SUPPLEMENTARY MATERIAL

Title: Gonorrhoea and chlamydia diagnosis as an entry point for HIV pre-exposure prophylaxis: A modeling study

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1 HIV SIMULATION MODEL DESIGN

Overview

Our agent-based simulation model of the HIV epidemic among MSM in Baltimore City is structured as a collection of modules that govern population demographics, sexual partnerships, the epidemiological aspects of disease with regard to HIV natural history, cascade of care and transmission. Each "agent" represents a single MSM in Baltimore City, characterized by age, race, and place of residence, and the model is evaluated in a series of one-week time steps. The HIV natural history module characterizes the progression of HIV among infected individuals according to disease stage. Each stage is associated with a different per-act risk of HIV transmission, and disease progression from stage 2 to stage 3 can be prevented (and/or reversed) by provision of ART. The HIV cascade of care estimates probabilities of HIV testing, linkage to care, disengagement/re-engagement, and ART provision/viral suppression at each time step. The sexual network and transmission module create and modify the population's sexual networks (as a series of stable and casual partnerships) at each step, modeling HIV transmission as a per-act probability among serodiscordant partnerships according to frequency and safety of sex act, HIV stage of the infected partner, and ART/PrEP use. Sexual partnerships are modeled as assortative according to age, race, and location of residence. Finally, the population demographic module accounts for aging, death, and birth processes.

1.1 Population Demographic Module

This module characterizes the initial population structure and governs various procedures for aging, death, and birth at end of each simulated year. We model the population of MSM in Baltimore City between the ages of 15 to 75. The population is structured as a collection of population groups corresponding to Baltimore's Community Statistical Areas (CSA) [1]. CSAs are clusters of neighborhoods and are organized according to census tract boundaries, which are consistent statistical boundaries. In some cases, CSA boundaries may cross neighborhood boundaries. There are 55 CSAs in Baltimore City. Neighborhood lines often do not fall along CSA boundaries, but CSAs are representations of the conditions occurring within those particular neighborhoods. Simulated population groups are characterized with regard to their geographical location (CSA of residence) and racial structure (black and non-black). We do not model the spatial distribution of individuals within each CSA; rather geographical assignments are made at the CSA level by assigning the corresponding CSA-center coordinates to each MSM living in that CSA. The initial HIV distribution across CSAs is estimated according to publicly available data from Maryland's Department of Health and Mental Hygiene (MDHMH) [2].

Individuals age with the simulation clock (years) and exit the model according to an age-specific natural mortality rate [3], or by reaching the age of 75, or via an additional mortality rate associated with HIV infection. To maintain the initial population decomposition without disturbing the CSA structures, we model a natural birth process at the CSA level for replenishing the population size over time. The birth process is modeled via a non-stationary Poisson process tuned to maintain each CSA's population at a constant mean over time. Newborns enter the MSM population at age of 15 to 20 years old and follow the corresponding racial structure of the CSA of residence.

Using the current estimate of Baltimore City male population (approximately 287,000) who are 15 year or older in age (about 232,000), and estimated percentage of adult MSMs in each racial group (7.5% of non-black males and 5.8% of black males [4]), we estimate the size of Baltimore City's MSM population at approximately 15,000.

Forming CSA-groups: To determine groupings of similar CSAs, we first ranked the CSAs according to the median income level and racial makeup based on available information from Baltimore City census [1].

For simplicity, levels of income (Figure S1-left panel) and proportion of population that is Black/African-American (Figure S1-right panel) were coded into values from 1 to 5 (representative of various shades in Figure S1), and two values were assigned to each CSA. For example, CSA "Midtown" (T-shaped in the center of the map) was assigned a rank of 3 for median household income, and 2 for the proportion of population that is Black/African-American.

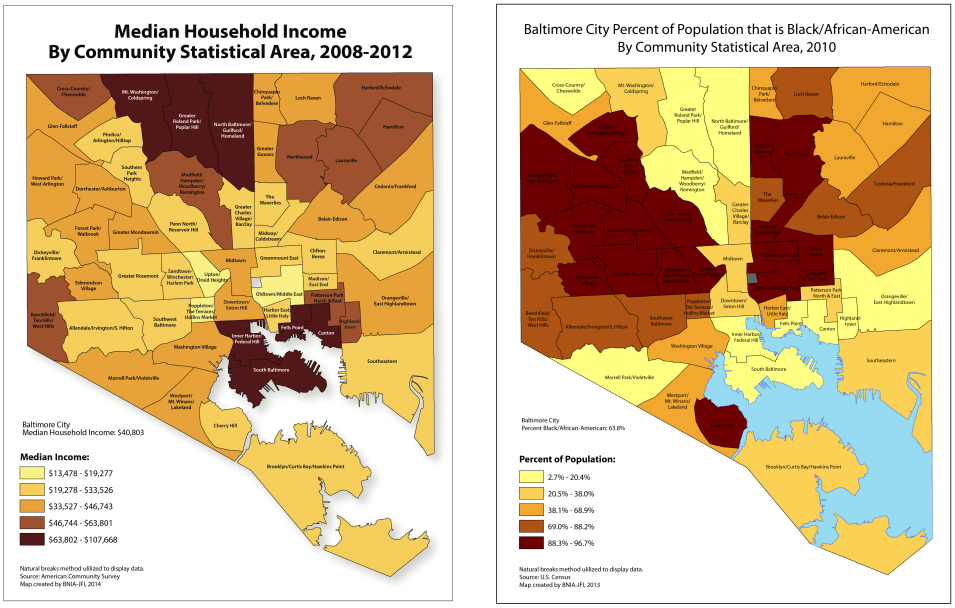

Figure S1: Baltimore City CSA ranking according to median income and racial structure [1].

We defined a CSA-group to include a number of neighboring CSAs (sharing a border) with at most a one-level difference in their ranked levels of income and racial makeup. To determine the CSA-groups throughout the city, we implemented a random search mechanism using a branch and bound logic. The search was started from a random CSA and branched through all neighboring CSAs to determine how many could belong to the same CSA-group. The search was bounded by those CSAs representing a difference of more than one level in ranked income and racial makeup but continued for those CSAs that belonged to the same group and branched further to test their other neighbors, until it was bounded in all directions. At the end of each iteration, a list of CSAs grouped by relative similarity across the whole city was generated. This search was repeated many times and the CSA groups that were most likely (i.e., high frequency) to form were identified. Overlapping CSA-groups were further checked for the possibility of combination into a single group. Finally, we had 16 CSA-groups across Baltimore City, representing geographically approximate neighborhoods with similar levels of income and racial makeup (Figure S2). Using CSA numbers as identifiers, a complete list of CSA groups is provided in Table S1.

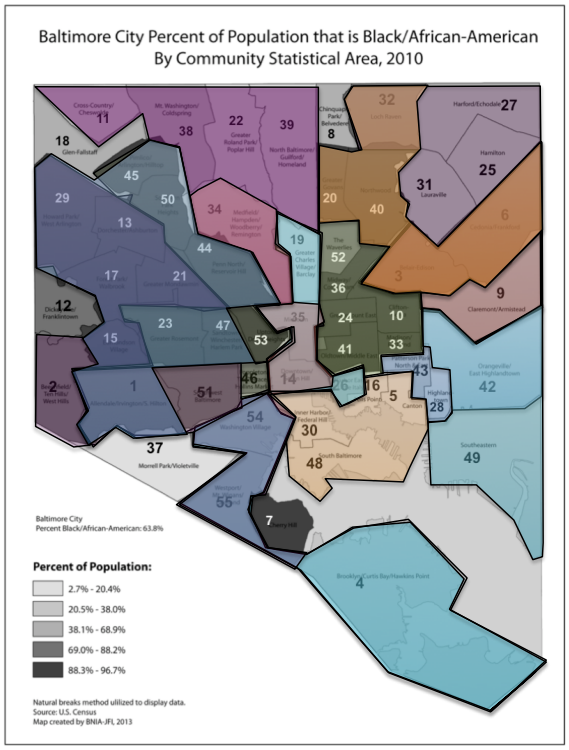

Figure S2: Baltimore City CSA ID's and CSA groups structure. Each CSA group is marked with a closed border in a different color. Some groups overlap such that some CSAs belong to more than one group. Some CSAs may not belong to any groups and are considered by themselves.

Table S1: List of CSA group and member CSAs

Group ID	CSA members
1	11 22 34 38 39
2	3 6 9
3	28 42 43
4	3 6 8 25 27 31 32
5	42 49
6	10 24 33 36 41 52
7	5 16 28 30 43 48
8	3 6 20 32 40
9	4 14 19 26 35 54 55
10	14 34 35
11	1 23 44 45 46 47 50 51 53
12	1 51 54 55
13	4 14 19 26 35 54 55
14	2 13 15 17 21 29
15	1 12 13 15 17 21 23 29 44 45 47 50 51
16	3 6 10 20 24 33 36 52

1.2 Sexual Partnership Module

This module governs the network of sexual partnerships and runs in discrete time steps, each representing a week. Following previous models of sexual contact networks [5–7], we conceptualize the network of sexual partnerships at an individual level (with regard to age, race, geography, sexual positioning, etc.) and calibrate the simulation parameters using local behavioral surveillance data available through the BESURE study, the Baltimore City branch of the National HIV Behavioral Surveillance System (NHBS) [8]. BESURE is a CDC funded project operated by the Maryland Department of Health and Mental Hygiene and the Johns Hopkins Bloomberg School of Public Health. Starting in 2004, BESURE has conducted four venue-based sampling surveys among Baltimore's MSM (Table S2). We use this data to extract information on several behavioral parameters at the individual level (e.g., preference toward using condoms in each type of partnerships) that will be directly implemented at the agent level, as well as population-level estimates for calibrating the unknown variables (e.g., frequency of the annual sexual partnerships). For those measures available across multiple BESURE waves, we use a pooled estimate of the reported values.

Table S2: Survey methods and sample characteristics, BESURE MSM 2004-2010

	Wave 1	Wave 2	Wave 3	Wave 4
Date	June 04-April 05	Jul-Oct 2008	Aug-Dec 2011	Jun-Dec 2014
Total MSM	645	448	404	455
HIV prevalence	37.7%	37.5%	42.6%	30.6%
Proportion of HIV that was unrecognized	58.4%	78.4%	67.3%	33.1%

1.3 Partnership types and formation

We model two types of partnerships representing long-term "stable" and short-term "casual" partnerships. Stable partnerships can last for several years [5], while casual partnerships will only last a single time step (one week) in the model. We assume that individuals can have multiple casual partnerships from one week to the next [9], but they can only engage in a maximum of one stable and one casual partnership at any time step. All partnerships are updated at the end of each simulation week, and those partnerships reaching their pre-specified duration will be dissolved. At the beginning of each following week, individuals' tendency to engage in a new partnership is evaluated and "eligible" individuals will select the geographical search domain for meeting their future partners based on their location of residence. Once the partnership domains are established for all eligible MSM, individuals will follow a search mechanism based on a combination of race- and age-dependent mixing patterns, as well as sexual role preference, to select their future partner from the pool of eligible people at the selected domain. This process is modeled in 3 steps:

1.3.1 Step 1. Evaluating an individual's probability of engaging in a new partnership

Each individual's likelihood of engaging in a new partnership is modeled as a function of his age, the level of sexual activity, and current partnership status.

In accordance with the heterogeneous frequency of reported partnerships by age, we define a partnership coefficient for modeling the likelihood of engaging in new partnerships as a function of individual's age ($c_{Part|Age}$) (assumed to be a fixed level for each age group).

Sexual activity class: In order to represent the heterogeneous level of sexual activity among MSM, we defined three sexual activity classes ("low", "medium" and "high"), each corresponding to a lifetime level of engagement in casual partnerships. An individual's sexual activity class (c_{SA}) is determined at the time of birth (entry to population) and remains fixed throughout his life (though within each sexual activity class, the actual level of partnership formation changes with age – for example, partnership formation declines with older age in all three classes). This attribute represents a combination of factors determining an individual's tendency for engaging in casual partnerships, reflecting the diversity of sexual activity seen in real populations. As described in a previously published modeling construct [10], we implement the simplified definition of the 3 sexual activity classes in order to more accurately represent "tails" in the observed distribution of (self-reported) sexual activity in data from Baltimore City. Individuals with particularly high sexual frequency are potentially important drivers of STI transmission dynamics but are not easily represented assuming a simple Poisson process of sexual partnership formation. We therefore arbitrarily assign equal numbers of individuals to these three sexual activity classes, and then calibrate the relative frequency of casual partnership formation in each of these classes to most closely fit the observed distribution among MSM in Baltimore City.

Finally, we model each agent's tendency for engaging in casual and stable partnerships at any point of time via two additional parameters (p_{Csl} and p_{Stb}) at the agent-level, and also define the conditional likelihood of engaging in new casual partnerships concurrent to an existing stable partnership via a separate parameter ($p_{Csl|Stb}$).

With these definitions, an individual's likelihood of engaging in a new stable (P_{new_stb}) or casual (P_{new_csl}) partnership at each timestep can be estimated as follow:

$$P_{new\_stb} = p_{Stb} \times c_{Part|Age}$$

$$P_{new\_csl} = p_{Csl} \times p^{*}_{Csl|Stb} \times c_{Part|Age} \times c_{SA}$$

$$p^{*}_{Csl|Stb} = \begin{cases} p_{Csl|Stb} & number\ of\ stable\ partnerships > 0 \\ 1 & o.w. \end{cases}$$

At each time step, an individual's likelihood for engaging in a new partnership is evaluated and eligible individuals are added to the pool of available people at their CSA of residence to find their potential partners in the next steps.

