**A modeling framework to inform PrEP initiation and retention scale-up in the context of Getting to Zero Initiatives: Supplementary Appendix**

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# A.1. Introduction

This Supplementary Appendix describes additional technical components of the agent-based network model (ABNM) described in the main body of the manuscript, particularly focusing on providing a more detailed explanation of the model processes along with the parameters and data sources. Computer programs and supporting documentation are available at: https://github.com/khanna7/BARS.

The modeling methods utilized a structure similar to prior ABNMs of HIV transmission [1–5] following the following steps:

* An initial population was generated, as described in Section A.2 below.
* Main and casual partnership networks were simulated on this initial population. The modeling process is described in Section A.3.
* Baseline HIV epidemics, resulting from HIV infections transmitted through networks of main and casual partnerships, were simulated to capture features of the epidemic among young (18-34 years) black men who have with men (YBMSM). The steps mentioned in the main body of the paper to model the HIV epidemics are described in Section A.4.
* Parameters for which the available estimates are variable or might be biased and sensitivity analyses that were conducted to produce reasonable estimates are described in Section A.5.
* Key model outputs were produced when the model was simulated with parameter estimates derived in Section A.6.
* At the conclusion of the baseline phase, interventions were simulated, including all of the key model processes. Additional information on these interventions can be found in Section A.7.

# A.2 Initial Population

The initial population consisted of 10,000 individuals, uniformly distributed between the ages of 18-34 at the start, consistent with empirical data [6]. As time evolved, the rates of departure and entry of individuals were set so that the overall population grew slowly consistent with observed growth rates as per census data**.** The population was randomly seeded with 10% HIV prevalence at the start, sufficient to sustain an epidemic, as has been done in previous agent-ABNM studies to design HIV interventions [2,4,5,7]. The model was simulated over a long period (100 years) to allow epidemic outcomes to become consistent with empirical data; similar “burnin” periods have been instituted in previous ABNM studies [2,4,5,7]. The simulations incorporated a number of demographic, network, biological, and behavioral features mentioned in the Methods section of the main body of the manuscript; these features are described in detail below.

# A.3 Models for Main and Casual Partnership Networks

The theoretical framework for modeling main and casual partnership networks is based upon the exponential random graph models (ERGMs), described elsewhere [8], and implemented in the *statnet* suite of packages [9] in the R programming language.

*Main and Casual Partnerships.* Two different partnership networks were simulated in the model. The log-odds of formation of each partnership type were dependent upon the number and distribution of existing partnerships within the network, and the absolute difference in the relative ages of partners for each partner type. The log-odds of the dissolution of each partnership were derived on estimates of the mean partnership duration.

The log odds of the formation of partnerships in both the main and casual networks was specified as  
where and are two individuals in the network; is a time step (simulated forward in daily units in this model), is the previous time step; is the number of edges; is the number of nodes with degree , specified for degrees 0, 1, and 2 in both the main and casual networks; and is the difference in the absolute values of the ages of individuals individuals who are in main and casual edges multipled by the number of main and casual partnerships The functions corresponding to each of these model terms represent the change in their value corresponding to the “toggle” of one dyad (defined as removing one existing tie, or adding a non-existent one); the change statistic functions are needed to estimate the coefficients , and , corresponding to the edges, degree distribution and age mixing terms respectively. These coefficients are estimated using Markov Chain Monte Carlo techniques [10], as per the algorithmic routines contained in the *statnet* package [11].

For both main and casual networks, the persistence of each partnership was defined as  
where is the coefficient associated with the dissolutoin of one tie. The model simulations, described in Section 4 below, incorporated the formation and dissolution coefficients derived here.

# A.4 Simulating Baseline Epidemics

The estimated models for main and casual partnership networks were simulated forward in daily time steps. These baseline epidemics were simulated for a long burnin period, allowing the model interdependencies sufficient time to equilibrate (100 years in this case). Each step of the simulation included the following processes: (1) entry of individuals into the modeled population; (2) departures of individuals from the modeled population; (3) modeling main and casual sexual networks; (4) HIV testing and diagnosis; (5) temporal evolution of CD4 counts; (6) temporal evolution of HIV RNA (“viral load”); (7) dynamics and effects of antiretroviral (ART) use; (8) dynamics and effects of preexposure prophylaxis (PrEP) use, (9) incidence of external HIV infections; and, (10) transmission of infection within serodiscordant main and casual partnerships. The estimation of the demographic, biological, and treatment parameters required to model these processes is described below.

A.4.1 Arrivals: Individuals aged into the model at 18 years. The arrival of new agents in the model was simulated as a Poisson process, with the mean set to 2.0. Thus, the entry rate was empirically determined, to balance the various departure processes (see Section A.4.2 below), so that the population grew at approximately the same growth rate as the population of interest (see Section A.4.2 below).

