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Network Targeting of HIV Preexposure Prophylaxis to
Men Who Have Sex with Men

By

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Master of Public Health

Epidemiology

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Faculty Thesis Advisor

Acknowledgements

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Bachelor of Science
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Contents

ABSTRACT

Background Partnership concurrency plays a critical role in HIV/STI transmission dynamics. Network connectivity is expanded due to concurrency, allowing for rapid HIV transmission within sexual networks of men who have sex with men (MSM). Because of this, network-based behavioral indications may be efficient strategies for targeting HIV preexposure prophylaxis (PrEP).

Methods We used stochastic network-based models of HIV transmission dynamics among MSM to estimate the impact of PrEP delivered based on network features. Connectivity within the network was determined by index and partner degree. We estimated the percentage of infections averted (PIA) and the number of person-years on PrEP to prevent one HIV infection (NNT) under the CDC's clinical practice guidelines (standard of care) compared to network-based indications. We modeled the contribution of network indications while varying the partner thresholds for them, also considering varied coverage, risk window, and risk reevaluation parameters.

Results Compared to a counterfactual model in which there was no PrEP coverage, the CDC guidelines scenario averted 15.1% of HIV infections, while the network-based scenario (index and partner degree) averted 11.4%. However, the network-based scenario only required 18 person-years on PrEP to prevent 1 new HIV infection, while the CDC scenario had an NNT of 24. The index degree indication on its own performed better than the partner degree indication in every variation of parameters. Increasing the probability of starting PrEP from 35% (base parameter) to 60% was associated with an increase in the percent of averted infections in both the CDC scenario (23.4%) and the network scenario (18.7%).

Conclusions Using network-based indications to target MSM for PrEP in place of the current CDC indications averts fewer overall infections but require less person-time on PrEP. As PrEP coverage continues to increase, network indications provide insight into an efficient way to distribute men along the MSM population.

INTRODUCTION

In 2017, the state of Georgia had almost 2,700 new HIV infections, almost 80% of these infections being in men.[1] More than 50% of these infections were from the Atlanta area (Dekalb and Fulton county). This makes Georgia the US state with the 5th highest HIV incidence.[2] Seventy percent of HIV infections in the state are categorized as "male-to-male sexual contact" transmissions.[1] Preexposure prophylaxis (PrEP) has been shown in randomized control trials as well as observational studies to effectively prevent MSM from acquiring HIV, even in the presence of behavioral risk compensation (e.g., decreased condom use).[3,4,5] In 2014, the Centers for Disease Control and Prevention (CDC) established clinical practice guidelines that provide recommendations on which MSM are ideal candidates for PrEP.[6] These guidelines were revised in 2017, and the current PrEP indications for MSM are: 1) Any male sex partners in the past 6 months; 2) Not in a monogamous partnership with a recently tested, HIV negative man; and 3) Any anal sex without condoms in the past 6 months OR a bacterial sexually transmitted disease (gonorrhea, syphilis, or chlamydia) diagnosed in the past 6 months.

There is strong evidence for PrEP's pharmacological ability to prevent HIV infection,[3,4,5] but understanding how PrEP can effectively target those within underserved and high-risk populations is a complex challenge for HIV implementation science. Mathematical modeling has been useful in projecting the potential HIV prevention levels that may be achievable with PrEP. One model in the United Kingdom estimated a reduction in HIV incidence in 25%, 50%, 75%, and 100% PrEP coverage models compared to a no-PrEP model.[7] Only about 35% of MSM are estimated to be on PrEP, though this proportion has increased every year since PrEP was approved by the Federal Drug Administration in 2012.[8] In a different iteration of this work, the 2014 CDC indications for PrEP in an MSM population in Atlanta were modeled to that the new indications resulted in declines in HIV prevalence and incidence.[9] PrEP coverage and adherence levels are driving forces of HIV outcomes in the MSM network.[10] While increasing PrEP coverage is important to HIV prevention, quantifying connectivity in the MSM network's role in HIV infection proliferation can provide insight into how to better indicate individuals for PrEP.[11]

The current CDC indications focus individual-level characteristics and behaviors, as described previously. However, networks are important: the interconnectivity of MSM networks is one reason HIV transmission among MSM is disproportionately high compared to heterosexual networks.[12] Concurrency

(the number of concurrent partnerships) has been studied as a possible driving factor of HIV transmission because overlapping partnerships can exponentially increase chains of transmission.[12,13] Concurrency is a function of network degree, or the number of ongoing and overlapping partnerships (concurrency is a binary categorization of a degree of 2 or more). Another downstream quantification of network connectedness is the degree of one's partners. There has been no previous study in HIV modeling that has used these network statistics to evaluate the impact of indicate MSM for PrEP based on network criteria. Exploring index and partner degree as PrEP indications in comparison to the CDC guidelines can provide insight into how targeting prevention techniques based on connectivity can reduce HIV incidence and improve prevention targets among MSM.

In this study, we compared predicted HIV outcomes of the three current CDC indications to network-based indications, parameterized by data from a previous study of Atlanta MSM. We analyzed the prevalence and incidence of each scenario, but also calculated the number and percent of infections averted, the number of years on PrEP needed to prevent one HIV infection, and also the proportion of MSM eligible for PrEP in each scenario. The two network-level characteristics measured and then subsequently used as PrEP indications in this analysis are individual (or index) degree and partner degree. Additionally, we examined how varying the degree indication thresholds, the risk window, the risk reevaluation period, and coverage affect HIV outcomes.

METHODS

Study Design. We used a network-based mathematical model of dynamic HIV transmission, building on a previous modeling study that explored the racial disparities in HIV incidence in the US.[14] We built this model with EpiModel software package in the R statistical computing environment.[15] The model parameters for sexual behavior were derived from two empirical studies, where the study population was MSM in Atlanta, Georgia, ages 18-40.[9,16]

HIV Transmission and Progression. As in previous studies,[17] we modeled sexual contacts over the network using exponential random graph models.[18] An important network stratification in this model was partnership type, of which there were three: main, casual, and one-off.[19] Partnership formation was determined by individual and partner age, race, and sexual role (insertive versus receptive) distributions

based on empirical data.[14] Partnership duration (and subsequent dissolution) was similarly determined by the distribution of partnership durations.