1.3.2 Step 2. Choosing the partnership domain

The partnership domain is determined according to a discrete mixing structure at the CSA level (Figure S3). In order to model the spatial mixing patterns across the population and among various subgroups, we first define sets of "neighboring" CSA groups with regard to geographical proximity and similar socioeconomic status (income levels) and racial structure [1]. Upon seeking a new partnership, an individual's search scope (for choosing the new partner) is determined according to a discrete geographical mixing probability (*pGM*) for selecting one's own CSA (p_0), a random neighboring CSA in the same CSA group (p_1) or non-neighbor CSA (p_2). The geographical mixing probability ($pGM=(p_0, p_1, p_2)$)

represents a measure of geographical/socioeconomic clustering in the network of partnerships, where *pGM*=(1,0,0) translates into an isolated mixing pattern for partnership only with individuals in one's CSA of residence, and *pGM*=(0.33,0.33,0.33) translates into a homogeneous mixing structure across the entire population. In our initial analysis, we calibrate the geographical mixing likelihoods at *pGM* = (0.5, 0.3, 0.2) according to available estimates from [11].

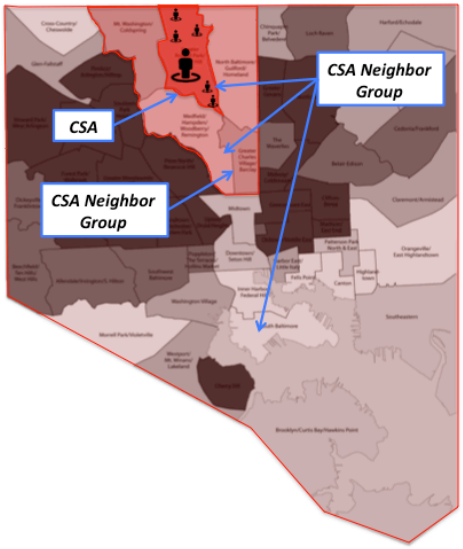

Figure S3: Partnership search domains. Individuals can choose their future partner from their own CSA or a random CSA within or outside their neighbor group.

1.3.3 Step 3. Modeling the search mechanism within the partnership domain

Once the partnership domain is established, individuals follow a search mechanism for finding their new partners from the pool of eligible members in the selected domain. The probability of partnership between two people is evaluated according to an age- and race-mixing structure, as well as sexual role preference. Assuming independent patterns of age- and race-specific mixing, the age-race mixing probability is computed as the product of age-mixing and race-mixing probabilities for each pair of potential partners. A random search mechanism is implemented to evaluate the probability of partnership with each potential partner in the selected domain until a successful match is found or the entire domain is searched. Potential partners are also checked for their compatibility with regard to sexual role and incompatible pairs (e.g., receptive-receptive or insertive-insertive) are dismissed. Upon a successful match, a new partnership is formed for both parties, who are then excluded from the pool of eligible partners for other individuals.

1.3.4 Age-Specific Mixing

Age-specific mixing is modeled based on absolute difference in the square root (ADSR) of men's ages [5]. The ADSR provides a closer fit to the observed age-mixing matrix than does age directly. This statistic also has the desirable property that the same absolute difference in age becomes less important over time. Using data on participant's age and their last male partner's age from BESURE, we estimate the reported ADSR level for main/casual partnerships ($ADSR_{partnership}$) as shown in Table S3. The probability of age-mixing between person *p* and *q* for each partnership type (*pAgeMixing*) is then computed as a function of

partners' age and the target ADSR level for each type of partnerships. Figure S4-A and S4-B compare the simulated distribution of ADSR values among casual and stable partnerships in the baseline simulation model.

$$pAgeMixing = \text{Min}(ADSR_{p,q,2} \times ADSR_{partnership} - ADSR_{p,q}) / ADSR_{partnership}$$

where

$$ADSR_{p,q} = \left| \sqrt{p_{age}} - \sqrt{q_{age}} \right|$$

$$ADSR_{partnership} = (ADSR_{Stb}, ADSR_{Csl})$$

Table S3: Estimates of reported ADSR for Stable/Casual partnerships in BESURE. Estimates are made based on the participant's age and their last male partner's age.

BESURE Waves:	$ADSR_{Stb}$ (Number of reported partnerships)	$ADSR_{Csl}$ (Number of reported partnerships)
Wave 2	0.62 (66)	0.72 (75)
Wave 3	0.68 (71)	0.73 (87)
Wave 4	0.51 (62)	0.76 (77)
Average estimate	**0.6**	**0.74**

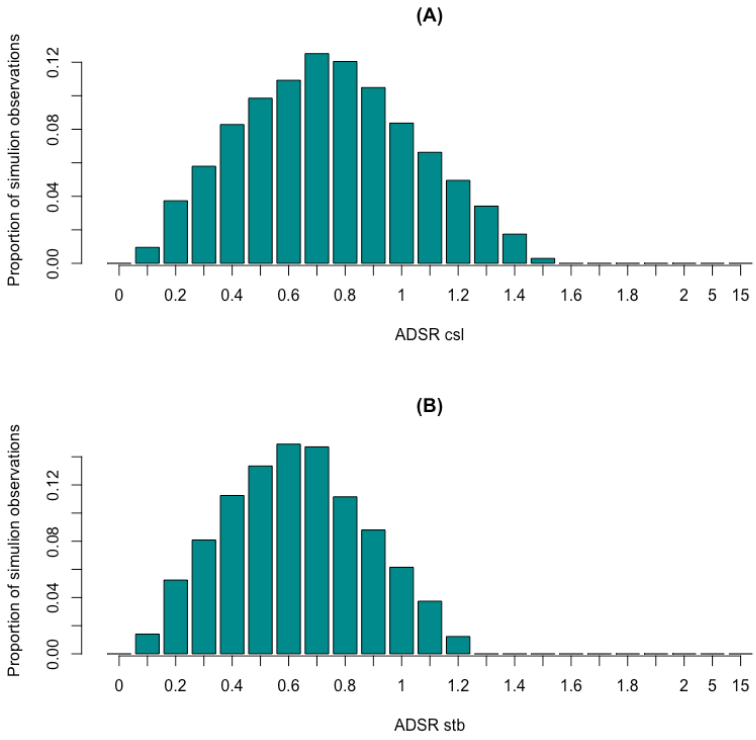

Figure S4: Distribution of ADSR in simulated casual (Panel A) and stable (Panel B) partnerships at the baseline model.

1.3.5 Race-Mixing

We model the probability of partnership between MSM of the same sex by estimating the reported ratio of same-sex partnerships for Black MSM at 90% and for White MSM at 75% through BESURE data.

1.3.6 Sexual Role Preference

Each MSM is assigned an individual sexual role preference (insertive only, receptive only, versatile) at the time of birth (entry to population). The sexual role preferences prohibit the partnerships between two men who are insertive only or those who are receptive only (allowing for 5 partnership configuration). The type of sexual act in partnerships between two versatile men is determined via uniform probability distribution between 0 and 1 (e.g., 50% chance of insertive/receptive act for each man) and will be updated at each time step for their active partnerships. Using data from BESURE, we estimate the proportions of population that fall within each category at 42% insertive-only, 26% receptive-only, and 32% versatile.

1.4 HIV Epidemiological Module

This module governs various aspects of HIV natural history and cascade of care, and it is updated at the end of each time step (week).

1.4.1 HIV Natural History

Upon a successful HIV transmission event, individuals experience a gradual increase in viral load (VL) and move through various stages of disease (Figure 1, main manuscript). We consider three disease stages in absence of ART, including stage 1 (CD4 count > 500 cells/ μL), stage 2 (CD4 count between 200-500 cells/ μL) and stage 3 (CD4 count <200 cells/ μL). Each disease stage is characterized with regard to duration of disease (as a crude measure of CD4 decline over time), mean VL level (determining the level of infectiousness) as well as the HIV mortality rate. In this model, we do not model the dynamics in the number of CD4 counts directly, but rather use the defined disease stages as surrogate marker of VL and mortality level for all HIV+ individuals.

1.4.2 HIV Cascade of Care

The continuum of care for infected individuals is modeled in five levels corresponding to those 1) unaware of their HIV infection, 2) diagnosed with HIV but not linked to care, 3) linked to care but not engaged in care, 4) engaged in care and on ART, and 5) engaged in care but not taking ART (Figure 1, main manuscript).

HIV-positive individuals are subject to a probability of screening for HIV at the beginning of each week. Upon diagnosis with HIV, individuals experience a fixed likelihood of linking to care over the following weeks. Once linked to care, individuals are assumed to engage in HIV care and start ART immediately. Individuals who are adherent to their ARV regimens and do not harbor resistance mutations to the component drugs can generally achieve viral suppression 8 to 24 weeks after ART initiation; rarely, in some patients it may take longer. Taking ART will further lower the disease mortality rate at each disease stage to a certain degree [12–14]. We assume that individuals starting ART through stage 3 (with CD4 count < 200 cells/ μL) will continue to experience the stage 3 mortality level (adjusted with ART reduction factor) for one year before reverting back to stage 2 (and experiencing stage 2 mortality level adjusted with ART reduction factor).

Those on ART can become non-adherent to treatment over time and/or become disengaged in care[1]. These individuals are subject to a weekly probability of reengagement in care and reinitiating ART in the future, but cannot reinitiate ART for 6 months after discontinuation [15]. Once off ART, individuals are assumed to lose viral suppression immediately and to experience a rapid decline in their CD4 counts. For simplicity, we assume that the effect of ART on CD4 count levels is maintained for one year following discontinuation (unless the agent was not previously on ART for a year, in which case the duration of ART is used) – and we also add this amount of time to the individual's "clock" of progression for HIV disease. Thus, for example, an individual starting ART in stage 2 and taking ART for 6 months before discontinuation will go back to stage 2, but the time until progression to stage 3 is prolonged by 6 additional months. We further assume that those starting ART in stage 1 will return to stage 2 if they discontinue treatment, and

[1] At ART discontinuation, if the person has started ART during Chronic disease, they are assumed to return to stage 2 with the same level of infectiousness and will be subjected to the corresponding mortality level. The duration of stage 2 is assumed to be the lesser of the preceding duration of ART (before loss to follow-up) or one year. If the person had started ART during stage 3, they will can return to stage 2 or stage 3 depending on the duration of treatment:

- If duration of treatment is smaller than the time spent in stage 3, agents return to stage 3 with the same level of infectiousness and mortality. The duration of stage 3 is extended for the duration of treatment up to one year.
- If duration of treatment is greater than the time spent in stage 3, agents return to stage 2. The duration of stage 2 will be expanded for the duration of treatment minus time spent in stage 3.

those beginning ART through stage 3 can revert to stage 2 or stage 3 depending on the duration of treatment.

1.5 HIV Transmission module

HIV transmission is evaluated for all active partnerships between HIV-positive individuals and susceptible partners at the end of each week. The probability of transmission is modeled as a function of an infected partner's infectiousness for transmitting HIV, the immunity of the negative partner toward transmission with HIV (through PrEP), potential protection through condom use, and an additional coefficient tuning the overall probability of transmission. HIV infectiousness is modeled as a function of an individual's VL corresponding to his disease stage and care status, as noted in Table 1 of the main manuscript. An individual's immunity to infection is modeled as a function of PrEP use and adherence, ranging from 0 (in absence of PrEP) to 1 (full adherence to PrEP). The probabilities of condom use in casual and stable partnerships are estimated based on reported levels through BESURE (Table S4). Finally, the transmission coefficient captures the baseline probability of HIV transmission per contact and is calibrated to reflect disease prevalence at equilibrium.

Table S4: Reported frequency of condom use in stable and casual partnerships from BESURE.

	Never	Part-time	The whole time
Stable partnership	0.45	0.55	0
Casual partnership	0.47	0.12	0.4

With these definitions, the weekly likelihood of HIV transmission through an active sexual contact is estimated as follow:

$$Ptrans(\mathrm{X},\mathrm{Y},\mathrm{Q}) = C \times X_{Inf} \times Y_{sus} \times (1 - pCondumUse(Q) \times cCondomEffectiveness) \times Y_{sexualPositionCoef}$$

where

Ptrans(*X,Y,Q*): Per week probability of transmission from person *X* (infected) to *Y* (susceptible) in a partnership type Q (stable, casual)

C: Simulation coefficient

Y_{Inf}: Person Y's infectiousness

X_{Sus}: Person *X's susceptibility* toward infection

pCondomUse(*Q*): Probability of using condom in partnership type Q

cCondomEffectiveness: condom effectiveness in reducing the risk of transmission

$Y_{sexualPositionCoef}$: Person Y's increased probability of transmission based on sexual positioning

1.6 GC Epidemiological Module

We consider NG/CT as a 'SIS'-type disease; specifically, individuals become infectious after an initial infection and remain infectious until treatment or spontaneous resolution, at which time they become immediately susceptible to recurrent infection. We assume that NG/CT is spread through sexual (genital-genital, genital-rectal, genital-oral, or oral-rectal) contact, and that infection may be either symptomatic or asymptomatic. Symptomatic individuals experience a fixed probability of seeking care in each week. We include only those care-seeking episodes that would trigger a clinical decision to test for NG/CT at the appropriate site and would result in treatment if the test were positive; other care-seeking episodes (whether for unrelated conditions [e.g., upper respiratory infections] or for symptoms of NG/CT that are either not recognized or would not result in treatment even if the test were positive) are ignored. We assume that individuals remain infectious during the week of treatment and one week thereafter [16–18]. In addition to this symptomatic testing behavior, all MSM (whether infected with NG/CT or not) can further undergo regular screening for NG/CT (i.e., in the absence of symptoms) according to CDC recommended criteria for MSM based on their HIV status, PrEP status, and STI history [19]. The duration of untreated disease (d) is based on literature estimates, and the weekly probability of spontaneous resolution is set to inverse of this duration ($1/d$).

