP at any time. This yielded a 5-percentage point decline in HIV prevalence (39.9% versus 45.2%) and a 23% decline in incidence (HR = 0.77). The cumulative PIA was 14.1% over the intervention horizon. We then modeled changes to individual steps. For awareness, while the observed values were equal for both races, increasing the probability for BMSM had a strong impact on PrEP use, and with that, declines in incidence. For access, setting the BMSM parameter to the observed WMSM value (95%) resulted in a smaller decline in incidence than changes to awareness. Conditional on access, empirical differences in prescription were relatively small (73% for WMSM versus 63% for BMSM); setting the BMSM parameter to observed WMSM values marginally increased the prevention effects. Increasing the proportion highly adherent did not impact the overall proportion of BMSM “on PrEP” (which includes the full distribution of adherence levels); this also resulted in a relatively small gain in the prevention effect. Increasing levels of retention on PrEP were associated with greater PrEP prevention benefits.

In Table 2, we present the projected impact of scaling the BMSM continuum parameters jointly on HIV incidence for BMSM and WMSM. Compared to the observed BMSM scenario, if all BMSM parameters were set to observed WMSM values we project that 17.7% of BMSM would actively be on PrEP. This compares to 23.4% of WMSM, with the difference due to WMSM’s higher level of CDC PrEP indications even when all continuum parameters were equal. In this observed WMSM scenario, incidence would decline faster (HR = 0.53 versus 0.77) than in the observed BMSM scenario. Scaling up BMSM continuum parameters to even higher levels (150% or 200% of observed BMSM values) would result in even greater numbers of BMSM on PrEP, with stronger incidence reductions to all BMSM.

Figure 1 graphically depicts this relative scaling of the joint BMSM parameters. Changes in outcomes are non-linear over these relative parameter changes, with the greatest marginal gains from scaling up the parameters from observed (100%) to 150%. Although we never modified the WMSM PrEP

continuum parameters (the proportion on PrEP remains at 23% across all scenarios), WMSM incidence declines from 0.93 per 100 person-years at risk (PYAR) in the observed BMSM scenario to 0.69 in the 200% scenario as a result of indirect effects (11% of sexual partnerships on average were cross-race).

The impact of PrEP on HIV disparities is shown in Figure 2 and Table 2. The absolute disparity index in the no-PrEP reference scenario was 6.08 per 100 PYAR, depicted by the dashed horizontal line. Implementing PrEP under the observed BMSM scenario would reduce the absolute disparity index compared to the reference scenario (4.95 per 100 PYAR), a 19% decline. If BMSM parameters were set to WMSM values, incidence would decline by 47% (HR = 0.53), with an absolute disparity index of 3.30 per 100 PYAR, a 46% decline. A doubling of BMSM parameters (200% scenario) would lead to an absolute disparity index of 1.04, an 83% decline. The relative disparity index suggests increasing disparities under the observed BMSM scenario (6.32 vs. 4.68), with reductions in the disparity only possible when BMSM continuum parameters are higher than WMSM values. The prevention index, the difference in hazard ratios, was effectively zero (0.01) in the scenario with BMSM parameters set to WMSM values (see Table 2), and even lower (indicating a greater prevention effect for BMSM) as the continuum is scaled up. Reductions in the absolute disparity index coincide with reductions in the prevention index. Parity in the hazard ratios by race is not necessary to reduce absolute disparities (compared to the reference scenario) but is necessary when quantifying disparities on a relative scale.

Figure 3 aggregates the PrEP continuum into two factor groups of initiation (awareness, access, and prescription) and engagement (adherence and retention). We projected the PIA and NNT across relative changes to BMSM parameters along each factor. In Panel A, greater gains in the PIA for BMSM are projected by a 10% increase in the initiation factors (moving left to right) compared to the same increase in the engagement factors (moving bottom to top), shown by the relatively vertical orientation of the bands at the 1.0/1.0 intersection. At worse than observed initiation levels, little is gained by improving engagement. In Panel B, the NNT at observed initiation factor levels ranges from approximately 6 to 14 years of BMSM person-time on PrEP to prevent one new BMSM infection. The NNT is lower as engagement is scaled up and is higher as initiation factors are scaled up. Because engagement includes adherence, scaling up adherence among BMSM increases the per-dose prevention effects; efficiency declines at higher initiation levels because of the overall decline in HIV incidence, requiring more PrEP to prevent an infection. At these higher initiation levels, improvements in the NNT would be possible through increased engagement.

DISCUSSION

Our study projected that implementation of PrEP could reduce HIV disparities on an absolute scale between BMSM and WMSM even despite current racial gaps in the HIV PrEP continuum from initiation to engagement in PrEP care. Further disparity reduction on both the absolute and relative scales with PrEP

could be achieved with interventions targeting each of the PrEP continuum steps for BMSM. Primary gains in population-level impact of PrEP would require focusing on initiation factors (awareness, access, and prescription) over engagement factors (adherence and retention), given the currently observed PrEP continuum.

Given the large HIV racial disparities among MSM in the United States [1], few HIV prevention interventions have been successful at simultaneously reducing HIV incidence overall while lowering disparities. Because of a confluence of race-specific gaps in clinical care for testing and treatment of HIV and related STIs [6], the most highly effective prevention strategies, such as early antiretroviral therapy, have benefited WMSM at greater levels than BMSM as a function of differential access to healthcare [47]. We rooted our model structure and parameters in empirical data to forecast how realistic representations of the PrEP continuum could impact HIV incidence for both black and white MSM over the next decade [30]. Our model suggests that it is possible to reduce, although not entirely close, the absolute gap in disparities in HIV incidence by race while at the same time lowering HIV incidence overall.