When serodiscordant partnerships were formed in the model, infection of the HIV-negative partner was dependent on the transmission probability specific to that partnership. Transmission probability per sexual act was a function of HIV-positive partner viral load (including HIV-positive partner use of anti-retroviral therapy),[20,21] number of sexual acts, per-act condom use,[22] circumcision of the insertive partner,[23,24] presence of the allele of the CCR5 gene,[25,26] and sexual position.[17] After infection, individuals were assigned a HIV clinical care continuum trajectory that matched empirical estimates of these states: receiving HIV diagnosis, initiating anti-retroviral therapy, or becoming virally suppressed.[14]

PrEP Indications. To compare current CDC guidelines clinical practice guidelines that have specific recommendations for targeting PrEP, we represented the 2017 CDC PrEP guidelines for MSM (Table 1).[6] Meeting any of the following conditions in the past 6 months indicated that a physician should offer PrEP as an option for any individual who falls under the indication definition. The CDC indications were as follows: 1) Condom-less anal intercourse in a monogamous and seroconcordant negative partnership if one of the individuals has not been tested in 6 months; 2) Not being in a monogamous partnership with recently (6 months) tested HIV negative man; and 3): Any sexually transmitted infection (STI) diagnosis, specifically gonorrhea and chlamydia in this model.

The network measures this study aims to compare with the CDC indications were index degree and partner degree. Index degree (Condition 2) was the total number of partners, up to 5 for the sake of this study, an individual has at any one time during the risk window. Partner degree (Condition 3) was the total number of partners the individual's partners have, also with a maximum of 5, during the risk window. The partner degree was calculated by summing the index degrees of each partner node.

PrEP coverage was the number of people in the network who go on PrEP once they meet the indications, estimated to be about 15–20%.[8] PrEP adherence refers to how individuals adhere to their doctors' directions to take PrEP once daily. Individuals were placed into either the low-, mid-, or high-adherence groups based on the following respective probabilities: 8.9%, 12.7%, and 78.5%.[27] Adherence affected the relative risks of HIV infection because PrEP because low-adherence individuals benefited less from PrEP than high-adherence individuals.

PrEP uptake was determined by indications occurring within a six-month risk history window.[6] The risk window is varied in a sensitivity analysis. Individuals were simulated to attend the clinic, and when they had at least one PrEP indication specified for the given scenario within the risk history window, they were indicated for PrEP use.

PrEP discontinuation was determined during reevaluation, which was weekly (instantaneous) by default in the model. We explored the effect of different intervals in a sensitivity analysis. This parameter represents formal PrEP discontinuation. Our model also accounts for spontaneous PrEP discontinuation, which occurred among MSM based on lack of access or reduced perceived risk.

Model Simulation. This model was calibrated using approximate Bayesian computation methods.[28] The burn-in model began with 10,000 MSM for a fifty-year period, in which men entered the network at sexual maturity and exited the network at death or age 40. After model calibration to simulate the HIV epidemic before the presence of PrEP, the simulation continued with a 5-year period in which the CDC indications only are implemented. The current understanding was that about 20% of MSM in the target population would currently be on PrEP, so this 5-year period aimed to simulate the current level of PrEP use. From this point, we modeled each PrEP scenario separately for 10 years (Table 1) at which index and partner degree thresholds were 2. In order to further understand the dynamics of these network measures in targeting MSM for PrEP use, we also examined Scenarios 4 and 5 with different index and partner degree thresholds, ranging from 1–5 for one threshold while holding the other threshold at 2. Each time step was one week. We simulated each scenario 250 times and presented the means and 95% credible intervals for each summary measure based of the stochastic nature of these models.

The following measures were calculated from epidemic simulation data: HIV incidence, HIV prevalence, number of infections averted (NIA), percentage of infections averted (PIA), and number of person-years on PrEP needed to prevent one new HIV infection (NNT). The base scenario was used to calculate HIV outcomes in a no-PrEP scenario that runs for 65 years. HIV incidence at the end of each intervention was reported as the average incidence over the last year of the intervention. We reported the HIV prevalence at the very end of the intervention. NIA was calculated by subtracting the cumulative incidence over the PrEP indication years (the last 10 years of the simulation) of the intervention scenario

from the cumulative incidence of Scenario 1. PIA was calculated by dividing NIA by the cumulative incidence of Scenario 1. NNT was calculated by dividing the number of person-years on PrEP by the NIA.

RESULTS

The base scenario represents a no-PrEP scenario used as the comparison for all other scenarios in Table 1. The scenario used for the sake of comparison throughout this paper is Scenario 1, as this simulated how PrEP prevented HIV infection following CDC indications (standard of care).

Table 2 and Figure 1 depict the HIV outcomes for all five scenarios, with index and partner degree thresholds held at 2 for the network indications. The CDC indications performed well in that they averted approximately 414 infections after indicating about half of the population for PrEP. However, in the context of NNT, the CDC indications scenario performed less efficiently, in that it required 24 person-years on PrEP to prevent one HIV infection. The scenario with all five indications (Scenario 5) performed best but was not far superior to the scenario with just CDC PrEP indications.

Only indicating PrEP based on their partner degree (Scenario 3) performed poorly in terms of eligibility and percent of eligible individuals who are currently on PrEP. However, when comparing the NNT of each scenario, there was no difference between Scenario 5 and Scenario 1. The number of person-years on PrEP needed to treat prevent one HIV infection was effectively the same. On the other hand, the network PrEP indications (Scenarios 2, 3, and 4) required less person-years on PrEP to prevent one HIV infection, though preventing fewer infections overall. Targeting based on network connectivity, rather than based on the CDC guidelines, prevented fewer infections overall but prevented infections more efficiently. While targeting individuals in the network based on their partner degree had an effect on the overall HIV outcomes, it did not significantly improve outcomes when used in combination with index degree.