1.6.1 Site of infection

We differentiate three types of NG/CT infections based on the site of infection as Urethral, Rectal or Pharyngeal infections. Given the low degree of overlap for simultaneous infections in multiple sites, and the higher likelihood of symptomatic disease in urethral infections for those co-infected with rectal and pharyngeal infections, we only allow for a single-site NG/CT infection in each individual and will exclude the possibility of simultaneous infections in various sites (allowing for no reinfection while the original infection lasts). Each type of infection is further associated with a specific likelihood of developing symptomatic disease (Table 1 of the main manuscript). Among HIV- individuals, a rectal/urethral NG/CT can increase the transmissibility of HIV to sexual contacts among HIV infected MSM and also increase the susceptibility for HIV acquisition among HIV uninfected MSM.

1.6.2 NG/CT Transmission dynamics

NG/CT-infected individuals can transmit the disease to other individuals through exiting network of sexual contacts (previously built and calibrated for the HIV model). Due to complications in conceptualizing all various pathways for transmission of disease from one site to another with regard to different types of sex acts, unknown level of individuals' preferences for each sexual role and the degree of versatility to change this role in each partnership, in addition to the lack of data informing the risk of NG/CT infection through each mode of transmission, we adopt a simplifying assumption to combine various modes of transmission for all types of infections through a single transmission event modeled over each active sexual contact between an infected and uninfected MSM at each time step. Upon transmission with NG/CT, the clinical site of the recipient infection is randomly assigned in such a way as to replicate the relative incidence of infection at each site as estimated from local surveillance report in Baltimore City (see Table 1 of the main manuscript).

1.6.3 Computing the probability of presenting to STI care

MSM may present to HIV/STI care providers (e.g., STD clinics, community health centers, HIV counseling programs) for a variety of reasons, and get tested for HIV and other STIs. We model visits for STI screening as a fixed weekly probability that reflects an individual's age-group (modeled in 12 classes for MSM age 15 to 75) and sexual activity level (modeled in 3 classes of sexual activity), such that younger MSM with higher propensity of partnerships experience a higher likelihood of visits [20,21].

We let *S* represent the individuals' sexual activity class (values ranging from 1 to 3 representing low-, medium- and high-activity classes) and we let A represent the individual's age-group (values ranging from 1 to 12 representing age groups of 5 years each: [15,19], [20-24], …, [70,75]). Finally, according to previous assumptions for lower level of access to HIV care among Black MSM compared to White MSM in the baseline simulation model, we modify the probability of accessing to STI care (*pAccessCare*) by race (R) set at 50% for Black MSM relative to White MSM [22]. Given these assumptions, an individual's probability of presenting to STI care (*PPSC*) at each week is computed as follow:

$$PPSC\ (\mathrm{S},\mathrm{A},\mathrm{R}) = {}^{(13-\mathrm{A})}/_{12} \times {}^{(\mathrm{S})}/_{3} \times pAccessCare(\mathrm{R}) \times C$$

where C is the fixed coefficient for fine-tuning the probability of presenting to STI care.

1.7 PrEP module

PrEP Eligibility criteria: Our primary outcome for the current analysis is the projected incidence of HIV after 20 years of delivering PrEP to MSM in Baltimore City. We measure this outcome in three different PrEP delivery scenarios, selected for purposes of evaluating the added benefit of targeting PrEP at individuals diagnosed with NG/CT. In all three scenarios, indication for PrEP use (eligibility) is considered in accordance with CDC recommendations [23] and Baltimore City's PrEP guidelines [24].

The CDC guidelines for PrEP use among MSM use the following criteria as indications for PrEP: sexually active HIV negative adult MSM who are not in a monogamous partnership with an HIV-negative male partner and who in the last 6 months: report any condomless anal sex, have any STI reported or diagnosed, or report having an ongoing sex partner with HIV [23]. The PrEP guidelines in Baltimore City further suggest that all HIV negative MSM who 1) may not have access to condom or always ask a partner to use a condom, 2) are diagnosed with a STI in the last 6 months, 3) are in a serodiscordant relationship with a HIV-infected partner (who may or may not be on HIV treatment), 4) are unsure of HIV-status of their sexual partner, or 5) inject drugs or are in a sexual partnership with a person who inject drugs should consider PrEP. As such, we modelled the criteria for PrEP eligibility among MSM to include HIV-negative MSM who are diagnosed with NG/CT in the last 6 months, live in a serodiscordant partnership, or report an unprotected sex act or a new casual partnership in the last 6 months.

2 SIMULATION CALIBRATION

Individual-level parameters in our models fall into two categories: "fixed" parameters estimated based on available literature or data, and "variable" parameters that are unknown and will be calibrated based on epidemiological setting. Fixed (known) parameters include those associated with the natural history of HIV (such as viral load levels in each disease stage) and those defining behavioral characteristics (e.g., likelihood of condom use). Variable parameters include descriptors of HIV and NG/CT transmission and

care that are defined at the individual-level and will be calibrated to provide the corresponding calibration targets (at the population-level) from Baltimore City (e.g., tuning the individual's probability of presenting to care for HIV screening to provide the target proportion of infected population diagnosed in Baltimore City). Table 1 in the main manuscript includes a list of main calibration targets for HIV and NG/CT modules.

2.1 Calibration Targets

2.1.1 HIV prevalence and continuum of care

Using the latest report of public HIV surveillance data from Baltimore City (year 2012) [2], we estimate the prevalence of HIV among MSM at a total of 3329 people, which corresponds to a prevalence of 22% in our simulated population. Furthermore, we estimate the reported proportion of HIV-infected MSM in each step of the cascade at 86% for those diagnosed but not linked to care, 62% for those linked to care but not engaged, 50% for those engaged but not on ART, 39% for those on ART but not virally suppressed and finally 27% for those virally suppressed.

2.1.2 NG/CT incidence

In this section, we provide details of our estimation procedure for NG/CT incidence using data made available to us through several sources including 1) the gonorrhoea Surveillance dataset, 2) STD Surveillance Network, and 3) BCHD facility dataset in Baltimore City.

Estimating the annual diagnosis of gonorrhoea infection in Baltimore City: The gonorrhoea Surveillance dataset includes all males residing in Baltimore City who were reported to the Baltimore City Health Department for infection with gonorrhoea at one or more anatomic site, regardless of sex partner gender, beginning with cases diagnosed on 1/1/09 and ending with cases reported through 5/31/16. Due to changes in testing technology, we only consider data from 2011 and later for estimating gonorrhoea diagnosis as that is when the STD clinics started using NAATs for extragenital swabs (due to the lab becoming validated for this) which is more in line with practices moving forward. We further restrict the data to the end of 2015, to cover the annual number of diagnosis in each full year (Table S5). We further analyze this data by reported site of infection and estimate the range of reported gonorrhoea diagnosis in each body site (Table S6).

Table S5: Annual number of reported gonorrhoea diagnosis among men in Baltimore City.

	2011	2012	2013	2014	2015
Gonorrhoea diagnosis	1139	901	1052	1083	1297

Table S6: Annual gonorrhoea diagnosis among men by site of infection in Baltimore City.

Site of infection	Lower bound	Upper bound
Urethral	681	1026
Rectal	46	83
Pharyngeal	58	151

Adjusting for MSM risk group: The surveillance dataset does not include information on gender of sex partners for all persons diagnosed with gonorrhoea infection. This information is however available for a

subset of population through STD Surveillance Network (SSuN). SSuN attendees are randomly selected from MSM diagnosed with gonorrhoea who will then agree to complete a SSuN interview. Within this group, 26% to 30% of all male patients identified themselves as MSM in Baltimore City.

Adjusting for non-overlapping Chlamydia infections: The BCHD facility dataset provides information on diagnosis of gonorrhoea or chlamydia infection among all male patients visiting the two STD clinics in Baltimore City. This data is further stratified for MSM by including men who reported male sex partners in the past 3 months OR self-identified as gay or bisexual. For patients who visited the clinic multiple times, if he was classified as MSM at any visit, we included all his clinic visits. The dataset provides information on all episodes of visit and diagnosis with gonorrhoea or chlamydia infection among these men. Based on the reported number of diagnosis, we estimate the proportion of diagnosed chlamydia infection that did not overlap with gonorrhoea infection relative to overall number of gonorrhoea diagnosis at 40%, and use this value to adjust the annual number of gonorrhoea diagnosis among MSM to include non-overlapping chlamydia infections as well. This estimate also agrees with the reported level of chlamydia infection relative gonorrhoea infection in Baltimore City through the STD Surveillance Network (SSuN) 2013 [25].

Adjusting for proportion of symptomatic cases not seeking care: In order to derive the true incidence of disease from the current estimates of the number diagnosis, we further adjust our estimate to account for the proportion of symptomatic cases not seeking care. Based on literature, we estimate that approximately 60% symptomatic population may not seek direct care for their disease (56% for Urethral infection, 60% for Rectal and 70% for Pharyngeal infection) [26], and inflate the number of symptomatic cases in our sample (approximately 78% of sample) by 250% to account for these cases.

Adjusting for the number of asymptomatic infection: Given the restrictions in capturing the underlying level of asymptomatic disease from the estimated of NG/CT diagnosis, we rely on our estimate of the symptomatic NG/CT incidence, and assume that each episode of NG/CT infection is associated with a 74% likelihood of symptomatic infection for urethral, 20% for Rectal, and 10% for Pharyngeal disease [26–28]. Based on this assumption, we derive the estimate for annual incidence of NG/CT among MSM by site of infection as follow:

- Incidence of urethral infection [725 − 1135] Person/year
- Incidence of rectal infection [144 − 259] Person/year
- Incidence of pharyngeal infection [327 − 852] Person/year

Challenges in interpreting local estimates: Despite general expectations, our estimated ratio of rectal/pharyngeal to urethral infections is very small. This pattern does not agree with the previously reported prevalence of extragenital relative to genital NG/CT in different populations that estimate the average prevalence ratio of rectal to urethral infections at 4.1 (ranging from 2.43 to 6.23) and pharyngeal to urethral infections at 1.5 (ranging from 1.35 to 1.71) [29–31]. In a previous analysis of SSuN data, researcher reported a similarly low proportion of extragenital to genital NG/CT infections among MSM attending STD clinics [32], and attributed it to low rate of extragenital NG/CT screening at STD clinics that results in missing those infections [33].

Given that our estimates of the genital and extragenital NG/CT infections based on local datasets from Baltimore City are more in line with the observed trends in the SSuN data, we believe that the same pattern of underestimation is evident for the true incidence of extragenital NG/CT infection in this population. In order to fix this problem, we chose to rely on the estimated incidence of genital (urethral)

NG/CT infection from the surveillance dataset in Baltimore City (assuming appropriate level of genital-site testing/screening and reporting), and to estimate the incidence of rectal and pharyngeal infections by applying the reported prevalence ratio of each infection site relative to urethral infection.

Estimating the incidence of rectal and pharyngeal infection: We assume that diagnosed NG/CT will be treated very rapidly, such that the relative duration of disease is driven by the proportion of infections for which people are not treated - whether because they are asymptomatic, symptoms are not sufficient to drive care-seeking, or the clinical presentation (e.g., sore throat) does not prompt testing or treatment for NG/CT. Screening is assumed to have relatively little impact on the *relative* duration of infection (i.e., screening can occur, but it does not pick up so many more prevalent urethral infections than pharyngeal infections, for example, that it drives the ratio of disease duration in the population to a significant degree). We further assume that the asymptomatic disease is likely to go undetected and therefore 26% of urethral infections, as well as 80% of rectal and 90% of pharyngeal infections will go untreated [26–28].

Based on these assumptions, we derive the incidence ratios based on prevalence ratios as follow:

- Incidence ratio of rectal to urethral disease: 4.08 (prevalence ratio) * 0.26 /0.8 (proportion of untreated cases) = 1.33
- Incidence ratio of pharyngeal to urethral disease: 1.5 (prevalence ratio) * 0.26 /0.9 (proportion of untreated cases) = 0.43

Using the estimated incidence ratios, we estimate the incidence of rectal and pharyngeal NG/CT among MSM as follow:

- Incidence of urethral NG/CT among Baltimore's MSM: [735-1135] Person/year
- Incidence of rectal NG/CT among Baltimore's MSM: [998-1505] Person/year
- Incidence of pharyngeal NG/CT among Baltimore's MSM: [326-492] Person/year

2.2 Calibration procedure

Upon collection of all individual-level data and incorporation into the model (fixed parameters), we calibrated the model as a whole against population-level targets (above) to ensure that the model provides realistic outputs. This was done via a random search mechanism to find the best combination of parameter values that minimizes the observed difference between simulated outputs and the calibration targets.

Burn-in Period: The model starts from a randomly generated population of MSM with no active partnership at time zero with a randomly assigned pattern of HIV infection (randomly according to age, race and location of residence). In order to create a realistic pattern of sexual partnerships with age, we allowed the original population to age and evolve for at least one generation before reaching a stable level of HIV incidence in the absence of PrEP – thus generating a full burn-in period of 100 years (a decision made on an a-priori basis).