In this analysis, we quantified the disparities on two different scales, an absolute scale that subtracts the standardized incidence rate of WMSM from the BMSM incidence rate, and a relative scale that takes their ratio. Many policy documents and cross-sectional surveillance studies use the ratio scale: the National HIV/AIDS Strategy, for example, sets a goal to reduce racial disparities in new HIV diagnoses by a relative measure [8]. In the context of a dynamic intervention, however, we suggest that ratios are less suitable than differences for several reasons. First, the population-level burden of disease is quantified by the overall incidence rate of disease per unit of person-time. Using the absolute scale allows for expressing disparities with this same denominator approach, such as the total number of incident cases over a specific time period that could be averted under different scenarios. This parallels the choice of attribute risks (risk differences) versus relative risks to quantify public health impact of a risk factor in epidemiological studies [48]. Second, ratio scales may be misleading for some interventional scenarios, as a PrEP intervention that performs marginally better for WMSM, while reducing the difference in the number of incident infections between races, has the counterintuitive effect of increasing the disparity ratio. Third, the ratio scale is particularly unstable when the denominator is small relative to the numerator, as it is here. Therefore, we recommend that disparities in interventional studies be quantified as absolute differences rather than ratios.

Given either comparative framework for disparities, the five steps of the PrEP continuum have been useful here in conceptualizing the racial gaps in PrEP service delivery [26]. First, awareness of PrEP was the step most strongly associated with incidence reduction for BMSM in our model, due to the marginally declining conditional probabilities for the subsequent steps. There has been a wide range of findings on the awareness and willingness of BMSM to use PrEP [13,14], related to lack of knowledge about PrEP and perceived stigma related to its use [15,49,50]. Second, access to PrEP-related healthcare is

complex: even though some assistance programs are available to cover medication costs in most cases [51], PrEP requires ongoing monitoring services covered through health insurance, which may be a barrier for some BMSM [16–18]. Third, receiving a prescription depends on indications for PrEP being accurately queried by clinicians willing to prescribe PrEP and reported by their patients. BMSM are less likely to be “out” to their doctors [52], and some clinicians may be less willing to prescribe to BMSM even if they have the same indications as WMSM [53]. Fourth, adherence is critical to the ongoing success of PrEP to prevent infections, but race/ethnicity has been strongly associated with less than optimal dosing across many implementation studies [54–56]. If proven safe and effective, long-acting formulations like cabotegravir injections may benefit some BMSM with adherence barriers [57]. Fifth and lastly, greater retention in PrEP care was found to be strongly associated with both infections averted and NNT in our model. PrEP discontinuation for reasons other than lapsed indications has been a growing challenge in clinical practice as PrEP users mature [58]; parallels to suboptimal levels of patient retention for HIV medical care may be useful in considering how to address PrEP discontinuation [26]. Increasing patient engagement in PrEP care for active users, across both adherence and retention, should be an ongoing priority for BMSM in particular, given observed differences in these continuum steps [19,21].

Limitations. Our model conceptualizes racial disparities by simulating a two-race population of MSM with empirically data-driven behavioral and biological parameters for non-Hispanic black and white MSM in the Atlanta area. This analysis did not model other racial/ethnic groups, such as Hispanic MSM, for whom the gaps in the PrEP continuum may also be suboptimal [59]. Continuum parameters were also based on two studies with race-stratified estimates [21,23], and these BMSM study populations may not represent the larger populations of HIV-uninfected BMSM. Further parameter data are needed for other demographic groups or geographic settings to expand the model scope, and the generalizability of our Atlanta-focused parameters may be limited in other socioeconomic and healthcare delivery settings. Our model may be limited by the assumption that routine HIV screening is the primary point for entry into PrEP, based on the requirement that HIV testing be performed before PrEP initiation [41]. Initiation of PrEP before specific sexual risk events has also been observed [12], and our future work will explore variations in reasons for starting PrEP.

Conclusions. PrEP interventions and clinical practice should be designed and delivered to target specific steps along the PrEP continuum. Implementation of PrEP care following this paradigm at current estimated rates could achieve the dual goals of reducing HIV incidence overall and decreasing the absolute disparities in incidence between BMSM and WMSM over the next decade. Targeting the existing race-specific gaps along the PrEP continuum could make critical advances in addressing these goals.

NOTES

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REFERENCES

1 Wejnert C, Hess KL, Rose CE, Balaji A, Smith JC, Paz-Bailey G. Age-Specific Race and Ethnicity Disparities in HIV Infection and Awareness Among Men Who Have Sex With Men-20 US Cities, 2008-2014. *J Inf Dis* 2016; **213**:776–83.

2 Maulsby C, Millett G, Lindsey K, Kelley R, Johnson K, Montoya D, *et al.* HIV among Black men who have sex with men (MSM) in the United States: a review of the literature. *AIDS Behav* 2014; **18**:10–25.

3 Hess K, Hu X, Lansky A, Mermin J, Hall HI. Estimating the Lifetime Risk of a Diagnosis of HIV Infection in the United States. In: *Conference on Retroviruses and Opportunistic Infections*.; 2016. p. O-5 52.