When using just the index and partner degree PrEP indications, the strictest threshold, where index or partner degree thresholds were held at 1, indicated more than half of the population for PrEP. The median number of infections averted dropped by 45% between an index threshold of 1 and an index threshold of 2 (holding partner degree threshold at 2). However, targeting index degree of three, four, and five was a more efficient way to target the most connected people in the network, as the median number

of years on PrEP needed to prevent one HIV infection is around 16 years for each of these while the median number of years on PrEP needed to prevent one HIV infection is over 25 with an index threshold of 1. We saw a similar trend when varying partner degree thresholds, though just less extreme. The range of median number of infections averted was not as wide when varying partner degree versus when index degree thresholds. With the exception of index degree threshold equaling 1, varying the partner degree performed much better than varying the index degree thresholds: incidence ranged from 2.71 to 2.80 for the former and from 2.36 to 3.08 for the latter. It was more common for individuals in this network to have a partner degree of five than an index degree of five, and it was more common to have an index degree of 1.

Table 4 presents the sensitivity analysis for both network parameter thresholds with all five indications (Scenario 5). Similar to Table 3, there was a significant drop off in most of the outcomes between the index threshold of 1 and index threshold of 2. However, the percent currently on PrEP was fairly consistent between both the index and partner degree threshold variations, unlike in Table 3. Because of this, all of the other outcomes were similar across the threshold variations. The CDC indications were highly effective at identifying high-risk individuals, such that adding the network parameters on top of them did not particularly enhance the way individuals were targeted within the network. Overall, the number of years on PrEP needed to prevent one HIV infection in each part of this sensitivity analysis were similar to that in Scenario 1 (Table 1).

Table 5 presents a sensitivity analysis for the risk history window in Scenario 1 in which meeting at least 1 indication of the three CDC guidelines during this period indicated the individual for PrEP. As the risk window increased, the NIA changes by 100 between 30 and 90 days and 90 and 180 days. After that point, the number of infections averted did not change as drastically. A risk window of 30 days gave a conservative number of years on PrEP needed to prevent one HIV infection, but the number of infections averted was also conservative. The 180-risk-window was a balanced estimate with not too high of an NNT justified by an impactful NIA.

In Table 6, we present a sensitivity analysis on the timing of reevaluating individuals for PrEP use impacted the NIA and NNT. Instantaneous risk reevaluation (indications are reevaluated at each timestep) removed MSM from the at-risk pool immediately. Even though they were not indicated by PrEP,

their discontinuing PrEP does not mean that they have 0% risk of infection, which is why the yearly and no risk reevaluation performed better in terms of HIV prevention. Scenario 2 performed better overall, and although there was a trade-off between NNT and NIA, the NNT was almost identical between the scenarios. This implies that index degree might be both more effective and more efficient than partner degree as an indication.

Table 7 shows the effects of varying coverage in each targeting scenario. Each scenario shows a dramatic increase in number of infections averted, the primary role of coverage on model outcomes. Figure 2 compares NNT and PIA across coverage values of 10% to 60% for each scenario. For the PIA, Scenarios 1 and 5 exhibited similar results, meaning that the network parameters did not necessarily enhance the CDC indication. Also, Scenarios 2 and 4 showed similar results, meaning that partner degree did not contribute greatly after accounting for index degree. Scenario 3 followed a similar increasing trend. The NNT was low and relatively concistent for all of the network indication-only scenarios at high coverage values, though the partner degree indication performed best at the lowest coverage levels.

DISCUSSION

PrEP has been proven to be effective in preventing HIV-negative MSM from acquiring HIV, though it still remains a challenge identify the most at-risk HIV-negative MSM as a means for targeting this biomedical HIV prevention intervention. In this study, we explored how network degree as a indication for of PrEP could be used in combination or as a replacement to the current standard of care: CDC's clinical practice guidelines.

Concurrent sexual partnerships have been identified as a key part of HIV transmission among MSM.[30,31,32] When there is an overlap in partnerships, the number of connected MSM is large at any point in time and infection is able to propagate to other partners easily as the sexual partnerships continue.[13] Understanding this phenomenon as a defining characteristic of the HIV epidemic among MSM allowed us to pose the question: what happens to the efficacy and efficiency of PrEP as an intervention at the population-level if we use network features to target PrEP?

Our findings demonstrate the balance between effectiveness and efficiency. While indicating MSM for PrEP based on their individual behavior (CDC guidelines) indicated a larger percentage of the population and averted more infections than the network measures, we saw a dramatic difference in how much more efficiently PrEP works among the network indication scenarios. In the risk window and risk reevaluation sensitivity analyses, we found that the seasons of risk matter for catching people at the right time for PrEP uptake and PrEP discontinuation. Finally, we found that while changing the group of people who are indicated for PrEP is important for HIV infection aversion, coverage was still of primary importance.

The public health implications of these findings are complex. It is not feasible to determine an individual's place within their sexual network in the traditional clinical setting where people are being indicated for PrEP today. A study found that Atlanta, despite having a high burden of HIV infection among MSM, was a city ranked lowest in familiarity with prescribing PrEP and actually having previously prescribed PrEP among both primary care and HIV providers.[33] Because indication based on network connectivity might require fewer doses of PrEP to reduce HIV infection than indicating on individual behavior, developing novel ways of distributing PrEP in non-clinical settings could lead to a more cost-effective method of HIV prevention with PrEP.

Limitations. There is overwhelming evidence of disparities in HIV prevalence and incidence between white and black MSM, and we did not stratify our model to show the disparities in this study. Black MSM are disproportionately burdened with HIV and are also less likely to have access to PrEP and antiretroviral therapy.[14,15,29,34] The model does consider differential parameters depending on race, but the primary results of this analysis did not display the disparities in HIV incidence, prevalence, and care continuum. Secondly, empirical data comes from a high-risk MSM population in Atlanta, Georgia. This population may not be representative of MSM populations elsewhere or other high-HIV burden populations. Lastly, this analysis only considered same-sex partnerships and acts for simplicity. In reality, MSM and heterosexual networks are not isolated and there is a portion of this network that has female partners and/or vaginal sex. This analysis does not consider the female nodes in this network and how they complicate the HIV transmission rates throughout this MSM network.

Conclusions. The 2017 CDC PrEP indications are able to indicate at-risk MSM for PrEP in an effective way. In terms of averting infections, they perform well. Keeping in mind that the CDC scenarios in this analysis are three different behavioral indications combined, the network indication results show us that network parameters used alone are able to perform on a comparable level to the CDC guidelines. Our results further support that network parameters capturing concurrency can identify at-risk individuals within a network in a more efficient way. Splitting the network into low-risk and high-risk groups based on their individual behavior does not capture the intricacies of the MSM network but is the way in which guidelines have been developed for clinical use. This analysis has proved that simplifying one's likelihood of contracting HIV in the previously mentioned way might not be the most efficient way to get PrEP to those who need it the most within the MSM network.