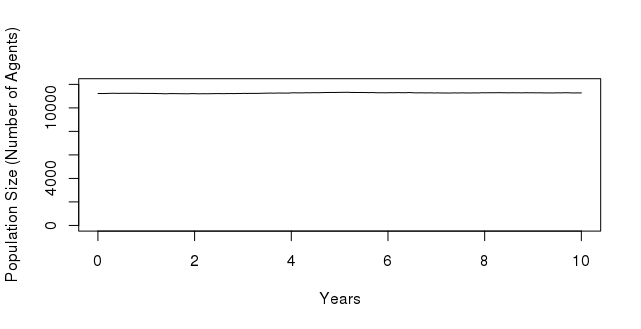
A.4.2 Departures and net population growth: Individuals departed from the model on account of the following reasons:

1. Aging out of the model at age >34 years;
2. HIV-uninfected individuals experience mortality, based on daily probabilities estimated from CDC Wonder data [12].
3. Untreated individuals with HIV infection had a maximum lifespan of 4279 days (approximately 11.7 years), estimated by summing the lengths of acute, chronic, and late-stage infection (details in Section A.4.10).
4. HIV-infected individuals on ART experienced an increase in the age-specific mortality rates, based on individual CD4 counts, in accordance with published data [13]. The increase in the daily mortality rates for HIV-infected individuals is below.

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| **Table A.1. Increased mortality rates for HIV-infected individuals who are not using ART.** | |
| CD4 count (cells/µl) | % increase in age-specific mortality rates |
| < 50 | 51% |
| 50 – 99 | 37% |
| 100 – 199 | 26% |
| 200+ | 0% |

The arrival and departure processes described above resulted in a net simulated growth rate of 0.047%; Figure A.1 below shows the simulated population size over 10 years, averaged over 30 simulations, with PrEP initiation and retention held at baseline levels.

**Figure A.1: Simulated population size over 10 years, averaged over 30 simulations, with PrEP initiation and retention held at baseline levels.**



Since empirical data for the population growth rate of YBMSM specifically in Illinois were not available, we considered the population of young (18-35 years) Black males in Illinois, which grew at about 0.88% per year from 2010-2017, as per data provided by the U.S. Census Bureau [14]. Thus, both the modeled and empirical data revealed a population growth rate of <1% per year.

A.4.3 Sexual network structure: Two different sexual networks within this population were modeled, based on two types of partnerships: “main” and “casual”. The formation and dissolution processes of both partnership types were set such that their cross-sectional structure remained consistent with empirical data. The key parameters for main and casual partnerships, estimated for a given day, were: the mean number and distribution of partnerships, the mean partnership duration, and the mean of the absolute difference in ages for partners.

Sexual networks were dichotomized as “main” and “casual”. The underlying cohort data [15,16] used to parameterize these networks also contained information on “exchange” partners; these partnerships were modeled within the “casual” partnership typology. The same cohort data were used to estimate other parameters used to model the sexual networks, namely the mean number of cross-sectional main and casual partnerships, the distribution of the number of main and casual partnerships (0, 1, 2), and age-mixing. The degree distributions were estimated by computing overlaps in the dates of first and last sex between the study respondent and each of their partners (each respondent reported on up to 5 partners in the last six months). Because the age ranges of agents in our model spanned a relatively narrow range (18 – 34 years), the age-mixing parameter was estimated as the mean of the absolute values of the difference in the ages of the partners, in contrast to other models that were developed for broader age ranges and used the difference in the square-roots of partner ages [1,17]. The durations of mean and casual partnerships were estimated using the last partner reports from NHBS data [18].

A.4.4 Temporal evolution of CD4 counts: The CD4 count of uninfected men was assumed to be constant at 916 cells/µl [19]. Upon HIV seroconversion, an individual’s CD4 count declined piecewise linearly, using a deterministic model where CD4 count was dependent on age at seroconversion, sex, and time since seroconversion, as described by Pantazis et al [20]:  
where was the CD4 count at years after seroconversion, was 23.53; was an indicator of African descent (set equal to 1 here), with a coefficient estimated at -0.76; was an indicator for female (set equal to 0 here), estimated at -1.49 and estimated at 0.34; was the age at seroconversion, with coefficient estimated at: 0 for , -0.1 for

A.4.5 Temporal evolution of HIV RNA (“viral load”): The viral load trajectory was modeled deterministically. For each infected, untreated individual, viral load was expressed as a six-parameter curve with a steep increase from 0 to peak viremia at 6.17 on the log10 scale over the first 45 days of infection, followed by a decline to the viral set point of 4.2 log10 over the next 45 days [21]. This viral set-point is maintained for the next 3550 days [22]. There is a final steady increase in viral load during late stage infection, where the viral load rises to 5.05 log10 [23], over the course of 728 days [22]. The viral load of individuals who initiated ART decreased until treatment is interrupted, at which time the viral load increased again, as explained above, as long as treatment remained interrupted.

A.4.6 HIV testing and diagnosis: A heterogeneity of testing behaviors were modeled. Consistent with population-based cohort data, 7.8% of individuals <26 years and about 2.3% of individuals >=26 years of age were designated as never testing [15]. The remaining individuals were classified into categories defined by the frequency of testing. An individual was diagnosed if, at the time of testing, they had been infected for longer than the detection window of the test (i.e. 22 days [24]). The distribution of the number of HIV tests in the last two years is given in Table A.2 below. Each individual was assigned to one of these categories, and a daily probability of testing for them was computed based on a number of tests parameter that was sampled from the discrete number of tests belonging to that interval.