4 Millett GA, Peterson JL, Wolitski RJ, Stall R. Greater risk for HIV infection of black men who have sex with men: a critical literature review. *Am J Public Heal* 2006; **96**:1007–19.

5 Maulsby C, Millett G, Lindsey K, Kelley R, Johnson K, Montoya D, *et al.* A systematic review of HIV interventions for black men who have sex with men (MSM). *BMC Public Health* 2013; **13**:625.

6 Rosenberg ES, Millett GA, Sullivan PS, Del Rio C, Curran JW. Understanding the HIV disparities between black and white men who have sex with men in the USA using the HIV care continuum: a modeling study. *Lancet HIV* 2014; **1**:e112–e118.

7 Mugavero MJ, Amico KR, Horn T, Thompson MA. The state of engagement in HIV care in the United States: from cascade to continuum to control. *Clin Infect Dis* 2013; **57**:1164–71.

8 White House Office of National AIDS Policy. National HIV/AIDS Strategy for the United States: Updated to 2020. ; 2015.

9 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. *N Engl J Med* 2010; **363**:2587–99.

10 Bush S, Magnuson D, Rawlings M, Hawkins T, McCallister S, Mera Giler R. Racial Characteristics of FTC/TDF for Pre-Exposure Prophylaxis Users in the US. In: *ASM Microbe*.; 2016. p. Abstract 2651.

11 Parsons JT, Rendina HJ, Lassiter JM, Whitfield THF, Starks TJ, Grov C. Uptake of HIV pre-exposure prophylaxis (PrEP) in a national cohort of gay and bisexual men in the United States. *J Acquir Immune Defic Syndr* 2017; **74**:285–292.

12 Elopre L, Kudroff K, Westfall AO, Overton ET, Mugavero MJ. Brief Report: The Right People, Right Places, and Right Practices: Disparities in PrEP Access Among African American Men, Women, and MSM in the Deep South. *J Acquir Immune Defic Syndr* 2017; **74**:56–59.

13 Khanna AS, Michaels S, Skaathun B, Morgan E, Green K, Young L, *et al.* Preexposure Prophylaxis Awareness and Use in a Population-Based Sample of Young Black Men Who Have Sex With Men. *JAMA Intern Med* 2016; **176**:136–8.

14 Eaton LA, Driffin DD, Bauermeister J, Smith H, Conway-Washington C. Minimal Awareness and Stalled Uptake of Pre-Exposure Prophylaxis (PrEP) Among at Risk, HIV-Negative, Black Men Who Have Sex with Men. *AIDS Patient Care STDS* 2015; **29**:423–9.

15 Fallon SA, Park JN, Ogbue CP, Flynn C, German D. Awareness and Acceptability of Pre-exposure HIV Prophylaxis Among Men Who have Sex with Men in Baltimore. *AIDS Behav* 2017; **21**:1268–1277.

16 Lelutiu-Weinberger C, Golub SA. Enhancing PrEP Access for Black and Latino Men Who Have Sex With Men. *J Acquir Immune Defic Syndr* 2016; **73**:547–555.

17 Marcus JL, Hurley LB, Hare CB, Silverberg MJ, Volk JE. Disparities in Uptake of HIV Preexposure Prophylaxis in a Large Integrated Health Care System. *Am J Public Health* 2016; **106**:e2-3.

18 Patel RR, Mena L, Nunn A, McBride T, Harrison LC, Oldenburg CE, *et al.* Impact of insurance coverage on utilization of pre-exposure prophylaxis for HIV prevention. *PLoS One* 2017; **12**:e0178737.

19 Arnold T, Brinkley-Rubinstein L, Chan PA, Perez-Brumer A, Bologna ES, Beauchamps L, *et al.* Social, structural, behavioral and clinical factors influencing retention in Pre-Exposure Prophylaxis (PrEP) care in Mississippi. *PLoS One* 2017; **12**:e0172354.

20 Smith DK, Toledo L, Smith DJ, Adams MA, Rothenberg R. Attitudes and program preferences of African-American urban young adults about pre-exposure prophylaxis (PrEP). *AIDS Patient Care STDS* 2012; **24**:408–21.

21 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 Intern Med* 2016; **176**:75–84.

22 Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis* 2011; **52**:793–800.

23 Kelley CF, Kahle E, Siegler A, Sanchez T, Del Rio C, Sullivan PS, *et al.* Applying a PrEP Continuum of Care for Men who Have Sex with Men in Atlanta, GA. *Clin Infect Dis* 2015; **61**:1590–7.

24 Sullivan PS, Rosenberg ES, Sanchez TH, Kelley CF, Luisi N, Cooper HL, *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**:445–54.

25 Nunn AS, Brinkley-Rubinstein L, Oldenburg CE, Mayer KH, Mimiaga M, Patel R, *et al.* Defining the HIV pre-exposure prophylaxis care continuum. *AIDS* 2017; **31**:731–734.

26 Mugavero MJ, Amico KR, Horn T, Thompson MA. The state of engagement in HIV care in the United States: from cascade to continuum to control. *Clin Infect Dis* 2013; **57**:1164–71.

27 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. *Sex Transm Dis* 2015; **42**:88–92.