TABLES

Table 1. Scenarios & Definitions for Models of PrEP in MSM for Behavioral and Network Indications

Indications	
Condition 1	UAI in monogamous, HIV status–unknown partnership: one-sided monogamy assessment
Condition 2	UAI outside monogamous partnership: nonmonogamy defined as nonmain partnership
Condition 3	Any STI Diagnosis in last 6 months
Condition 4	Index degree greater than given threshold
Condition 5	Partner degree greater than given threshold
Combinations	
Scenario 1	CDC indications only: Conditions 1, 2, & 3
Scenario 2	Condition 4
Scenario 3	Condition 5
Scenario 4	Degree indications only: Conditions 4 & 5
Scenario 5	All 5 indications
Definitions	
Ego degree	Number of sexual partners, or number of primarily connected nodes
Partner degree	Number of partners' partners, or number of secondarily connected nodes
Risk Window	Length of historical time window to conduct risk assessment
Coverage	Proportion of MSM who are on PrEP: 35.3%
Adherence	Proportion of MSM with low, middle, and high adherence to PrEP: 8.9%, 12.7%, 78.5% respectively

Table 2. Epidemiological Outcomes 10 Years After Initiation of PrEP in MSM, by Behavioral Indication Scenario

	Eligible for PrEP (%)	Currently on PrEP (%)	Prevalence Median (Middle 95%)	Incidence Median (Middle 95%)	NIA* Median (Middle 95%)	PIA** Median (Middle 95%)	NNT*** Median (Middle 95%)
Base	-	-	0.251 (0.235, 0.268)	3.35 (2.87, 3.93)	-	-	-
Scenario 1	52.9 (51.3, 54.5)	18.3 (17.5, 18.9)	0.211 (0.197, 0.227)	2.62 (2.16, 3.12)	413.5 (171.5, 654.4)	0.151 (0.065, 0.228)	24.4 (17.8, 39.9)
Scenario 2	43.2 (42.1, 44.3)	11.5 (10.8, 12.2)	0.219 (0.203, 0.234)	2.80 (2.33, 3.25)	316.5 (108.2, 593.1)	0.115 (0.041, 0.206)	16.3 (10.7, 33.4)
Scenario 3	26.6 (25.8, 27.5)	8.2 (7.4, 8.8)	0.235 (0.219, 0.251)	3.07 (2.58, 2.83)	121.5 (-181.1, 387.6)	0.044 (-0.069, 0.132)	16.7 (-91.5, 178.2)
Scenario 4	47.9 (46.7, 49.0)	11.5 (10.9, 12.1)	0.219 (0.205, 0.234)	2.77 (2.28, 3.25)	314.5 (51.2, 623.9)	0.114 (0.020, 0.215)	18.7 (12.1, 41.9)
Scenario 5	68.5 (67.4, 69.5)	16.0 (15.3, 16.7)	0.208 (0.192, 0.224)	2.59 (2.08, 3.04)	474.5 (228.3, 709.6)	0.174 (0.085, 0.246)	25.0 (17.8, 36.5)

*NIA, number of infections averted; **PIA, percentage of infections averted; ***NNT, number needed to treat

Table 3. Sensitivity Analyses of different thresholds for index and partner degree indications in Scenario 4

	Eligible for PrEP (%)	Currently on PrEP (%)	Prevalence Median (Middle 95%)	Incidence Median (Middle 95%)	NIA Median (Middle 95%)	PIA Median (Middle 95%)	NNT Median (Middle 95%)
Index							
1	85.0 (84.4, 85.5)	16.7 (16.0, 17.3)	0.200 (0.184, 0.215)	2.36 (1.92, 2.85)	598.0 (348.3, 821.6)	0.217 (0.132, 0.288)	25.3 (19.7, 35.9)
2*	48.0 (46.7, 49.3)	11.5 (10.8, 12.2)	0.219 (0.205, 0.233)	2.77 (2.31, 3.29)	330.5 (55.7, 581.8)	0.121 (0.022, 0.202)	18.2 (12.0, 40.4)
3	32.7 (31.7, 33.8)	9.4 (8.7, 10.2)	0.228 (0.213, 0.246)	2.98 (2.52, 3.64)	207.5 (-92.4, 478.3)	0.075 (-0.035, 0.165)	15.6 (-91.2, 55.4)
4	27.7 (26.7, 28.9)	8.4 (7.7, 9.1)	0.232 (0.217, 0.250)	3.07 (2.59, 3.62)	142.5 (-126.0, 412.9)	0.053 (-0.050, 0.141)	16.1 (-136.8, 124.3)
5	26.6 (25.7, 27.6)	8.2 (7.4, 9.0)	0.235 (0.217, 0.250)	3.09 (2.52, 3.64)	120.5 (-177.0, 426.2)	0.044 (-0.068, 0.149)	15.9 (-257.8, 300.6)
Partner							
1	63.2 (62.3, 64.2)	13.0 (12.2, 13.6)	0.214 (0.200, 0.230)	2.71 (2.19, 3.15)	407.5 (115.1, 612.3)	0.147 (0.045, 0.216)	22.4 (15.6, 39.0)
2*	47.9 (46.8, 49.0)	11.5 (10.8, 12.3)	0.218 (0.202, 0.236)	2.73 (2.31, 3.29)	338.0 (67.5, 634.0)	0.123 (0.025, 0.220)	17.7 (11.4, 40.7)
3	43.6 (42.5, 44.5)	11.4 (10.7, 12.1)	0.220 (0.206, 0.236)	2.79 (2.33, 3.31)	313.5 (60.4, 579.4)	0.116 (0.023, 0.201)	16.8 (11.1, 40.8)
4	43.4 (42.2, 44.5)	11.4 (10.8, 12.1)	0.219 (0.204, 0.235)	2.76 (2.28, 3.36)	318.5 (43.9, 599.3)	0.116 (0.017, 0.211)	16.8 (11.3, 41.4)
5	43.3 (42.2, 44.3)	11.5 (10.8, 12.1)	0.219 (0.202, 0.236)	2.80 (2.34, 3.28)	325.0 (73.9, 610.4)	0.120 (0.029, 0.211)	16.4 (10.5, 40.3)