2.3 Calibrating partnerships

BESURE surveys (2004 – 2014) provided the main source of local information available on the network of MSM partnerships in Baltimore. The data included aggregate information on the reported number of sexual partners (by age group) and type of those partnerships in the last 12 months. Assuming a fixed mixing structure over time, we used this information to calibrate the individual-level likelihood of engaging in a stable or casual partnership at each simulated time step (week). We further used the coefficients of sexual activity to calibrate the right and left tail of the partnership frequency distribution

(for those MSM reporting 0 or more than 5 partners in a given year). The partnership calibration results are summarized in Figure S5.

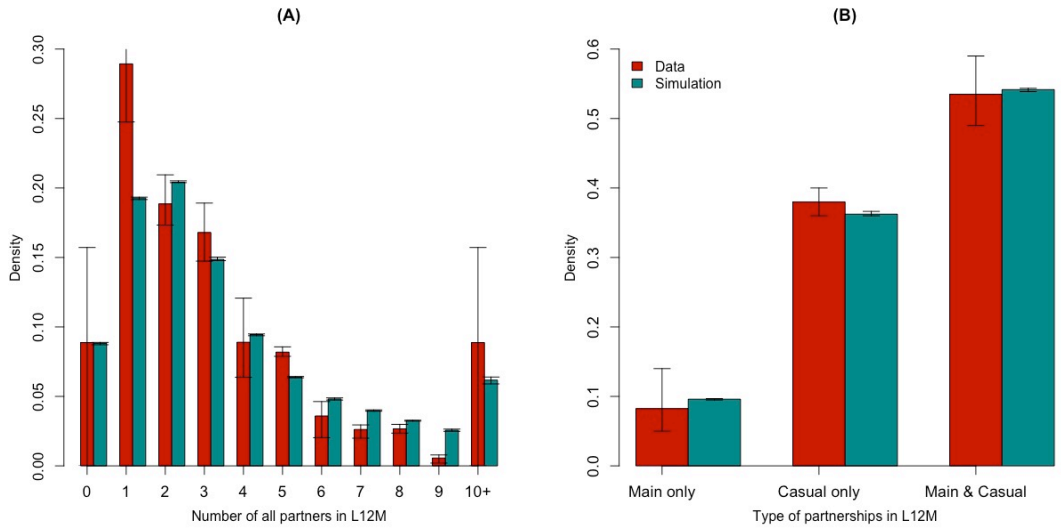

Figure S5: Model calibration to partnership data. Shown are the mean values of simulations (in green) compared against empirical data (in red). The error bars around simulated values represent the 95% uncertainty range of observations around each simulated measure, and the error bars around the data represent the range of annual observations through the 4 BESURE surveys from 2004 to 2014.

2.3.1 Frequency of partnerships by age and sexual activity

The age-dependent coefficients of partnerships in each sexual activity class were calibrated to accurately portray the right and left tails of the partnership frequency distribution for all MSM and in each age group. The calibration results are summarized in Figure S6.

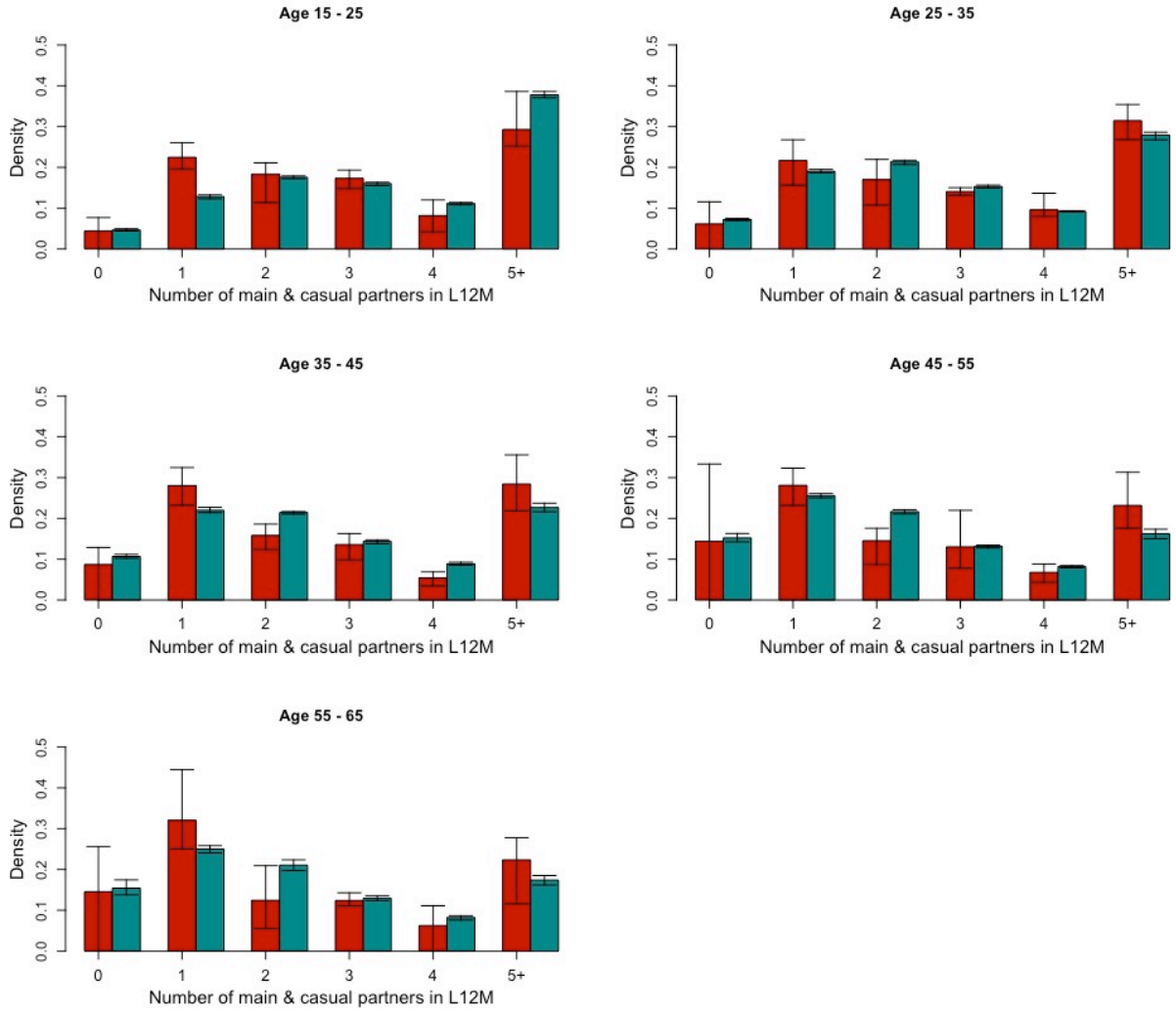

Figure S6: Frequency of reported partnerships in each age group in the last 12 months (L12M), comparing model results to the data against which the model was calibrated. Shown are the mean values across all simulations (in green) compared against empirical data (in red). The error bars around simulated bars represent the 95% uncertainty range of simulated values and the error bars around the data represent the range of annual observations through the 4 BESURE surveys from 2004 to 2014.

There were conceptual challenges with the use of BESURE data as the main data source for calibrating the network of sexual partnerships. Specifically, BESURE applies a venue-based sampling method, which is more likely to capture a representative sample of young (as opposed to older) MSM. Based on discussions with the BESURE investigators, we felt that the general population of older MSM was likely to have lower numbers of sex partners than reported in BESURE and therefore allowed for a lower frequency of partnerships among older MSM.

Furthermore, given the strong bimodal distribution of partnerships among young adults, we were not able to replicate these empirical distributions precisely and thus chose to minimize the estimation error at the tails of this distribution. To further assist the calibration of tails, we defined sexual activity classes

according to the mean number of casual partnerships to represent natural heterogeneity in in individual-level partnerships. Addition of high versus low/medium sexual activity classes allowed us to calibrate the overall frequency of partnerships in each age group with more precision. Figure S7 represents model projections of the frequency of partnerships in each sexual activity class. This figure illustrates that, after calibration to BESURE data, the low and medium sexual activity classes behave very similarly (and may likely be represented equally well as a single class). Given the lack of representative data against which to explicitly calibrate these distributions, this presumed distribution of sexual partnerships is an assumption/limitation of the current model.

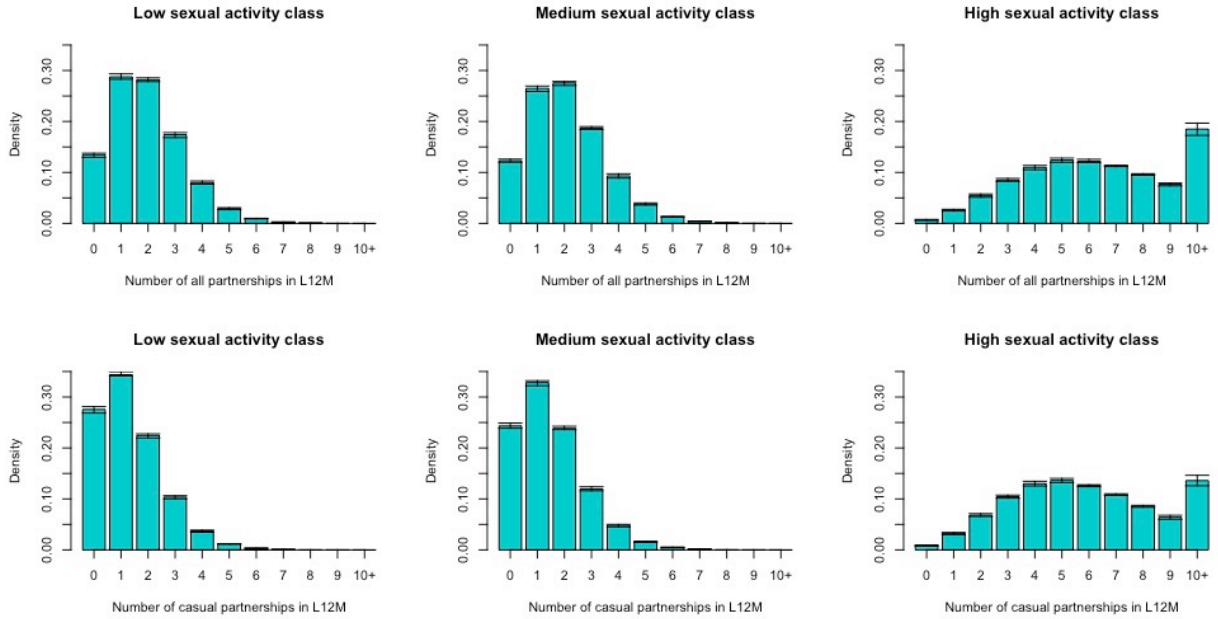

Figure S7: Model projections of the frequency of partnerships in the last 12 months (L12M) in each sexual activity class. Panels represent the distribution of all (top row) and casual (bottom row) partnerships in low, medium and high sexual activity classes. Shown are the mean values of simulations (in green) with error bars representing the 95% uncertainty range of observations around each simulated measure.

2.4 Calibrating HIV and NG/CT epidemiology

Using the population-level targets for annual diagnosis and incidence of NG/CT as well as HIV prevalence and cascade of care (section 3.1), we calibrate the simulation model to provide these outcomes within an acceptable range (Figure S8 A through D).