28 Jenness SM, Goodreau SM, Morris M. EpiModel: An R Package for Mathematical Modeling of Infectious Disease over Networks. *bioRxiv* 2017; :213009.

29 Krivitsky PN, Handcock MS. A Separable Model for Dynamic Networks. *J R Stat Soc Ser B Stat Methodol* 2014; **76**:29–46.

30 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. *Lancet HIV* 2017; **4**:e311–e320.

31 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. *J Inf Dis* 2016; **214**:1800–1807.

32 Hernández-Romieu AC, Sullivan PS, Rothenberg R, Grey J, Luisi N, Kelley CF, *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**:505–12.

33 Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G, *et al.* Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. *J Inf Dis* 2012; **205**:358–365.

34 Beer L, Oster AM, Mattson CL, Skarbinski J. Disparities in HIV transmission risk among HIV-infected black and white men who have sex with men, United States, 2009. *AIDS* 2014; **28**:105–14.

35 Beer L, Mattson CL, Bradley H, Shouse RL. Trends in ART prescription and viral suppression among HIV-positive young adults in care in the United States, 2009-2013. *J Acquir Immune Defic Syndr* 2017; :1.

36 Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al.* Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; **365**:493–505.

37 Jenness SM, Weiss KM, Goodreau SM, Gift T, Chesson H, Hoover KW, *et al.* Incidence of Gonorrhea and Chlamydia Following Human Immunodeficiency Virus Preexposure Prophylaxis Among Men Who Have Sex With Men: A Modeling Study. *Clin Infect Dis* 2017; **65**:712–18.

38 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. *J Acquir Immune Defic Syndr* 2015; **68**:337–44.

39 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.

40 Wiysonge CS, Kongnyuy EJ, Shey M, Muula AS, Navti OB, Akl EA, *et al.* Male circumcision for prevention of homosexual acquisition of HIV in men. *Cochrane Database Syst Rev* 2011; :CD007496.

41 Centers for Disease Control and Prevention. Preexposure prophylaxis for the prevention of HIV infection in the United States–2014: A Clinical Practice Guideline. ; 2014.

42 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. *Lancet Infect Dis* 2014; **14**:820–9.

43 Crosby RA. State of condom use in HIV prevention science and practice. *Curr HIV/AIDS Rep* 2013; **10**:59–64.

44 Hernández-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. *Sex Transm Infect* 2014; **90**:602–7.

45 Kim M, McKenney J, Khosropour CM, Prater AB, Rosenberg ES, Siegler AJ, *et al.* Factors Associated With Condom Breakage During Anal Intercourse: A Cross-Sectional Study of Men Who Have Sex With Men Recruited in an Online Survey. *JMIR Public Heal Surveill* 2016; **2**:e7.

46 Toni T, Welch D, Strelkowa N, Ipsen A, Stumpf MPH. Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. *J R Soc Interface* 2009; **6**:187–202.

47 Hall HI, Frazier EL, Rhodes P, Holtgrave DR, Furlow-Parmley C, Tang T, *et al.* Differences in human immunodeficiency virus care and treatment among subpopulations in the United States. *JAMA Intern Med* 2013; **173**:1337–44.

48 Rothman KJ, Greenland S, Lash T. *Modern Epidemiology, Third Edition*. ; 2014. doi:10.1002/hast.292

49 Eaton LA, Kalichman SC, Price D, Finneran S, Allen A, Maksut J. Stigma and Conspiracy Beliefs Related to Pre-exposure Prophylaxis (PrEP) and Interest in Using PrEP Among Black and White Men and Transgender Women Who Have Sex with Men. *AIDS Behav* 2017; **21**:1236–1246.

50 Brooks RA, Landovitz RJ, Regan R, Lee S-J, Allen VC. Perceptions of and intentions to adopt HIV pre-exposure prophylaxis among black men who have sex with men in Los Angeles. *Int J STD AIDS* 2015; **26**:1040–8.

51 Smith DK, Van Handel M, Huggins R. Estimated coverage to address financial barriers to HIV preexposure prophylaxis among persons with indications for its use, United States, 2015. *J Acquir Immune Defic Syndr* 2017; **Epub ahead**. doi:10.1097/QAI.0000000000001532

52 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.

53 Calabrese SK, Earnshaw VA, Underhill K, Hansen NB, Dovidio JF. The impact of patient race on clinical decisions related to prescribing HIV pre-exposure prophylaxis (PrEP): assumptions about sexual risk compensation and implications for access. *AIDS Behav* 2014; **18**:226–40.

54 Vaughan AS, Kelley CF, Luisi N, del Rio C, Sullivan PS, Rosenberg ES. An application of propensity score weighting to quantify the causal effect of rectal sexually transmitted infections on incident HIV among men who have sex with men. *BMC Med Res Methodol* 2015; **15**:25.

55 Amico KR, Stirratt MJ. Adherence to preexposure prophylaxis: current, emerging, and anticipated bases of evidence. *Clin Infect Dis* 2014; **59 Suppl 1**:S55-60.

56 Marcus JL, Hurley LB, Hare CB, Nguyen DP, Phengrasamy T, Silverberg MJ, *et al.* Preexposure Prophylaxis for HIV Prevention in a Large Integrated Health Care System: Adherence, Renal Safety, and Discontinuation. *J Acquir Immune Defic Syndr* 2016; **73**:540–546.