*These scenarios are equivalent to the reference

Table 4. Sensitivity Analyses of different thresholds for index and partner degree indications in Scenario 5

	Eligible for PrEP (%)	Currently on PrEP (%)	Prevalence Median (Middle 95%)	Incidence Median (Middle 95%)	NIA Median (Middle 95%)	PIA Median (Middle 95%)	NNT Median (Middle 95%)
Index							
1	84.9 (84.4, 85.5)	16.7 (16.0, 17.4)	0.199 (0.185, 0.215)	2.40 (1.94, 2.83)	594.5 (307.6, 869.0)	0.218 (0.120, 0.295)	25.0 (19.6, 36.5)
2*	68.5 (67.5, 69.3)	15.9 (15.3, 16.6)	0.209 (0.196, 0.224)	2.59 (2.11, 3.05)	463.5 (226.9, 718.3)	0.172 (0.087, 0.250)	24.7 (18.6, 41.8)
3	64.4 (63.4, 65.5)	16.2 (15.5, 16.8)	0.210 (0.194, 0.225)	2.59 (2.13, 3.09)	448.0 (209.2, 712.0)	0.164 (0.079, 0.250)	24.4 (17.5, 40.2)
4	63.6 (62.4, 64.6)	16.2 (15.5, 17.0)	0.210 (0.196, 0.225)	2.58 (2.12, 3.14)	435.0 (194.2, 704.6)	0.157 (0.075, 0.247)	24.7 (17.7, 38.2)
5	63.5 (62.5, 64.5)	16.2 (15.6, 16.9)	0.210 (0.197, 0.224)	2.60 (2.21, 3.05)	435.5 (190.5, 724.4)	0.160 (0.073, 0.246)	24.1 (18.2, 39.6)
Partner							
1	74.5 (73.7, 75.3)	15.4 (14.8, 16.1)	0.208 (0.191, 0.224)	2.56 (2.09, 3.00)	476.5 (216.5, 747.7)	0.175 (0.084, 0.259)	25.0 (18.6, 40.1)
2*	68.5 (67.5, 69.6)	16.0 (15.3, 16.8)	0.207 (0.192, 0.225)	2.58 (2.11, 3.05)	484.0 (199.3, 723.7)	0.178 (0.077, 0.254)	24.0 (18.4, 37.3)
3	66.3 (65.3, 67.3)	16.2 (15.5, 16.8)	0.208 (0.192, 0.223)	2.57 (2.01, 3.09)	464.0 (191.8, 747.1)	0.169 (0.073, 0.258)	24.5 (17.3, 38.4)
4	66.2 (65.1, 67.1)	16.2 (15.5, 16.9)	0.209 (0.193, 0.225)	2.57 (2.08, 3.04)	448.5 (203.7, 738.8)	0.168 (0.079, 0.258)	24.8 (17.9, 39.8)
5	66.2 (65.2, 67.1)	16.2 (15.5, 17.1)	0.208 (0.194, 0.224)	2.55 (2.12, 3.05)	470.5 (199.5, 743.9)	0.171 (0.079, 0.259)	23.9 (18.2, 36.8)

*These scenarios are equivalent to the reference

Table 5. Sensitivity Analyses of different risk history windows in days for Scenario 1

	Eligible for PrEP	Currently on PrEP	Prevalence	Incidence	NIA	PIA	NNT
	(%)	(%)	Median (Middle 95%)	Median (Middle 95%)	Median (Middle 95%)	Median (Middle 95%)	Median (Middle 95%)
Window							
30	30.1 (29.2, 31.4)	10.0 (9.3, 10.7)	0.229 (0.215, 0.251)	2.98 (2.46, 3.59)	224.5 (-35.0, 529.0)	0.082 (-0.013, 0.182)	14.2 (-18.5, 59.7)
90	42.0 (40.9, 43.3)	15.6 (14.8, 16.3)	0.221 (0.206, 0.236)	2.77 (2.25, 3.31)	325 (76.0, 575.5)	0.118 (0.030, 0.203)	21.5 (14.9, 50.5)
180	53.0 (51.6, 54.1)	18.3 (17.5, 19.0)	0.211 (0.195, 0.226)	2.61 (2.19, 3.08)	429.0 (140.1, 680.8)	0.158 (0.055, 0.239)	23.9 (17.3, 40.8)
270	60.6 (59.4, 62.1)	19.8 (19.0, 20.7)	0.206 (0.190, 0.222)	2.54 (2.13, 3.02)	487.5 (223.2, 760.3)	0.179 (0.086, 0.258)	26.1 (19.9, 42.9)
360	65.8 (64.2, 67.2)	20.8 (19.9, 21.5)	0.201 (0.187, 0.215)	2.44 (1.96, 2.87)	530.0 (263.2, 777.6)	0.192 (0.103, 0.269)	27.2 (20.9, 38.9)

Table 6. Sensitivity analysis of risk reevaluation window for network scenarios

	Eligible for PrEP (%)	Currently on PrEP (%)	Prevalence Median (Middle 95%)	Incidence Median (Middle 95%)	NIA Median (Middle 95%)	PIA Median (Middle 95%)	NNT Median (Middle 95%)
Scenario 2							
Instantaneous	43.3 (42.3, 44.3)	11.4 (10.7, 12.2)	0.219 (0.204, 0.234)	2.76 (2.34, 3.25)	329.0 (80.7, 587.0)	0.121 (0.031, 0.206)	16.1 (11.1, 35.1)
Yearly	43.2 (42.1, 44.4)	17.5 (16.6, 18.4)	0.213 (0.198, 0.230)	2.70 (2.23, 3.20)	396.0 (140.1, 619.8)	0.143 (0.052, 0.219)	21.1 (14.9, 40.2)
None	43.2 (42.1, 44.3)	20.8 (19.8, 22.0)	0.209 (0.193, 0.225)	2.61 (2.11, 3.09)	431.5 (183.0, 734.7)	0.157 (0.070, 0.253)	22.4 (16.3, 37.5)
Scenario 3							
Instantaneous	26.6 (25.6, 27.5)	8.2 (7.5, 9.0)	0.233 (0.218, 0.251)	3.09 (2.60, 3.64)	112.0 (-135.8, 365.8)	0.042 (-0.051, 0.129)	16.4 (-130.5, 284.8)
Yearly	26.6 (25.8, 27.5)	14.0 (13.0, 15.2)	0.227 (0.211, 0.244)	2.97 (2.47, 3.49)	207.5 (-66.6, 466.5)	0.074 (-0.026, 0.163)	21.2 (-49.9, 232.2)
None	26.7 (25.8, 27.6)	17.7 (16.4, 19.0)	0.223 (0.208, 0.239)	2.90 (2.38, 3.43)	250./0 (-26.4, 499.8)	0.090 (-0.010, 0.177)	22.6 (13.1, 63.4)