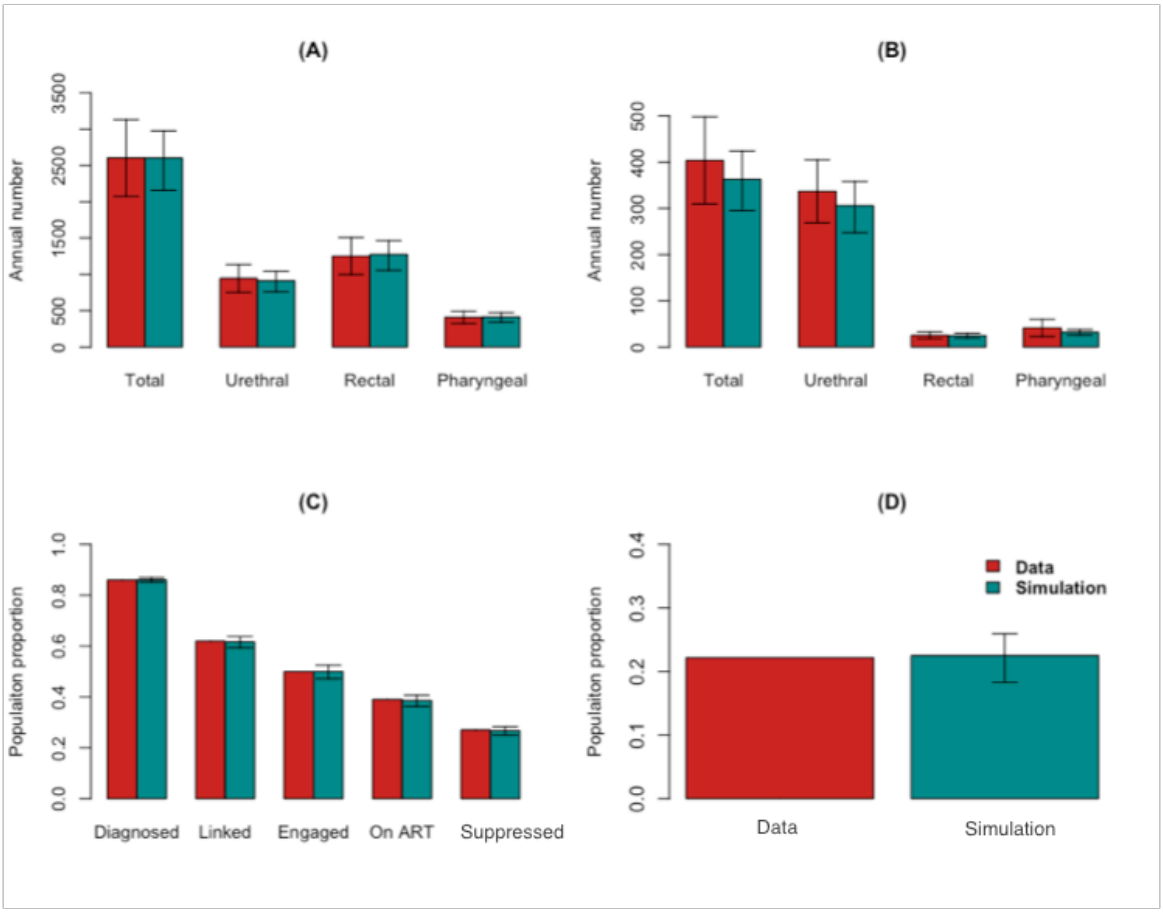

Figure S8: Closeness of model fit to epidemiological data for (A) annual incidence of NG/CT, (B) annual diagnosis of NG/CT, (C) Cascade of HIV Care, and (D) HIV prevalence. These graphs illustrate the effectiveness of the calibration procedure and are not a validation of the underlying data or the model itself. Shown are the mean values of 200 simulations (in green) compared against empirical data (in red). The error bars around simulated values represent the 95% uncertainty range of observations around each simulated measure, and the error bars around the data in panel A&B represent the range of annual observations through the Baltimore City surveillance dataset (2011 – 2015). Data used for calibration in panel C&D is only available as point estimate in year 2012.

Given the lack of data regarding the anatomical site of infection and the relative frequency of oral-only versus oral-plus-anal versus anal-only sex to model site-specific transmission dynamics for NG/CT, we adopted a simplified approach that does not fully capture the complete transmission dynamics but should result in the appropriate distributions of NG/CT infection at each anatomical site. For this purpose, we combined various modes of transmission for all types of infections through a single transmission event modeled over each active sexual contact between an infected and uninfected MSM at each time step. Upon transmission with NG/CT, the clinical site of the recipient infection was randomly assigned in such a way as to replicate the relative incidence of infection at each site as estimated from local surveillance report in Baltimore City (see Table 1). The final calibration results in a probability of 35% for urethral, 49% for rectal and 16% for pharyngeal infections modeled upon each successful transmission event. Since the goal of this model is not to comprehensively represent the dynamics of NG/CT transmission but rather to estimate the impact of PrEP strategies for HIV that incorporate NG/CT screening and treatment, we

adopted this simplified approach (which may have some inaccuracies regarding the specific transmission dynamics but should result in the appropriate marginal distributions of infection by each anatomical site), rather than incorporating data-free assumptions about the relative frequency of oral-only versus oral-plus-genital sex and the relative transmissibility of NG/CT from each anatomical site to the other.

2.4.1 HIV and NG/CT co-infection:

As described above, our calibration targets were limited to the marginal distributions of HIV and NG/CT infections among MSM, and excluded the co-infection rates due to data unavailability. Unpublished results from analysis of STD Surveillance Network (SSuN) data [34] from 2008 to 2013 in 12 jurisdictions suggest that 8% of patients diagnosed with NG had a previous HIV diagnosis, and among the remaining individuals diagnosed with NG, 69% received an HIV test within 30 days of their STI diagnosis. However, the proportion of patients diagnosed with HIV coinfection on that test is not recorded. We therefore took a conservative approach, assuming that the only correlations between HIV and NG/CT would be induced by age- and race-specific assortative mixing, plus differentiation of individuals into three different sexual activity classes. Figure S9A represents the projected levels of HIV and NG/CT prevalence at the end of each year in the model, corresponding to 22% of MSM infected with HIV (calibration target), 10% infected with NG/CT (calibration target) and 2.5% infected with HIV and NG/CT (a cross survey estimate). Figure S9B represents the proportion of incident cases who were co-infected with NG/CT and HIV at the time of HIV or STI infection. For example, this figure suggests that 20% of incident HIV cases are co-infected with NG/CT at the time of disease transmission. These results suggest that our underlying sexual activity assumptions do not impose a high rate of correlation between the two diseases; as a result, our estimates of the impact of STI-based PrEP may be conservative. To the extent that HIV and NG/CT co-locate among similar populations beyond age, race, and tertiles of sexual activity, one would expect that NG/CT-targeted PrEP strategies would have even greater impact than projected in this model.

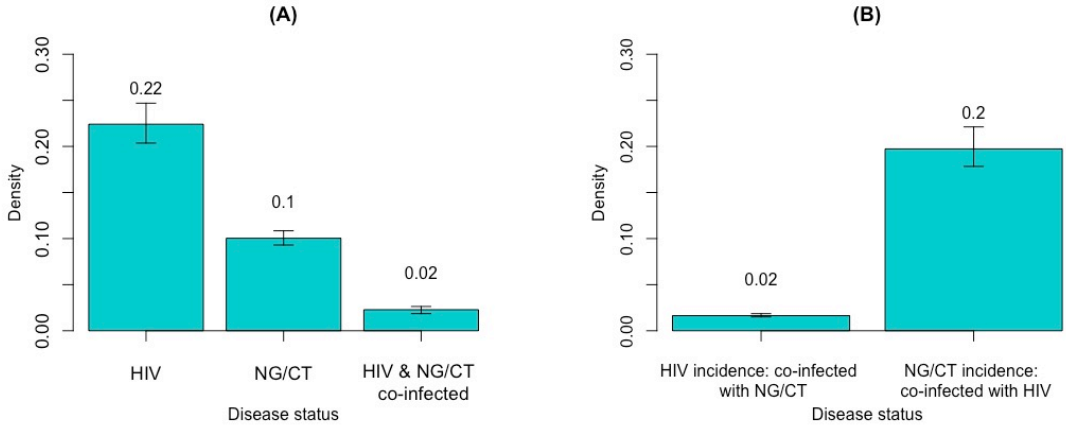

Figure S9: Model projections of the distribution of HIV, NG/CT, and coinfection among MSM (Panel A) and the proportion of HIV and NG/CT incident cases coinfected at the time of transmission (Panel B). Shown are the mean values of simulations (in green) with error bars representing the 95% uncertainty range of observations around each simulated measure.

2.5 Complete list of model parameters

Table S7 provides a complete list of model parameters and values.

Table S7: Complete list of model parameters and values.

Parameter	Value	References
Partnerships		
Proportion of population in each sexual activity (SA) **class**	0.33	
Rate of casual partnership formation in each sexual activity class relative to the medium sexual activity class	Low sexual activity class 0.85 High sexual activity class 5.0	
Rate of casual partnership by age group	[15-25): 0.5 [25-45): 0.3 [45-55): 0.25 [55-75+): 0.3	
Age Mixing (Absolute different in square root of ages) • Stable partnerships • Casual partnerships	 0.6 0.73	 [35]
Race mixing (Likelihood of mixing with a partner of the same race) - Black & Black - White & White	 0.9 0.75	[35]
Likelihood of condom use - Stable partnerships - Casual partnerships	[Never, Partially, Always] [0.45, 0.55, 0.00] [0.47, 0.12, 0.41]	 [35]
Sexual position preference - Insertive only - Receptive only - Versatile	 0.42 0.26 0.32	 [35]
Transmission coefficient for insertive relative to receptive sexual position	0.384	[36]
NG/CT		
Proportion of cases symptomatic - Urethral - Rectal - Pharyngeal	 74% 20% 10%	 [27] [26,37] [28,37]
Duration of infection in the absence of treatment	[3 – 12] months [2]	[16,38,47–51,39–46]
Duration of treatment	2 weeks	[16–18]
Regular GC screening intervals for HIV+ MSM on ART - All MSM - MSM with a history of NG/CT in the last 6 months	 12 months 6 months	 [52]
Likelihood of compliance with CDC guideline for NG/CT screening	40%	[53–58]
Efficacy of condoms to prevent NG/CT transmission	70%	[16,59,60]

[2] Values are selected over uniform distributions across the ranges presented

Increase in HIV transmissibility (from urethral or rectal infection)	[1.5 – 2] fold [3]	[61–65]
Increase in HIV susceptibility (from urethral or rectal infection)	[1 – 2.5] fold [3]	[16,28,65,66]
Probability of NG/CT transmission per act	0.294	Calibrated to provide the incidence of NG/CT
Proportion of NG/CT infections assigned to each site - Urethral - Rectal - Pharyngeal	 35% 49% 16%	Calibrated to provide the site-specific incidence of NG/CT
Weekly probability of symptomatic NG/CT testing - Urethral - Rectal - Pharyngeal	 0.009 0.001 0.04	Calibrated to provide the site-specific diagnosis of NG/CT
Weekly probability of screening high-risk (according to age and sexual activity class) MSM for HIV and NG/CT	0.014	Calibrated to provide the annual diagnosis of NG/CT and HIV
Probability that NG/CT screening only at urethral site	0.94	Calibrated to provide the relative diagnosis of extragenital to genital NG/CT
Relative likelihood of NG/CT screening among Black MSM relative to White MSM	0.5	[22]
HIV		
Disease stage duration - Stage 1 (CD4 >500 cells/µL): Acute - Stage 2 (CD4 200-499 cells/µL): Chronic - Stage 3 (CD4 <200 cells/µL)[3]: Late stage	 [6 – 9] weeks [3] [8 – 10] years [1 – 3] years	[5,67,68] [5,69] [5,67,69]
Time from ART initiation to full viral suppression	[4-24] weeks [3]	[70]
Time from ART discontinuation to pre-ART CD4 nadir[4]	ART treatment duration up to one year	[71–74]
Mortality rate [3] - Stage 1 & 2, no ART - Stage 3, no ART - Reduction in mortality due to ART	 5 per 1000 person years 1/duration of stage 3 58%	[12–14]
Average viral load (log10 copies/mL) - Stage 1, no ART - Stage 2, no ART - Stage 3, no ART - On ART, partially suppressed - On ART, fully suppressed	 6.5 4.5 5 3.5 1.5	[5]
Efficacy of condoms to prevent HIV transmission	80%	[75,76]
Infectiousness per sexual contact	$2.45^{(\log(VL)-4.5)}$	[5]

[3] Mortality rate in stage 3 is defined as 1/(duration of stage 3).

[4] Infectiousness assumed equal to that of stage 2

Individual's weekly likelihood of engagement in HIV care	0.00577	[77–79]
Weekly probability of ART discontinuation	0.0015	[80]
Gap in care after ART discontinuation	26 weeks	[15]
Weekly probability of - Screening for HIV only (not NG/CT) - Linkage to care (if HIV-positive and not linked) - Starting ART (if engaged)	 0.0065 0.0065 0.095	Calibrated to provide the HIV cascade of care
Relative likelihood of accessing HIV care among Black MSM	0.5	[22]

2.6 Additional analysis

Since sexual activity class is a modeling construct rather than a measurable feature of an individual (see section 1.3.1), there are no data to describe assortative mixing by activity class per se. Similarly, lacking data on serosorting among primary and casual partnerships, we did not explicitly incorporate this into the model. In order to further elucidate model dynamics, we have generated additional figures to report the simulated frequency of sexual partnerships by sexual activity classes (e.g., High-High, High-Med, etc.) and also HIV serostatus (Figure S10 and S11). Note that, since sexual activity class was assumed to reflect casual partnerships only, the frequency of stable partnerships is similar and randomly distributed across all classes (with partnerships across classes being twice as likely as partnerships within classes, reflecting the laws of probability with random assortment).