57 Markowitz M, Frank I, Grant RM, Mayer KH, Elion R, Goldstein D, *et al.* Safety and tolerability of long-acting cabotegravir injections in HIV-uninfected men (ECLAIR): a multicentre, double-blind, randomised, placebo-controlled, phase 2a trial. *Lancet HIV* 2017; **4**:e331–e340.

58 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. *J Int AIDS Soc* 2016; **19**. doi:10.7448/IAS.19.1.20903

59 Davey DJ, Bustamante MJ, Wang D, Young S, Klausner JD. PrEP continuum of care for MSM in Atlanta and Los Angeles County. *Clin Infect Dis* 2016; **62**:402–403.

TABLES

Table 1. Proportion on HIV Preexposure Prophylaxis (PrEP), HIV Prevalence and Incidence per 100 PYAR at Year 10, Hazard Ratio of Incidence at Year 10 and Percent of Infections Averted (PIA) over 10 Years Compared to the Reference (No PrEP) Scenario among Black MSM, by PrEP Continuum Step Values

Scenario	% On PrEP *95% CrI*[3]	HIV Prevalence *95% CrI*	HIV Incidence *95% CrI*	Hazard Ratio *95% CrI*	PIA *95% CrI*
Reference (No PrEP)	0.0 (0.0, 0.0)	45.2 (43.0, 47.4)	7.73 (6.51, 9.07)	-	-
Aware of PrEP (%)					
30%	5.0 (4.3, 5.5)	41.8 (39.8, 43.8)	6.54 (5.47, 7.68)	0.85, 0.68, 1.09)	9.3 (1.8, 15.3)
50% (Obs B & W)[1,2]	8.4 (7.7, 9.1)	39.9 (38.1, 41.6)	5.88 (4.66, 7.05)	0.77 (0.57, 0.99)	14.1 (8.2, 21.0)
70%	12.0 (11.2, 12.8)	37.7 (35.7, 39.5)	5.24 (4.43, 6.25)	0.68 (0.55, 0.88)	20.0 (13.8, 26.9)
90%	15.6 (14.8, 16.5)	35.9 (34.2, 37.8)	4.68 (3.88, 5.57)	0.61 (0.48, 0.78)	25.0 (18.7, 30.4)
Access to PrEP Given Awareness					
50%	5.4 (4.9, 5.9)	41.4 (39.6, 43.3)	6.43 (5.30, 7.52)	0.84 (0.65, 1.06)	10.1 (3.3, 16.4)
76% (Obs B)[1]	8.4 (7.7, 9.1)	39.9 (39.1, 41.6)	5.88 (4.66, 7.05)	0.77 (0.57, 0.99)	14.1 (8.2, 21.0)
85%	9.4 (8.8, 10.1)	39.1 (37.5, 41.0)	5.65 (4.73, 6.81)	0.73 (0.58, 0.95)	15.9 (10.3, 22.4)
95% (Obs W)[2]	10.6 (9.9, 11.5)	38.5 (36.3, 40.3)	5.54 (4.56, 6.48)	0.72 (0.56, 0.94)	18.2 (10.8, 24.9)
Prescribed PrEP Given Access					
50%	7.2 (6.5, 7.8)	40.4 (38.4, 42.2)	6.14 (5.13, 7.02)	0.81 (0.64, 0.99)	12.9 (4.8, 18.5)
63% (Obs B)[1]	8.4 (7.7, 9.1)	39.9 (38.1, 41.6)	5.88 (4.66, 7.05)	0.77 (0.57, 0.99)	14.1 (8.2, 21.0)
73% (Obs W)[2]	9.2 (8.5, 9.9)	39.5 (37.6, 41.3)	5.83 (4.84, 6.90)	0.75 (0.59, 0.98)	15.4 (8.8, 21.7)
85%	10.1 (9.4, 10.9)	38.9 (36.8, 40.5)	5.64 (4.54, 6.73)	0.74 (0.54, 0.95)	17.3 (9.5, 23.4)
Full Adherence Given Prescription					
50%	8.3 (7.7, 8.9)	39.8 (38.1, 41.8)	5.98 (4.78, 7.04)	0.78 (0.58, 1.02)	14.2 (6.0, 20.5)
60% (Obs B)[1]	8.4 (7.7, 9.1)	39.9 (38.1, 41.6)	5.88 (4.66, 7.05)	0.77 (0.57, 0.99)	14.1 (8.2, 21.0)
75%	8.6 (7.8, 9.2)	39.3 (37.2, 41.1)	5.70 (4.61, 6.73)	0.75 (0.56, 0.93)	15.6 (9.9, 23.3)
93% (Obs W)[2]	8.8 (8.1, 9.4)	38.9 (37.0, 40.6)	5.59 (4.66, 6.78)	0.74 (0.58, 0.95)	16.5 (10.1, 22.6)
Time on PrEP before Discontinuation Given Prescription					
1 year	7.9 (7.2, 8.6)	40.1 (37.9, 42.0)	5.97 (4.89, 7.02)	0.78 (0.60, 0.99)	13.7 (7.6, 20.0)
1.1 years (Obs B)[1]	8.4 (7.7, 9.1)	39.9 (38.1, 41.6)	5.88 (4.66, 7.05)	0.77 (0.57, 0.99)	14.1 (8.2, 21.0)
2 years	10.7 (9.9, 11.4)	38.6 (36.8, 40.6)	5.45 (4.41, 6.69)	0.71 (0.54, 0.93)	17.5 (11.0, 23.7)
3.16 years (Obs W)[2]	12.3 (11.6, 13.0)	37.8 (35.6, 39.4)	5.23 (4.11, 6.22)	0.68 (0.52, 0.87)	20.0 (13.5, 26.8)

[1] Observed PrEP Continuum value for Black MSM. [2] Observed PrEP Continuum value for White MSM. [3] CrI = credible intervals.