*Index and partner degree thresholds are set to 2

Table 7. Sensitivity analysis of the probability of starting PrEP (coverage)

Coverage	Eligible for PrEP (%)	Currently on PrEP (%)	Prevalence Median (Middle 95%)	Incidence Median (Middle 95%)	NIA Median (Middle 95%)	PIA Median (Middle 95%)	NNT Median (Middle 95%)
Scenario 1							
10%	48.9 (47.3, 50.2)	6.1 (5.6, 6.5)	0.237 (0.223, 0.256)	3.07 (2.57, 3.68)	148.5 (-129.7, 409.0)	0.055 (-0.049, 0.143)	18.8 (-180.5, 151.1)
30%	52.2 (50.8, 53.6)	16.1 (15.5, 16.8)	0.216 (0.201, 0.229)	2.67 (2.18, 3.26)	383.0 (161.6, 620.0)	0.139 (0.064, 0.215)	23.3 (16.7, 39.1)
50%	54.9 (53.6, 56.2)	24.1 (23.2, 24.9)	0.199 (0.185, 0.215)	2.43 (1.95, 2.85)	551.0 (320.1, 833.9)	0.203 (0.124, 0.290)	25.0 (19.0, 35.7)
Scenario 2							
10%	43.2 (42.2, 44.3)	3.5 (3.1, 3.9)	0.241 (0.225, 0.256)	3.15 (2.63, 3.79)	114.0 (-137.8, 357.0)	0.042 (-0.051, 0.125)	13.3 (-89.7, 175.0)
30%	43.2 (42.2, 44.3)	9.9 (9.2, 10.5)	0.222 (0.207, 0.239)	2.87 (2.35, 3.36)	283.5 (8.2, 532.7)	0.102 (0.003, 0.185)	16.3 (10.2, 47.5)
50%	43.2 (42.2, 44.5)	15.6 (14.8, 16.5)	0.209 (0.192, 0.223)	2.61 (2.14, 2.99)	428.5 (166.3, 729.2)	0.157 (0.065, 0.249)	17.1 (12.2, 29.8)
Scenario 3							
10%	26.3 (25.4, 27.4)	2.5 (2.1, 2.9)	0.247 (0.229, 0.261)	3.24 (2.77, 3.87)	25.5 (-245.7, 303.6)	0.009 (-0.094, 0.105)	5.2 (-48.2, 374.5)
30%	26.5 (25.7, 27.4)	7.1 (6.4, 7.8)	0.237 (0.222, 0.256)	3.15 (2.65, 3.80)	96.0 (-150.0, 369.8)	0.036 (-0.059, 0.130)	13.9 (-114.9, 171.2)
50%	26.6 (25.7, 27.6)	11.3 (10.3, 12.2)	0.229 (0.212, 0.247)	2.99 (2.51, 3.53)	170.0 (-89.8, 397.6)	0.063 (-0.034, 0.138)	17.6 (-77.6, 148.2)
Scenario 4							
10%	47.8 (46.6, 48.9)	3.6 (3.2, 3.9)	0.240 (0.224, 0.258)	3.13 (2.62, 3.70)	120.5 (-146.9, 386.8)	0.044 (-0.057, 0.135)	14.1 (-132.2, 201.6)
30%	47.9 (46.8, 49.2)	10.0 (9.2, 10.6)	0.223 (0.208, 0.240)	2.84 (2.36, 3.29)	284.0 (5.4, 533.2)	0.101 (0.002, 0.189)	18.0 (11.3, 41.9)
50%	47.9 (46.7, 49.0)	15.7 (14.9, 16.5)	0.209 (0.191, 0.223)	2.61 (2.05, 3.13)	455.5 (147.0, 718.6)	0.165 (0.056, 0.252)	18.4 (12.9, 30.5)
Scenario 5							
10%	67.0 (66.0, 68.0)	5.1 (4.7, 5.5)	0.237 (0.218, 0.255)	3.10 (2.60, 3.60)	156.5 (-154.9, 452.4)	0.057 (-0.059, 0.163)	22.4 (-105.4, 150.0)
30%	68.1 (67.1, 69.1)	14.0 (13.4, 14.6)	0.213 (0.199, 0.229)	2.64 (2.18, 3.19)	410.5 (181.3, 662.4)	0.151 (0.069, 0.232)	24.3 (18.1, 45.1)
50%	69.2 (68.2, 70.3)	21.4 (20.7, 22.2)	0.195 (0.182, 0.209)	2.32 (1.89, 2.80)	619.5 (361.7, 885.2)	0.225 (0.139, 0.306)	25.0 (20.2, 33.4)

*Index and/or partner degree thresholds are set to 2

FIGURES

Figure 1. Percent of infections averted and number of years on PrEP needed to prevent one new HIV infection for all five scenarios as described in Table 2.