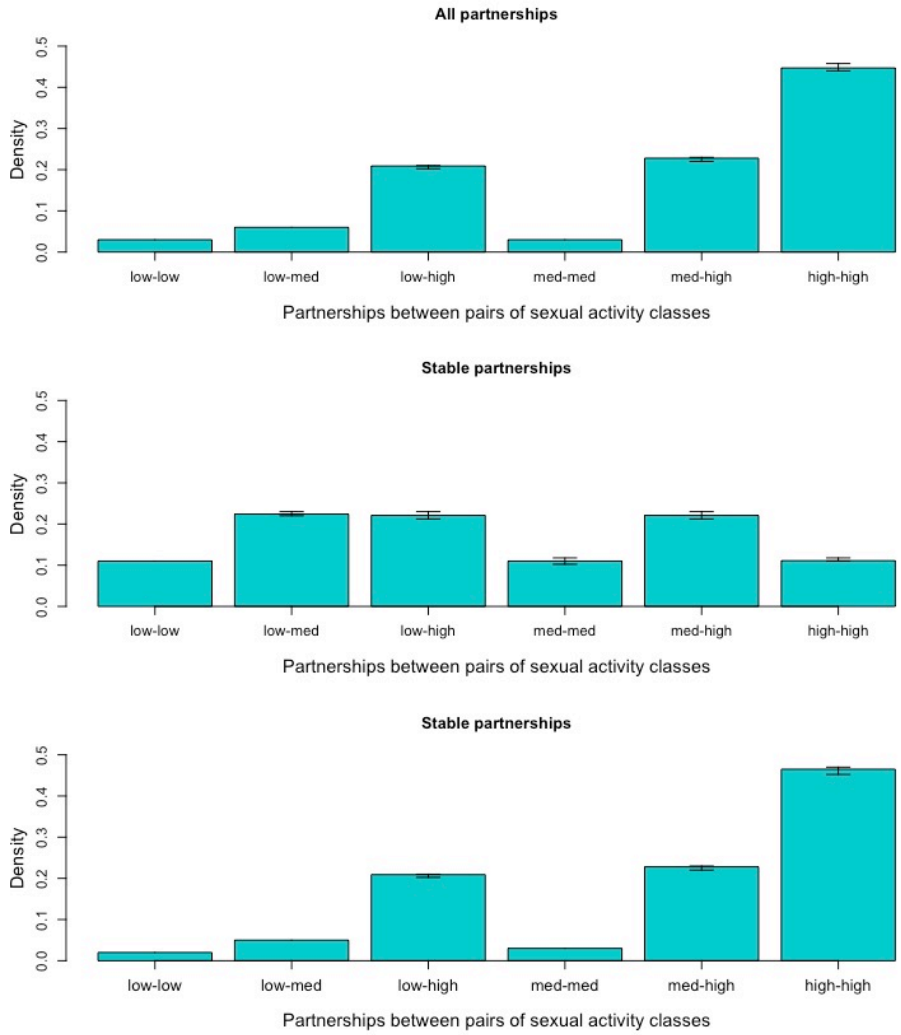

Figure S10: Model projections of the distribution of partnerships among MSM by sexual activity class. Shown are the mean values of simulations (in green) with error bars representing the 95% uncertainty range of observations around each simulated measure.

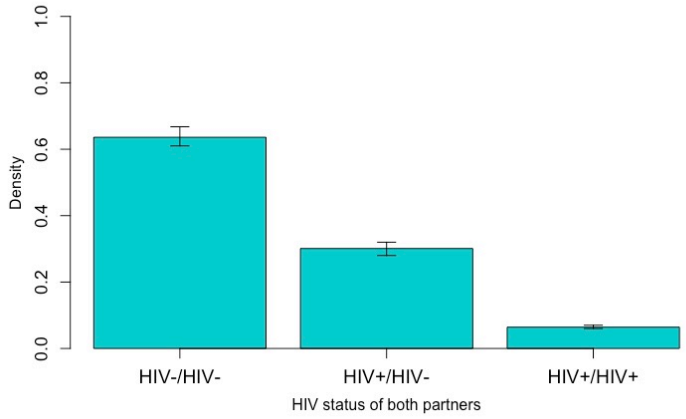

Figure S11: Model projections of the distribution of partnerships by HIV status. Shown are the mean values of simulations (in green) with error bars representing the 95% uncertainty range of observations around each simulated measure.

In order to better illustrate the implications of these modeling assumptions on impact of STI targeted PrEP, we also checked the distribution of MSM receiving PrEP in the model by sexual activity class an age (Figure S12). As expected, targeting PrEP at MSM diagnosed with STIs provides an efficient approach for providing PrEP to high-risk individuals in the high sexual activity class and younger age groups (Figure S12-Panels A & D)

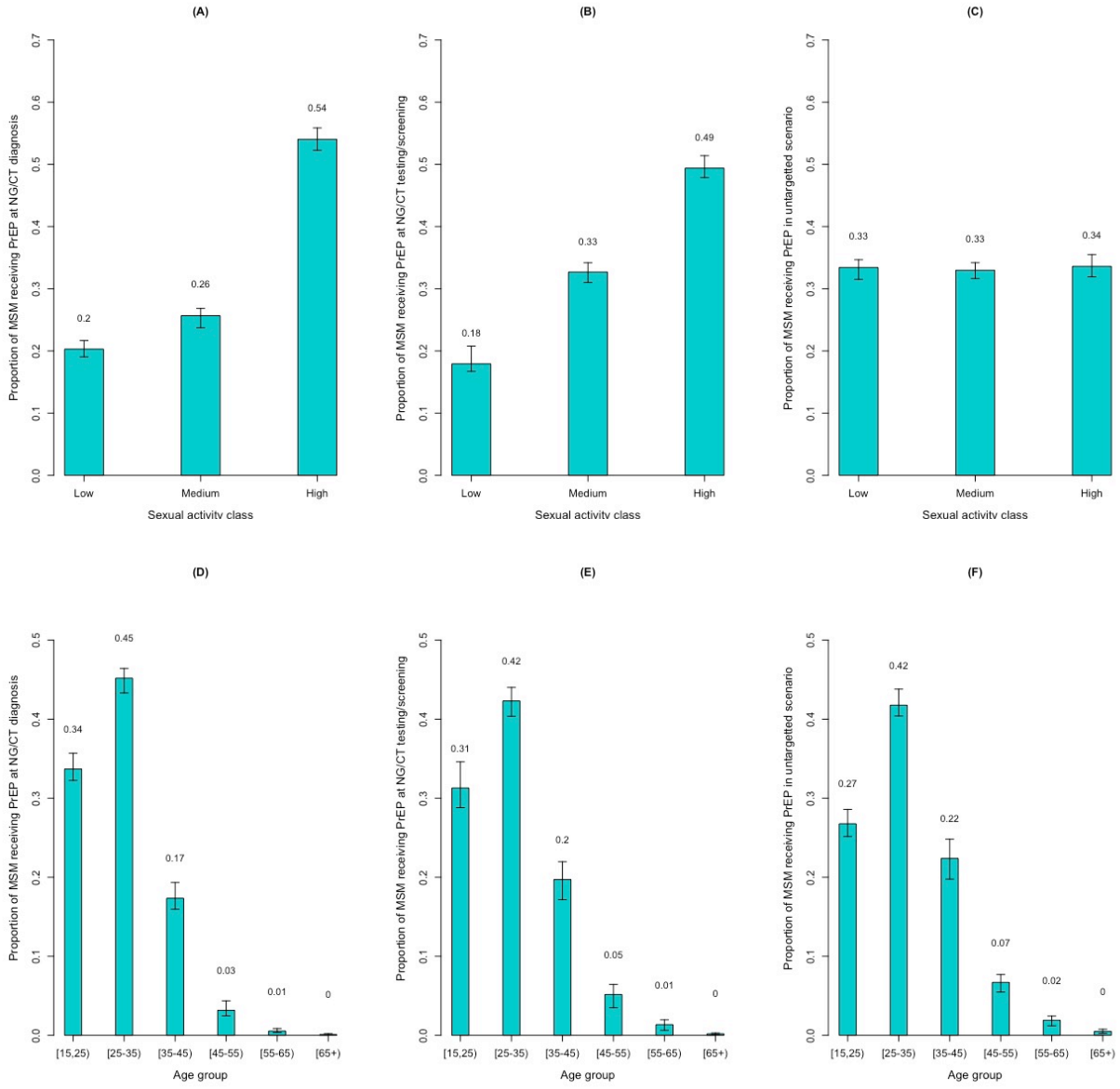

Figure S12: Model projections of the distribution of MSM receiving PrEP in each sexual activity class (top row) and each age group (bottom row) in each PrEP scenario. Panels A and D depict this distribution under NG/CT-targeted PREP; panels B and E illustrate PrEP evaluation at NG/CT screening and testing; and panels C and F represent untargeted PrEP. Shown are the mean values of simulations (in green) with error bars representing the 95% uncertainty range of observations around each simulated measure.

3 SENSITIVITY ANALYSIS

One-way sensitivity analysis of simulation results was performed with regard to all model parameters (listed in Table S7). For this purpose, we changed each parameter to +/- 25% of its original value, one at a

time (keeping all others fixed at the original value) and evaluated the main simulation outputs after such variation. The primary output of interest for the sensitivity analysis was HIV incidence at 10 years without PrEP (baseline) and with PrEP (under each PrEP campaign). For this analysis, we assumed an uptake and adherence of 60% to PrEP. The tornado graphs (Figure S13 to S16) represent the results of the one-way sensitivity analysis. Figure S13 presents the results for HIV incidence at year 10 in Baseline (absence of PrEP), and Figure S14 through Figure S16 present HIV incidence in year 10 of a PrEP campaign targeting MSM at the time of NG/CT-diagnosis (Figure S14), at the time of NG/CT screening (Figure S15) or through a community-wide campaign (Figure S16).

Assuming a threshold of 25% to detect significant changes, the projected HIV incidence at baseline and in absence of PrEP (Figure S13) was sensitive to variation of parameters relating to 1) transmission of HIV including the coefficient of HIV transmission, viral load as a measure of infectiousness, and condom use and effectiveness; 2) the coefficient of NG/CT transmission; and 3) parameters describing overall sexual activity including the probabilities of starting new partnerships, and the level of sexual activity in the most sexually active class. Similar behavior was observed in scenarios modeling the implementation of PrEP at NG/CT diagnosis (Figure S14), at the time of NG/CT screening (Figure S15) or through a community-wide campaign (Figure S16). None of the sensitivity analysis scenarios resulted in significant variation (>25%) of HIV incidence in PrEP scenarios compared to the baseline.

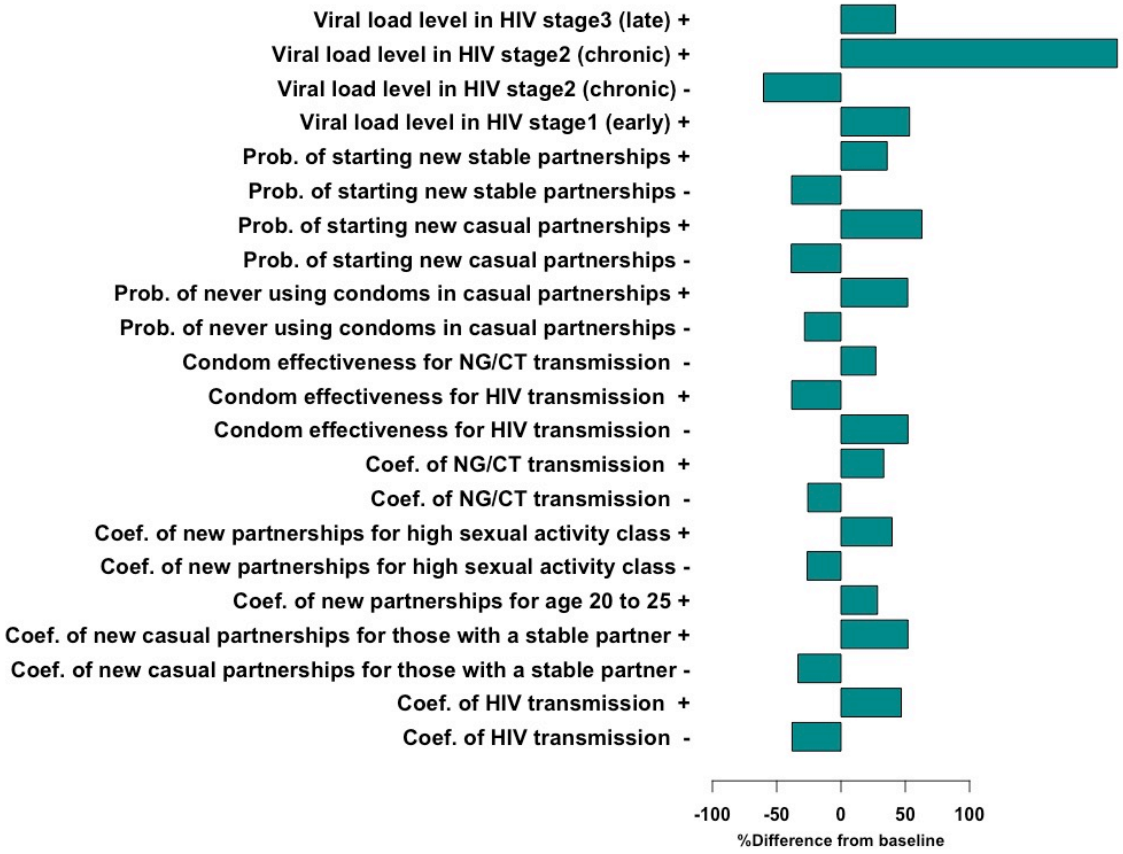

Figure S13: Sensitivity analysis of HIV incidence at year 10 to variation of model parameters in the Baseline (absence of PrEP) scenario. Input parameters are listed on the left, +/- corresponding to 25%

increases/decreases, and bars reflecting corresponding differences in output. The y-axis shows the percent difference in the value of selected output from the baseline model (before parameter change). Differences more than 25% are considered as significant.