Table 2. Proportion of MSM on HIV Preexposure Prophylaxis (PrEP), HIV Incidence per 100 PYAR at Year 10, Hazard Ratio of Incidence at Year 10 Compared to the Reference (No PrEP) Scenario, by Race, and Disparity Indices, Across Combined Relative PrEP Continuum Indicator Scenarios for Black MSM

Scenario	Black MSM Outcomes			White MSM Outcomes			Disparity Indices		
	% On PrEP *95% CrI*[4]	HIV Incidence *95% CrI*	Hazard Ratio *95% CrI*	% On PrEP *95% CrI*	HIV Incidence *95% CrI*	Hazard Ratio *95% CrI*	Absolute[1] *95% CrI*	Relative[2] *95% CrI*	Prevention[3] *95% CrI*
Reference (No PrEP)	0.0 (0.0, 0.0)	7.73 (6.51, 9.07)	-	0.0 (0.0, 0.0)	1.65 (1.27, 2.07)	-	6.08	4.68	-
Combined PrEP Continuum for BMSM									
Obs. B x 50% Rel.	0.8 (0.6, 0.9)	7.38 (6.20, 8.69)	0.97 (0.74, 1.19)	23.4 (22.3, 24.5)	1.00 (0.69, 1.32)	0.61 (0.40, 0.88)	6.38	7.38	0.36
Obs. B	8.4 (7.7, 9.1)	5.88 (4.66, 7.05)	0.77 (0.57, 0.99)	23.4 (22.4, 24.4)	0.93 (0.68, 1.23)	0.56 (0.40, 0.86)	4.95	6.32	0.21
Obs. W	17.7 (16.8, 18.7)	4.15 (3.36, 4.98)	0.53 (0.43, 0.70)	23.4 (22.2, 24.5)	0.85 (0.59, 1.15)	0.52 (0.34, 0.79)	3.30	4.88	0.01
Obs. B x 150% Rel.	27.2 (26.1, 28.4)	3.06 (2.33, 3.80)	0.39 (0.29, 0.51)	23.5 (22.4, 24.5)	0.77 (0.47, 1.10)	0.47 (0.28, 0.73)	2.29	3.97	-0.08
Obs. B x 200% Rel.	42.1 (40.8, 43.4)	1.73 (1.33, 2.17)	0.22 (0.17, 0.32)	23.5 (22.4, 24.6)	0.69 (0.48, 0.99)	0.42 (0.27, 0.66)	1.04	2.51	-0.2

[1] Absolute disparity index = BMSM HIV incidence - WMSM HIV incidence. [2] Relative disparity index = BMSM HIV incidence / WMSM HIV incidence. [3] Prevention index = BMSM hazard ratio - WMSM hazard ratio. [4] CrI = credible intervals.

FIGURES

Figure 1. Empirical distribution of model simulations (n = 250 in each scenario) for HIV prevalence and HIV incidence (per 100 person-years at risk) at Year 10 for BMSM and WMSM across relative values of the combined BMSM PrEP continuum (awareness, access, prescription, adherence, and retention). Relative value 1.0 is the observed BMSM continuum values, 0.5 is half of those observed, and 2.0 is twice those observed.