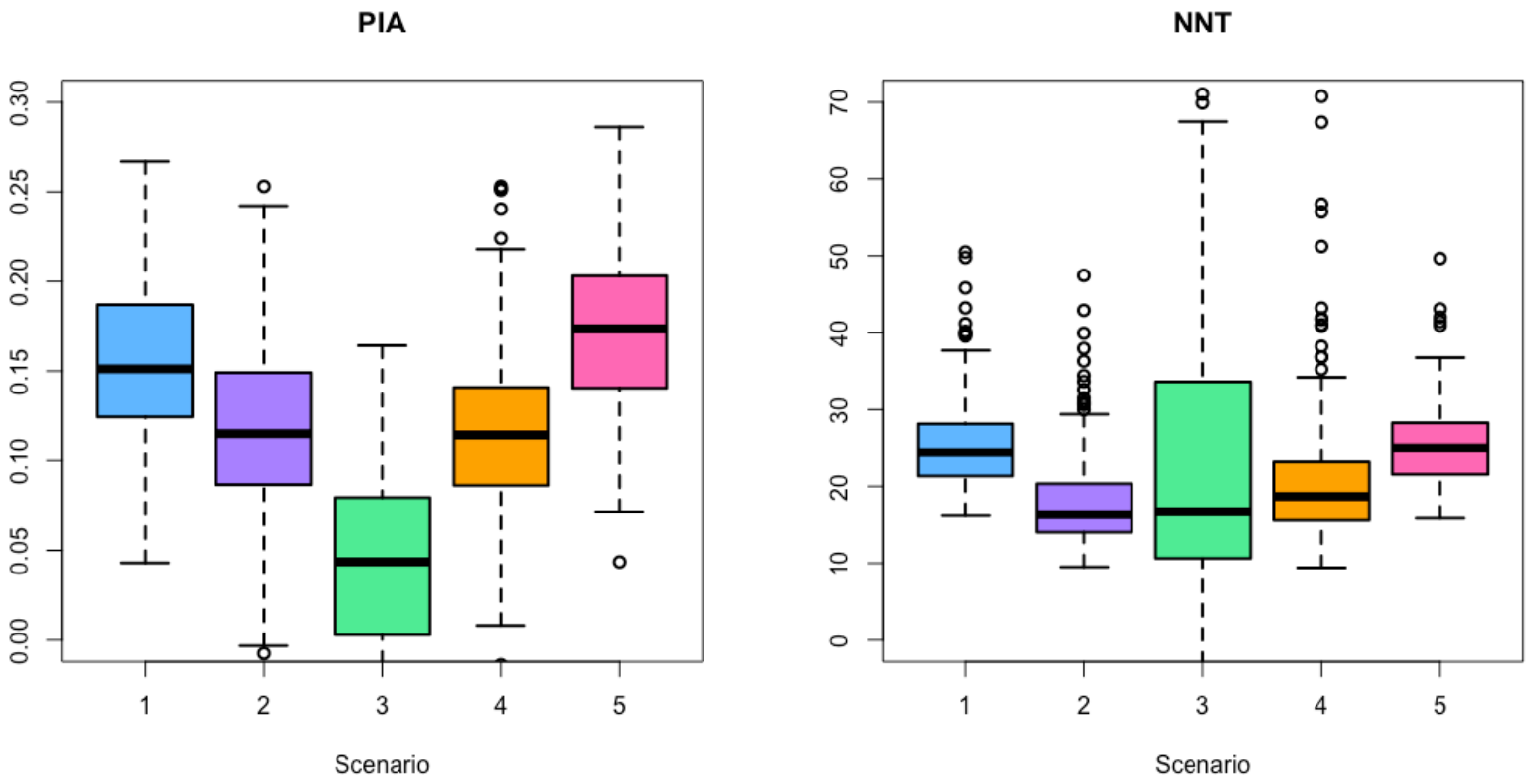
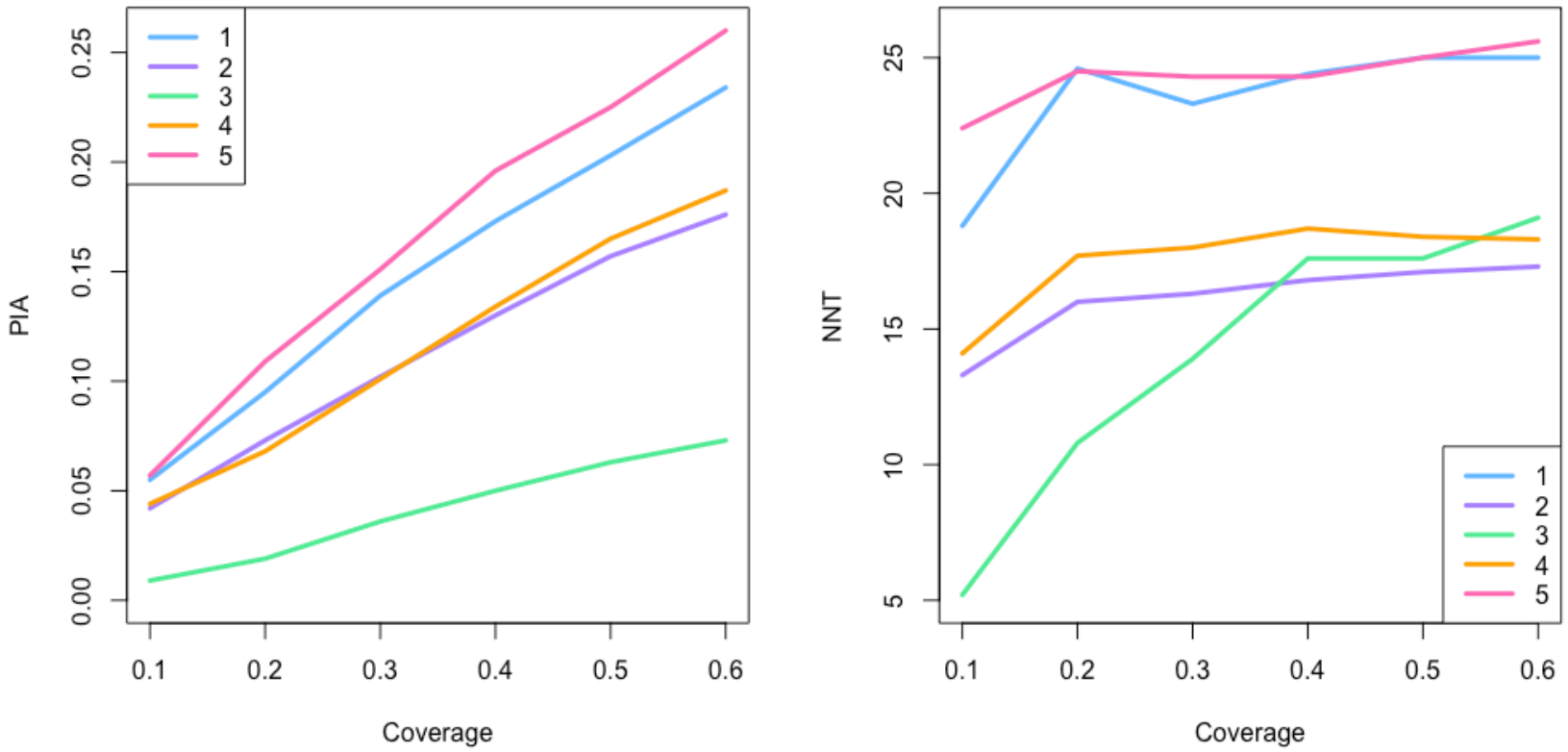


Figure 2. Percent of infections averted (PIA) and number of person-years on PrEP needed to prevent one HIV infection (NNT) with varying coverage for each scenario, with network scenarios (2, 3, 4, and 5) holding all indication thresholds at 2.