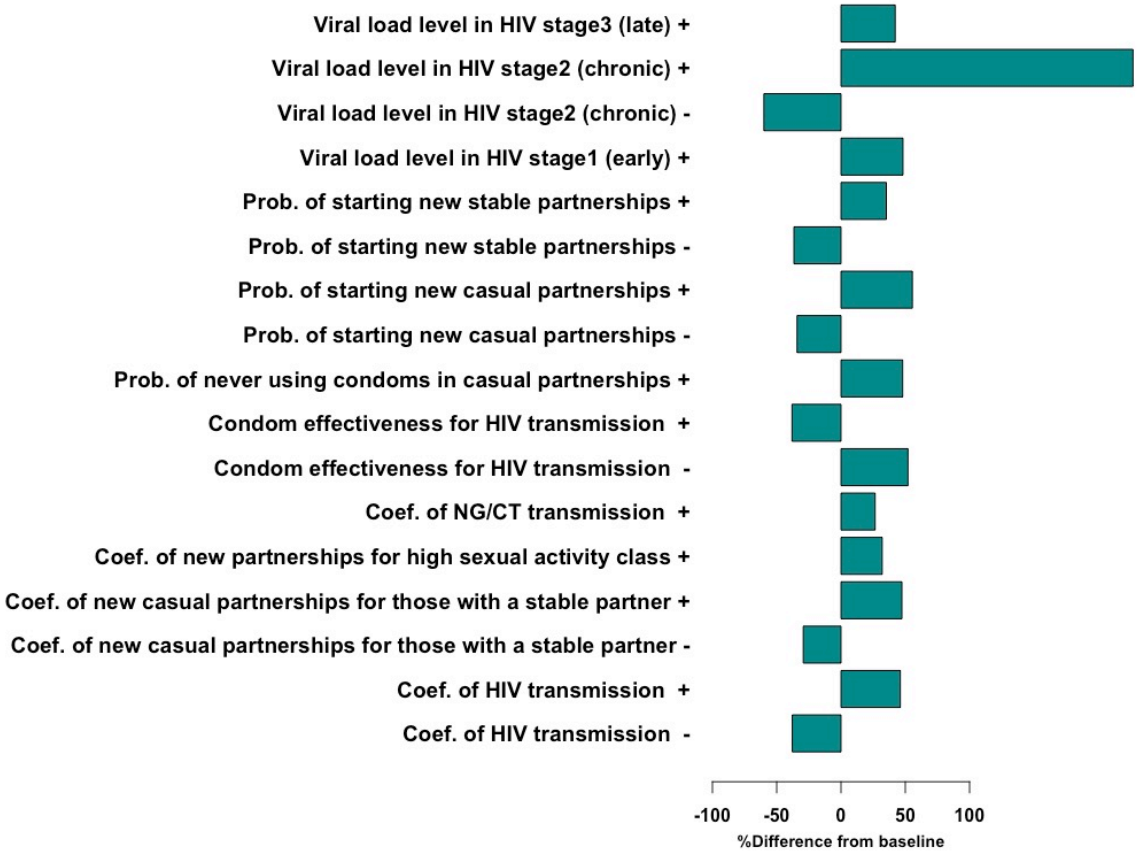

Figure S14: Sensitivity analysis of HIV incidence in year 10 to variation of model parameters in the scenario of a PrEP campaign targeting MSM at the time of NG/CT-diagnosis. Input parameters are listed on the left, +/- corresponding to 25% increases/decreases, and bars reflecting corresponding differences in output. The y-axis shows the percent difference in the value of selected output from the baseline model (before parameter change). Differences more than 25% are considered as significant

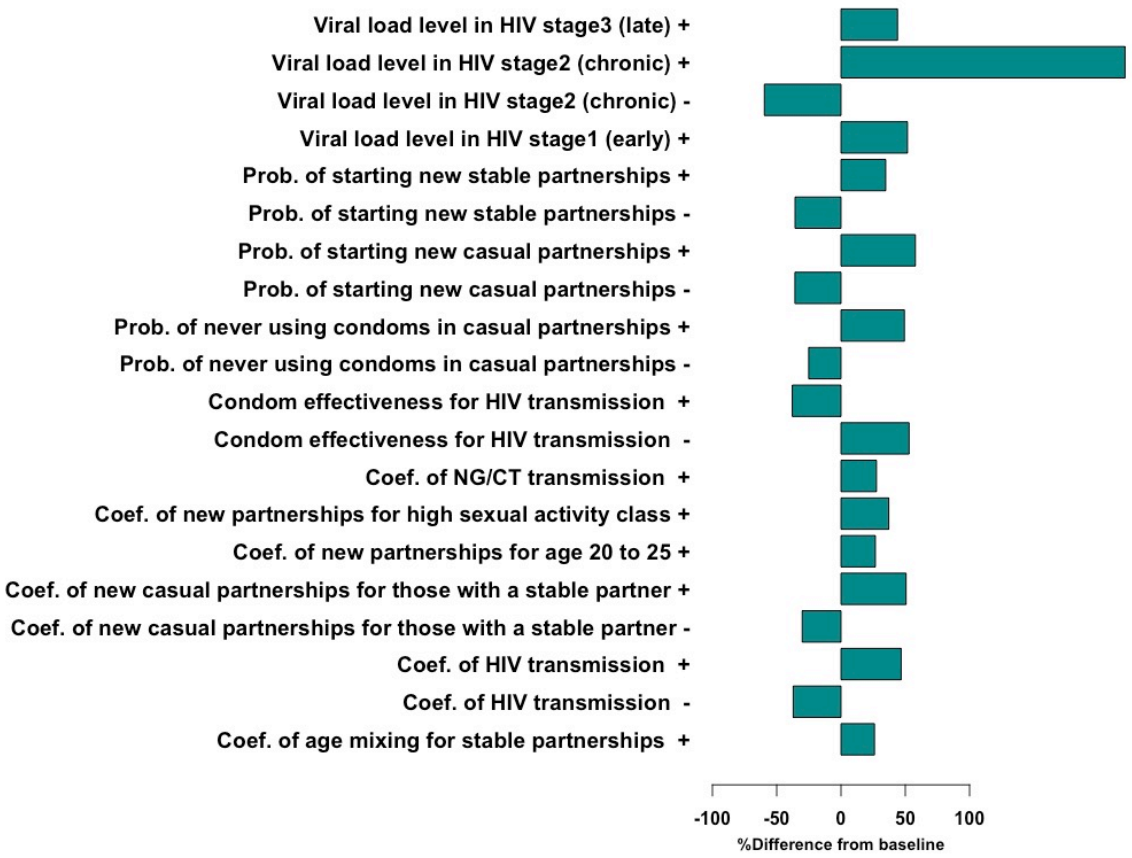

Figure S15: Sensitivity analysis of HIV incidence in year 10 to variation in model parameters in the scenario of a PrEP campaign targeting MSM at the time of NG/CT screening. Input parameters are listed on the left, +/- corresponding to 25% increases/decreases, and bars reflecting corresponding differences in output. The y-axis shows the percent difference in the value of selected output from the baseline model (before parameter change). Differences more than 25% are considered as significant

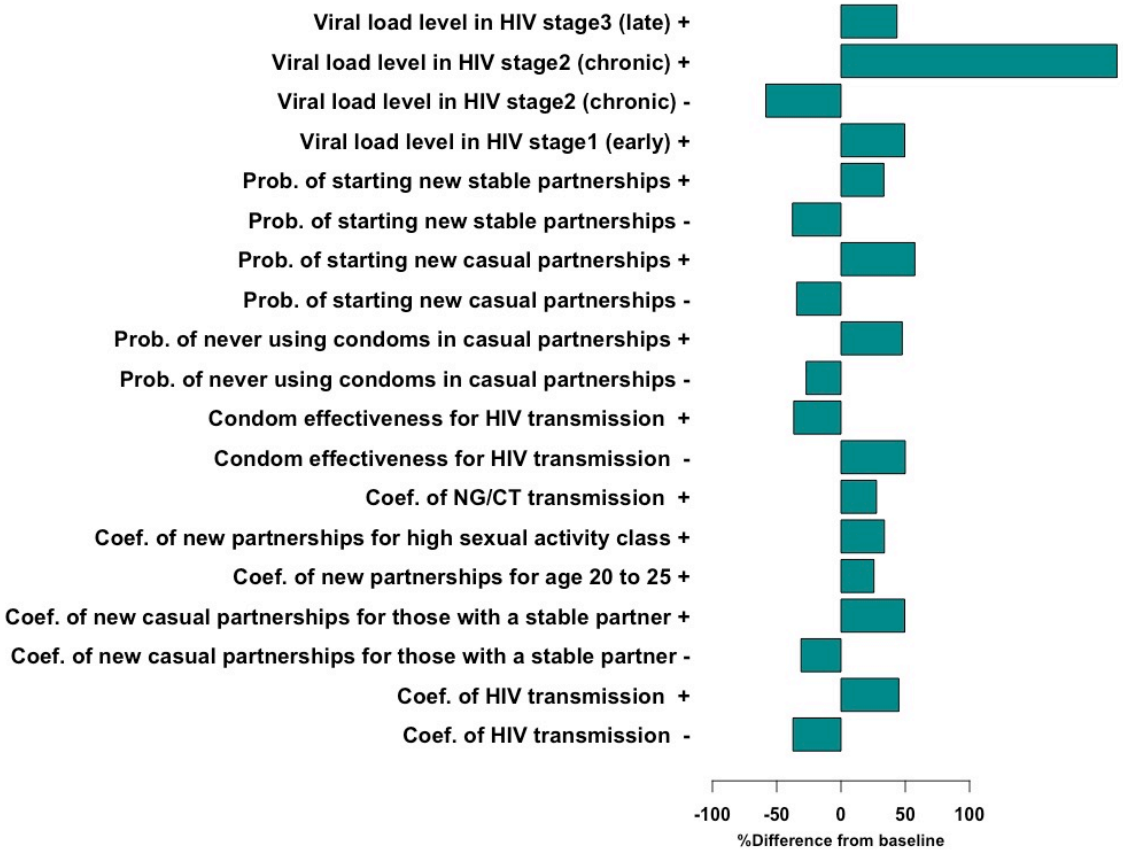

Figure S16: Sensitivity analysis of HIV incidence in year 10 to variation in model parameters in the scenario of a PrEP campaign targeting MSM through a community-wide campaign. Input parameters are listed on the left, +/- corresponding to 25% increases/decreases, and bars reflecting corresponding differences in output. The y-axis shows the percent difference in the value of selected output from the baseline model (before parameter change). Differences more than 25% are considered as significant.

3.1 Sensitivity analysis to impact of behavioral disinhibition

In the absence of strong data on existence of behaviour change for people on PrEP, we have elected to keep the model in the simplest format as possible. However, we acknowledge that this may limit the applicability of our findings to settings in which such behaviour may occur. To further study the impact of such assumption on our findings, we performed an additional sensitivity analysis of results to impact of behavioural disinhibition. For this purpose, we model behavioural disinhibition as %reduction in rate of condom use among MSM taking PrEP (reflected equally on rate of condom use in casual and stable partnerships), varied from 0% (no behavioural disinhibition) to 100% (no condom use).

Figure S17 compares the projected impact of NG/CT targeted PrEP at different rates of condom use reduction among PrEP users. The red line represents the baseline scenario in the model in absence of behavioral disinhibition. As expected, the projected impact of NG/CT-targeted PrEP on HIV incidence declines with reduced levels of condom use among PrEP users. For example, at baseline and in absence

of behavioural disinhibition, the NG/CT targeted PrEP results in 12% [10.4% - 14.1%] reduction in HIV incidence over 20 years. Decreasing the condom use among PrEP users by 25% and 50% will consequently results in lower impact of PrEP at the population level, corresponding to 9.8% [7.7% - 11.9%] and 7.2% [5.1% - 9.4%] reductions in HIV incidence over 20-years. Reduction in rate of condom use among PrEP users can further reduce the potential impact of PrEP (through increased STI screening) on incidence and prevalence of NG/CT. At very high levels of behavioural disinhibition (light green line representing a 75% reduction in condom use among PrEP users), implementation of PrEP can in turn increase the rate of STI transmission and incidence over time.

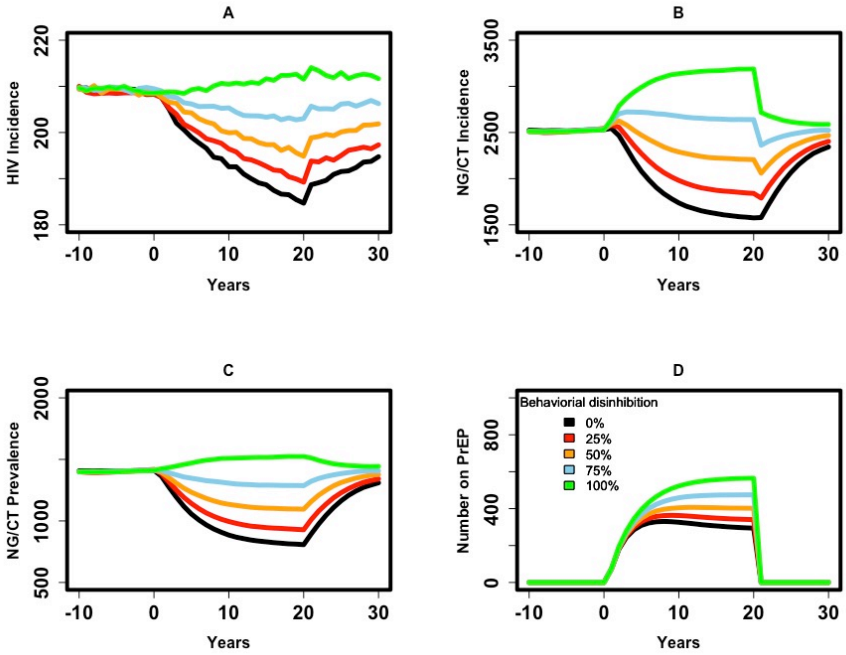

Figure S17: Sensitivity of the impact of NG/CT targeted PrEP to variation in rate of condom use among PrEP users. Shown on the y-axes are the annual incidence of HIV (A), incidence of NG/CT (B), prevalence of NG/CT (C) and number of MSM on PrEP and (D). Different colors represent PrEP scenarios at various levels of reduction in condom use among PrEP users, ranging from 0% (the baseline analysis in the main manuscript, shown in black) to 100% (no condom use among PrEP users, shown in light green).