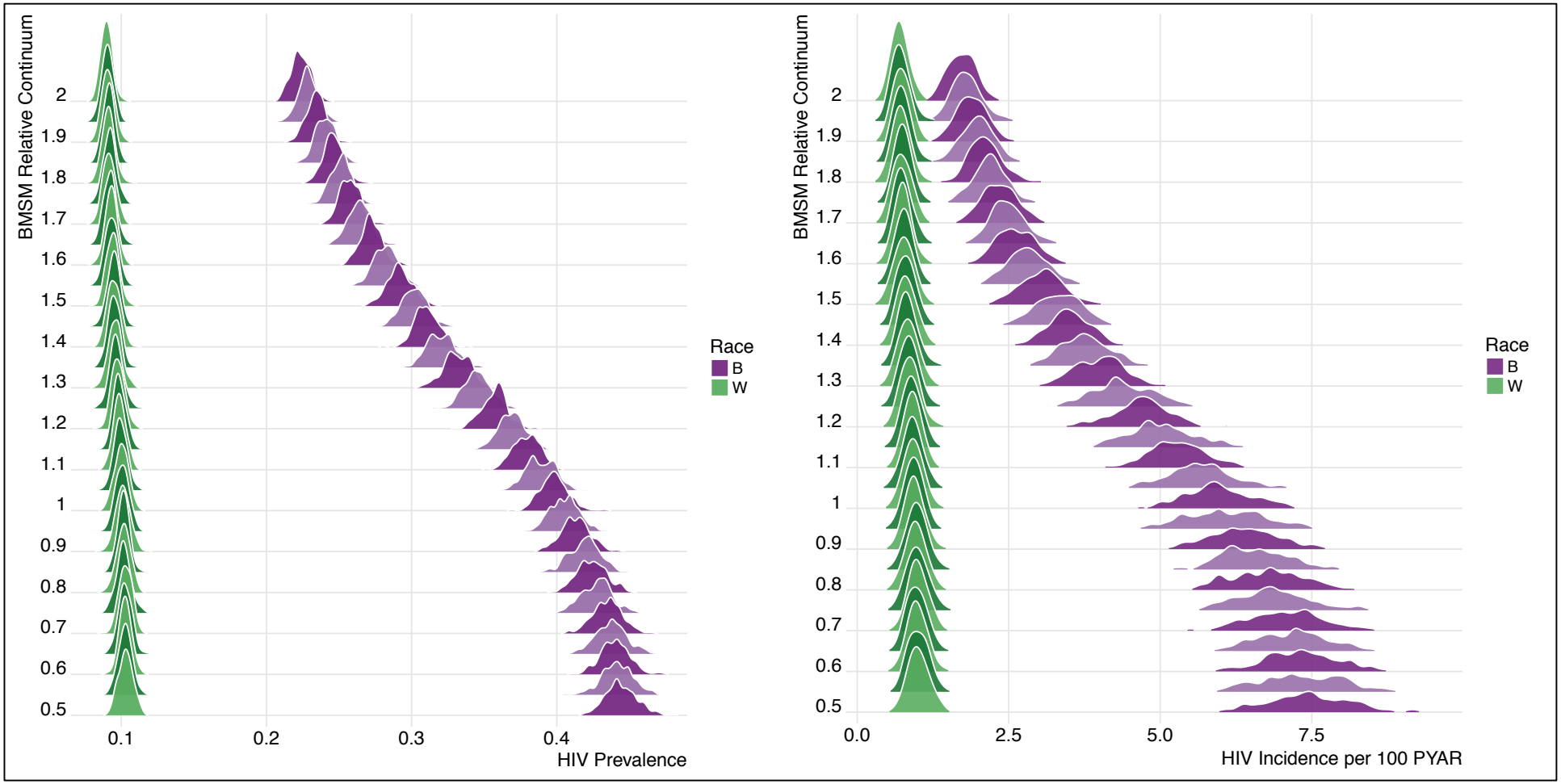

Figure 2. The absolute disparity index (HIV incidence in BMSM - HIV incidence in WMSM) and Prevention Index (HR from HIV preexposure prophylaxis [PrEP] for black MSM [BMSM] - HR from PrEP for white MSM [WMSM]) across relative values of the combined BMSM PrEP continuum, at year 10. Dashed horizontal line shows the pre-PrEP disparity index; dotted vertical line shows the empirical BMSM continuum values.