REFERENCES

1. Georgia Department of Public Health, HIV/AIDS Epidemiology Section. HIV Surveillance Summary, Georgia 2017. 2019 Feb.
2. Centers for Disease Control and Prevention. HIV Surveillance Report, 2017. 2018 Nov;29.
3. 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 Dec 30;363(27):2587–99.
4. Grant RM, Anderson PL, McMahan V, Liu A, Amico KR, Mehrotra M, et al. An observational study of preexposure prophylaxis uptake, sexual practices, and HIV incidence among men and transgender women who have sex with men. Lancet Infect Dis. 2014 Sep;14(9):820–9.
5. 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. 2015 Nov 15;61(10):1601-3.
6. Centers for Disease Control and Prevention: US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline. 2018 Mar;38.
7. 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 Feb;3(2):e94–104.
8. Finlayson T, Cha S, Denson D, Trujillo L, Xia M, Prejean J, Wejnert C. Changes in HIV PrEP Awareness and Use Among Men Who Have Sex With Men, 2014 vs 2017. Poster presented at: Conference on Retroviruses and Opportunistic Infections; 2019 Mar 4-7; Seattle, WA.
9. 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. Journal of Infectious Diseases. 2016 Dec 15;214(12):1800–7.
10. Fujimoto K, Wang P, Flash CA, Kuhns LM, Zhao Y, Amith M, et al. Network Modeling of PrEP Uptake on Referral Networks and Health Venue Utilization Among Young Men Who Have Sex with Men. AIDS Behav. 2018 Nov 14.
11. Friedman SR, Neaigus A, Jose B, Curtis R, Goldstein M, Ildefonso G, et al. Sociometric risk networks and risk for HIV infection. Am J Public Health. 1997 Aug;87(8):1289–96.
12. Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. AIDS. 1997 Apr;11(5):641–8.
13. 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. 2016 Nov 28;30(18):2875–83.
14. Sullivan PS, Rosenberg ES, Sanchez TH, Kelley C, Luisi N, Cooper H, et al. Explaining Racial Disparities in HIV Incidence in a Prospective Cohort of Black and White Men Who Have Sex With Men in Atlanta, GA: A Prospective Observational Cohort Study. Ann Epidemiol. 2015 Jun;25(6):445–54.
15. Jenness S, Goodreau S, Morris M. EpiModel: mathematical modeling of infectious disease. 2015; doi:10.5281/zenodo.16767.
16. Hernández-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; 42:505–12.
17. Goodreau SM, Carnegie NB, Vittinghoff E, et al. What drives the US and Peruvian HIV epidemics in men who have sex with men (MSM)? PLoS One 2012; 7:e50522.
18. Krivitsky PN, Handcock MS. A separable model for dynamic networks. J R Stat Soc Ser B Stat Methodol 2014; 76:29–46.
19. Carnegie NB, Goodreau SM, Liu A, 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. J Acquir Immune Defic Syndr 2015; 69:119–25.
20. Hughes JP, Baeten JM, Lingappa JR, et al. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. J Infect Dis 2012; 205:358–65.
21. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011; 365:493–505.
22. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database Syst Rev 2002; 1:CD003255.

23. Wiysonge CS, Kongnyuy EJ, Shey M, et al. Male circumcision for prevention of homosexual acquisition of HIV in men. Cochrane Database Syst Rev 2011; 6:CD007496.
24. Goodreau SM, Carnegie NB, Vittinghoff E, et al. Can male circumcision have an impact on the HIV epidemic in men who have sex with men? PLoS One 2014; 9: e102960.
25. Zimmerman PA, Buckler-White A, Alkhatib G, et al. Inherited resistance to HIV-1 conferred by an inactivating mutation in CC chemokine receptor 5: studies in populations with contrasting clinical phenotypes, defined racial background, and quantified risk. Mol Med 1997; 3:23–36.
26. Marmor M, Sheppard HW, Donnell D, et al. Homozygous and heterozygous CCR5-delta32 genotypes are associated with resistance to HIV infection. J Acquir Immune Defic Syndr 2001; 27:472–81.
27. 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 2015; 176:75–84.
28. 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.
29. Huang YA, Zhu W, Smith DK, Harris N, Hoover KW. HIV Preexposure Prophylaxis, by Race and Ethnicity — United States, 2014–2016. MMWR Morb Motral Wkly Rep 2018;67:1147-1150.
30. Amirkhanian YA. Social Networks, Sexual Networks and HIV Risk in Men Who Have Sex with Men. Curr HIV/AIDS Rep. 2014 Mar;11(1):81–92.
31. Leng T, Keeling M. Concurrency of partnerships, consistency with data, and control of sexually transmitted infections. Epidemics. 2018 Dec;25:35-46.
32. Morris M, Kurth AE, Hamilton DT, Moody J, Wakefield S. Concurrent Partnerships and HIV Prevalence Disparities by Race: Linking Science and Public Health Practice. Am J Public Health. 2009 Jun;99(6):1023–31.
33. Smith DK, Mendoza MCB, Stryker JE, Rose CE. PrEP Awareness and Attitudes in a National Survey of Primary Care Clinicians in the United States, 2009–2015. PLoS One. 2016 Jun 3;11(6):e0156592.
34. Jenness SM, Maloney KM, Smith DK, Hoover KW, Goodreau SM, Weiss KM, et al. Addressing Gaps in HIV Preexposure Prophylaxis Care to Reduce Racial Disparities in HIV Incidence in the United States. Am J Epidemiol. 2019 Apr 1;188(4):743-752.