Figure S18 further compares the impact of 3 PrEP scenarios that were discussed in the main text at various levels of behavioural disinhibition. Despite sensitivity of PrEP outcomes to variation in rate of condom use reduction in each scenario, the relative impact of NG/CT targeted PrEP scenario on HIV incidence compared to the other two scenarios (PrEP evaluation at NG/CT screening/testing and Untargeted PrEP) shows little sensitivity to underlying assumptions regarding behavioural disinhibition (Panel D in each set of graphs), and only begins to decline at very high levels of condom use reduction (last set of graphs for 75% reduction in condom use).

These results further characterize the impact of behavioural disinhibition on population-level impact of PrEP on incidence of HIV and other STIs as proposed by previous studies. This further highlight the need for additional behavioural surveillance data characterizing the changes in level of condom use and risky behaviours among PrEP users in local settings. Despite this behaviour, the main outcome of our analysis

for increased efficacy of PrEP implementation through a NG/CT targeted approach remains robust to variation in rate of condom use reduction.

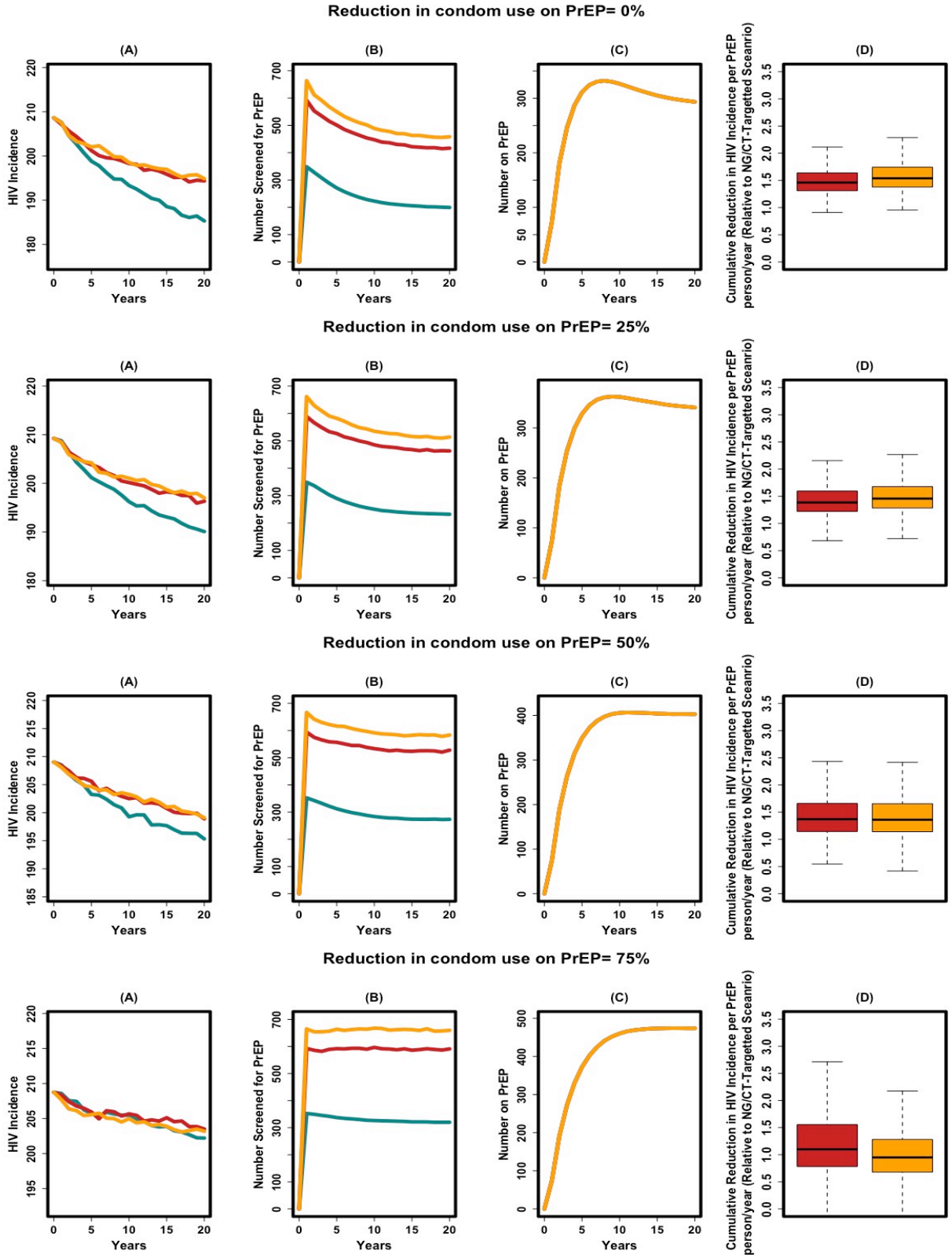

Figure S18: Sensitivity of the impact of all PrEP scenarios to variation in rate of condom use among PrEP users. Shown in this figure is the relative impact of NG/CT-integrated PrEP (in green) compared against

PrEP evaluation at NG/CT screening/testing (in red) and untargeted PrEP (in yellow), with full description of these scenarios given in the manuscript text. The three strategies are compared under the assumption that the same number of MSM would receive PrEP, at various levels of reduction in condom use among PrEP users. Panel A gives the annual incidence of HIV, panel B the number of MSM approached for PrEP, panel C the number of MSM on PrEP at any point in time (all three lines overlapping), and panel D the cumulative reduction in HIV incidence per PrEP person/year in untargeted scenarios relative to NG/CT-targeted scenario.

4 ADDITIONAL FIGURES

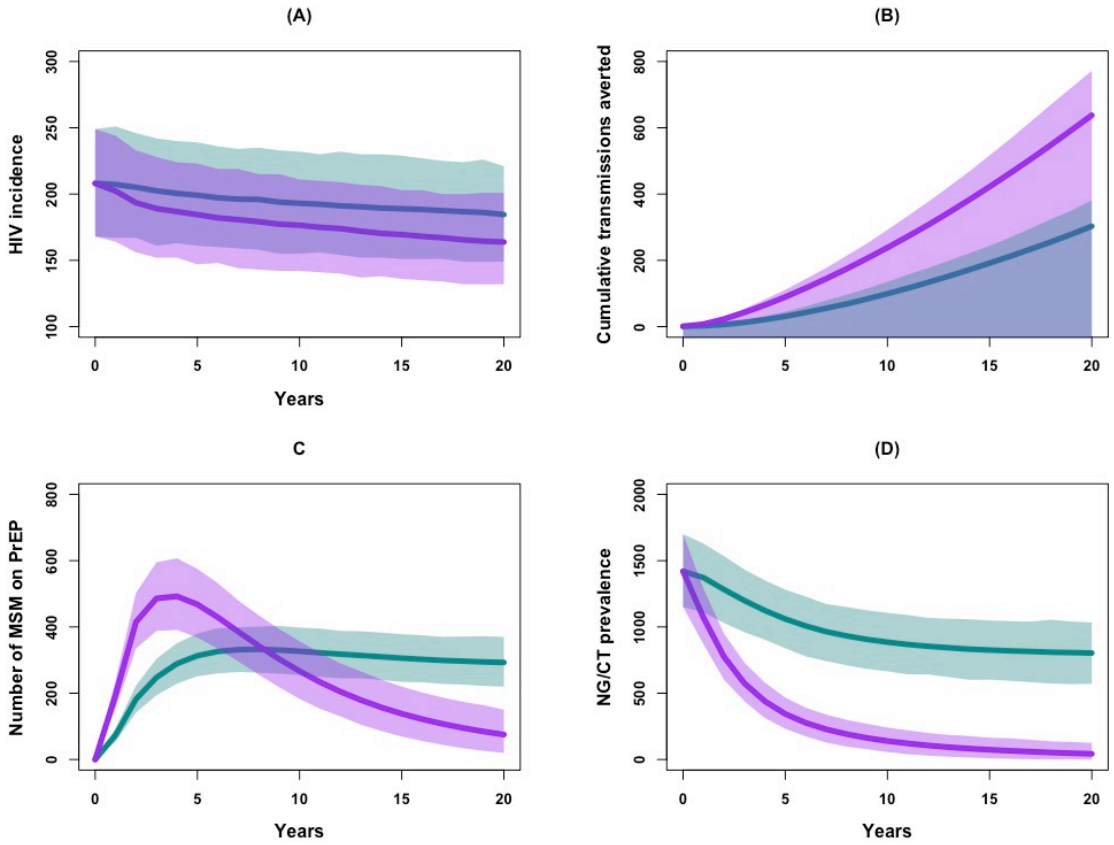

Figure S19: Impact of NG/CT-integrated PrEP, according to frequency of NG/CT screening/testing, with uncertainty ranges shown. Shown on the y-axes are the annual incidence of HIV (A), cumulative number of transmissions averted (B), (C) number of MSM on PrEP and (D) NG/CT prevalence. The green line depicts a scenario in which all MSM currently diagnosed with NG/CT are placed on PrEP with 60% uptake and adherence (NG/CT-integrated PrEP scenario in the main text), and the purple line shows a hypothetical scenario in which 50% of MSM are screened for NG/CT every year, with those testing positive for NG/CT also offered PrEP. Shaded areas represent the 95% uncertainty ranges of simulated data. This figure corresponds to Figure 3 in the main manuscript, but with uncertainty ranges given.

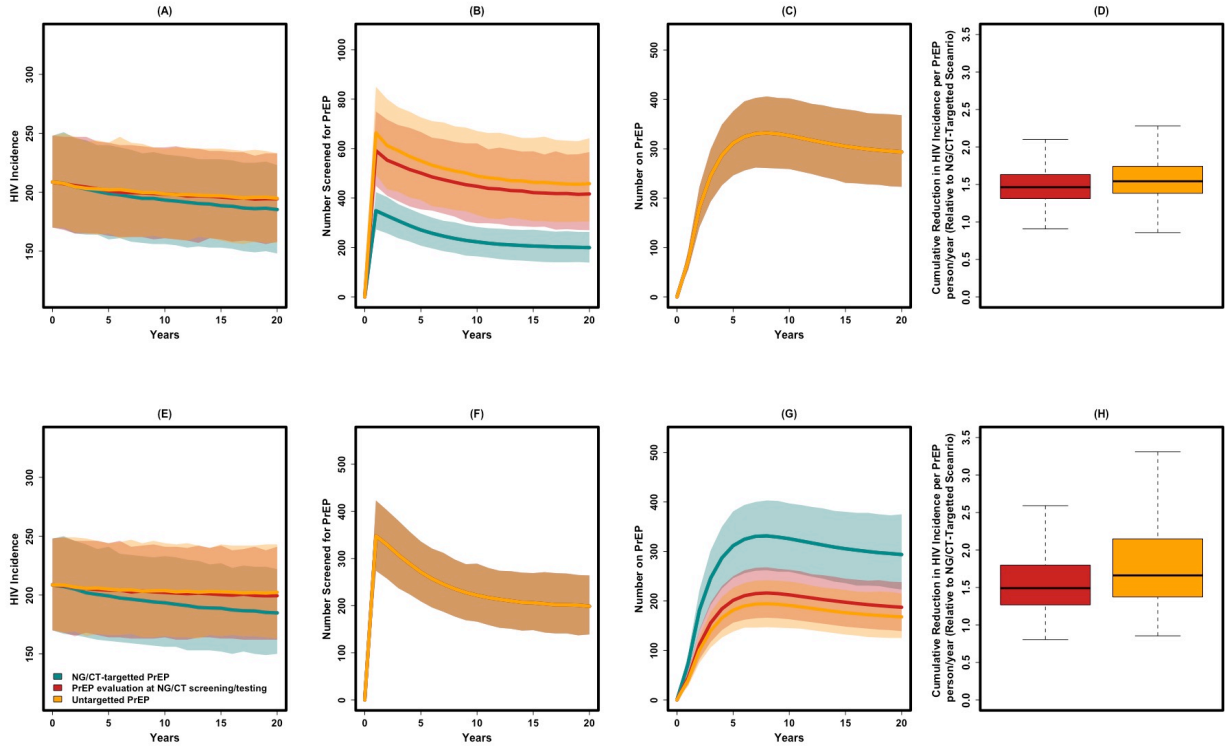

Figure S20: Relative impact of NG/CT-integrated PrEP with uncertainty ranges. Shown in this figure is the relative impact of NG/CT-integrated PrEP (in green, also corresponding to the green line in Figure S19), compared against PrEP evaluation at NG/CT screening/testing (in red) and untargeted PrEP (in yellow), with full description of these scenarios given in the manuscript text. In the first set of experiments, the three strategies are compared under the assumption that the same number of MSM would receive PrEP (panels A through D), or the same number of MSM would be screened for PrEP (panels E through H). Panel A gives the annual incidence of HIV, panel B the number of MSM approached for PrEP, panel C the number of MSM on PrEP at any point in time (all three lines overlapping), and panel D the cumulative reduction in HIV incidence per PrEP person/year in untargeted scenarios relative to NG/CT-targeted scenarios (similar pattern in panels E through H). This figure corresponds to Figure 4 in the main manuscript, but with uncertainty ranges given.

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