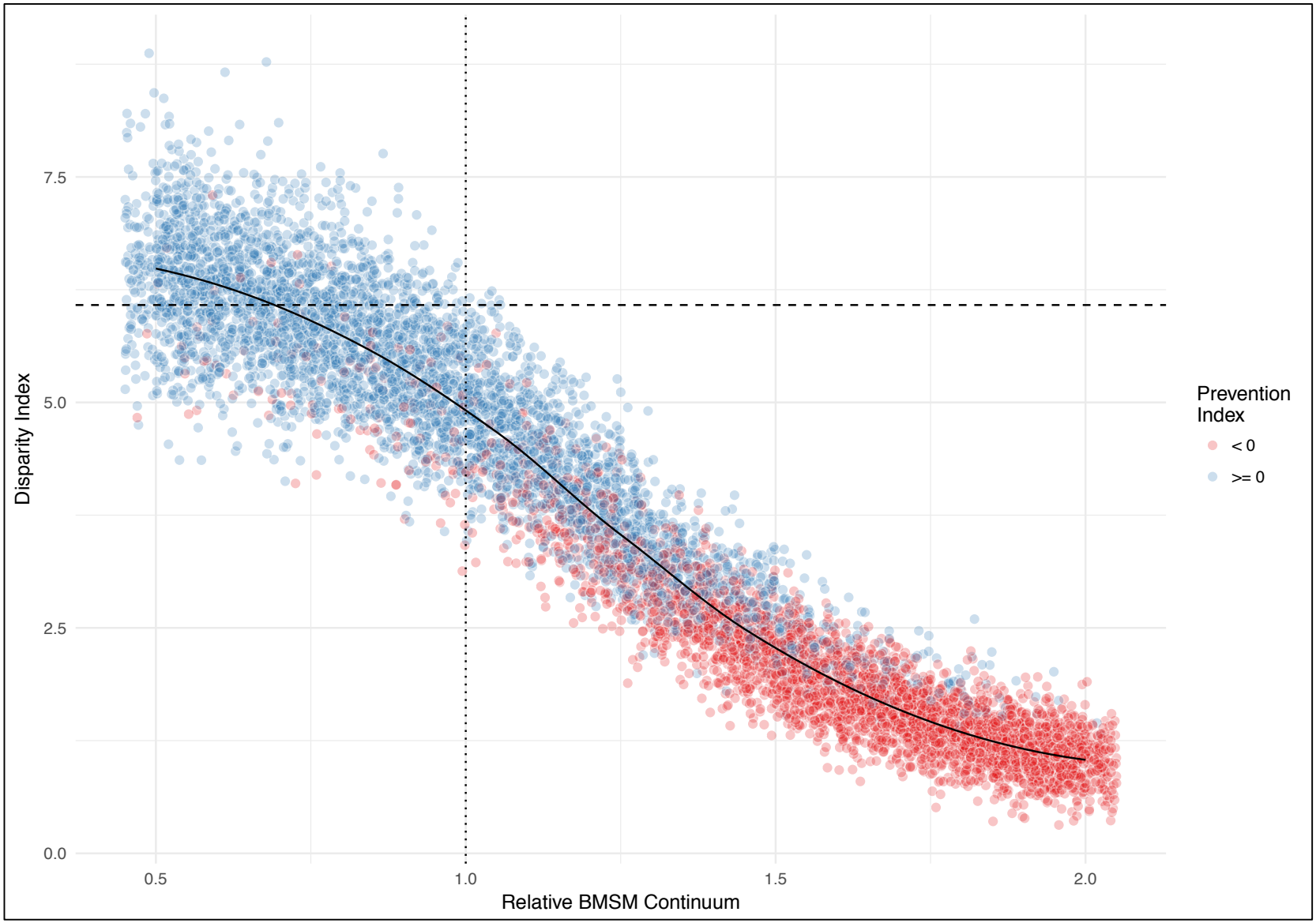
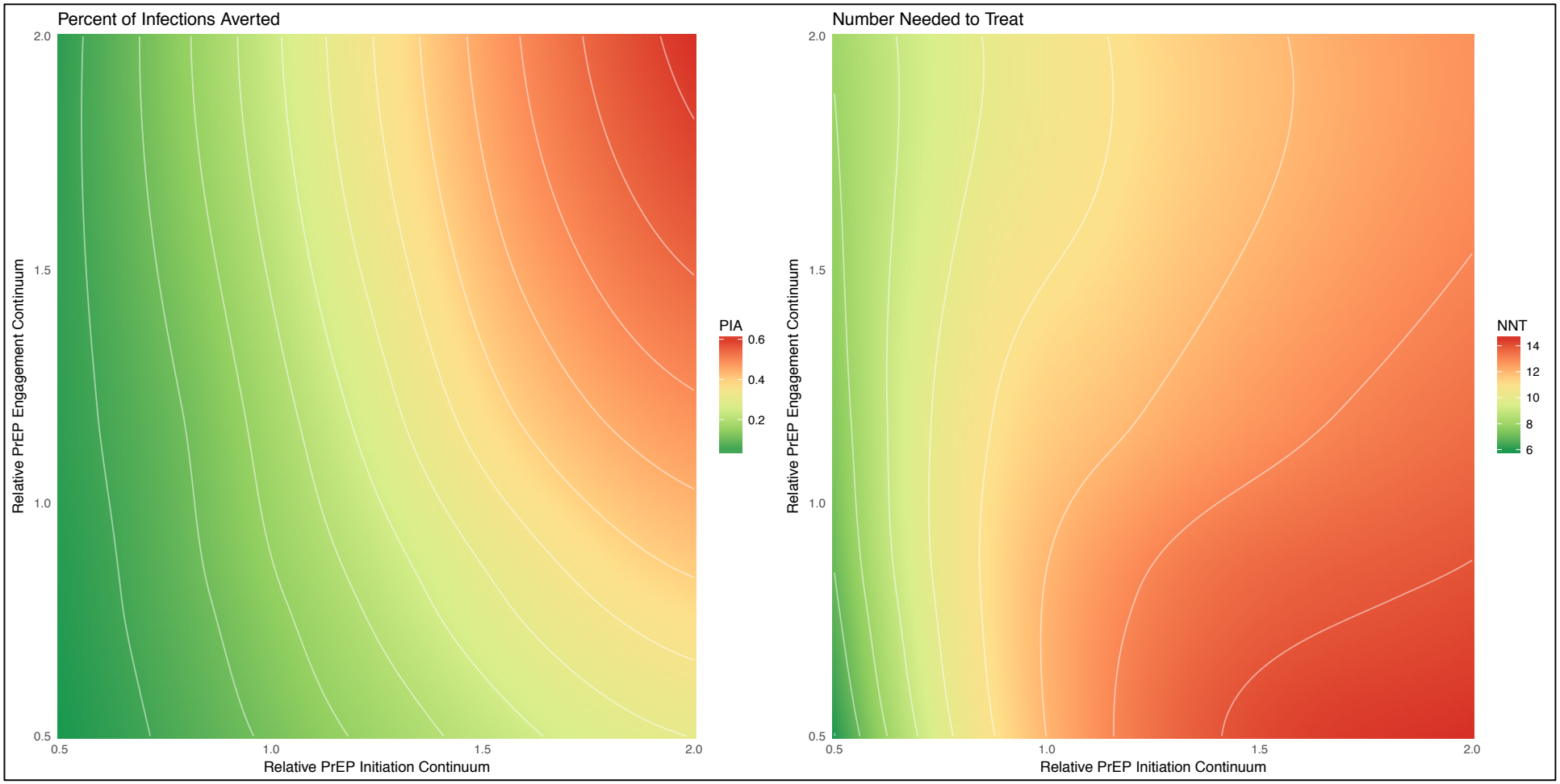
Figure 3. The percent of infections averted (PIA) and number needed to treat on PrEP for one year to prevent one new HIV infection across relative values of the combined BMSM PrEP continuum for initiation (factors = awareness, access, and prescription) versus engagement (factors = adherence and retention).