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| **Table A.2: Distribution of number of tests (among testers) in the last 2 years+** | |
| Number of tests in the last 2 years | % of testers |
| 1-2 | 45.7% |
| 3-4 | 29.9% |
| 5-6 | 10.9% |
| 7-8 | 5.5% |
| 9-10 | 3.9% |
| 11-12 | 1.2% |
| 13-16 | 0.008% |
| 17-20 | 0.011% |
| 21-30 | 0.007% |
| + Chicago, 2013-2014. | |

A.4.7 Dynamics of ART use: At the time of infection, each individual who was eligible for treatment was assigned to one of four states of ART adherence: adherence levels at the two extremes, almost always adherent (A), almost never adherent (N), and two categories of partial (P) adherence: usually (P+) and sometimes (P-). The distribution of ART adherence was estimated from longitudinal cohort data in the uConnect study [15,16]. Of the HIV-positive individuals completing all three visits (n=93), 32% were virally suppressed (<200 copies log viral load RNA) at all three visits (classified as category A defined above), 28% were suppressed at two visits (classified as category P+ above), 30% were suppressed at one visit (classified as category P- defined above), and 10% were never suppressed (classified as category N, defined above).

After 30 days, each person’s adherence for the next 30-day window was assessed, consistent with these four possible adherence states: 0.95 for A, 0.67 for P+, 0.33 for P-, and 0.05 for N. This cycle was repeated every 30 days given typical medication prescription patterns. (Typical medication prescription patterns for ART include a 30-day supply and 2-3 refills depending upon the client’s needs. This assumption was made in conjunction with our panel of HIV providers who care for YBMSM as well as the DHHS guidelines for ART treatment.) The distribution of times between diagnosis and ART initiation were empirically estimated from cohort data [15,16] and are given in Table 1 in the main body of the manuscript.

A.4.8 Dynamics of PrEP use: To model PrEP use, individuals were classified into four categories of adherence as per published data: 21.1% of men took 0 pills/week (non-adherent), 7.0% took <2 pills/week (low adherence), 10.0% took 2–3 pills/week (moderate adherence), and 61.9% took 4+ pills/week (higher adherence) [25]. PrEP use is assumed to reduce HIV infection probability in these adherence groups by 0%, 31%, 81%, and 95%, for non, low, moderate, and high adherence, respectively, in accordance with previous modeling work [26]. On average, PrEP uptake (i.e., the proportion of HIV-negative individuals using PrEP at any given time) was about 13.7% [15,16]. To model this, consider probability of stopping PrEP on any given day. If is the number of HIV-negatives and is the proportion of HIV-negative individuals using PrEP, then on any given day is the number of users who stop PrEP. From the above definitions, it also follows that the number of HIV-negatives who are not using PrEP is . If we define as the probability that any non-user initiates PrEP on a given day,

to maintain the same number of users at any given step, implying that A selection probability of as defined above was set for HIV-negative individuals to initiate PrEP, enabling the model to maintain a specified proportion of HIV-negative individuals on PrEP.

For the interventions that prioritized serodiscordant couples and network position, the selection procedure for new PrEP initiators was implemented in two steps. In the first step, the process to maintain baseline PrEP rates was operationalized by assigning a selection probability for new PrEP initiators, as described above. In the second step, additional individuals were sampled from the pool of the target intervention group (serodiscordant couples or individuals in the highest scoring network positions) to make up the difference in the baseline and target levels of PrEP uptake. Selection from the target intervention group was also implemented probabilistically; the numerator of this probability was computed by considering the number of individuals required to make up the difference in the baseline and target levels of PrEP uptake, and the denominator was the total number of HIV-negative individuals.

Additionally, as per the base assumption in the model, PrEP initiators are retained on PrEP for 12 months, and retention times were assumed to be geometrically distributed. At the time of initiating PrEP use in the model, each user was assigned a duration of use, that was randomly sampled from a geometric distribution with a mean of 12 months. This formulation allowed PrEP users to cycle on and off PrEP, with the specified mean duration of use. Consequently, about 37% of PrEP initiators in the model were retained on PrEP one year after they started using it. A recent analysis of data from the largest provider of PrEP in Illinois found a comparable proportion (43% of PrEP initiators in the general population) retained on PrEP after about one year [27].

A.4.9. Incidence of external HIV Infections: To model HIV infections from individuals not in the defined population (i.e. “external” infections), the following parameters were considered: (1) the overall incidence rate among YBMSM, estimated at 5-7 per 100 person years (py) from two different population-based Chicago cohorts of YBMSM [16,28,29]; (2) the proportion of this overall HIV incidence that consists of new HIV infections transmitted from older BMSM to YBMSM and vice versa, estimated at 28% [30]; the proportion of infections that are transmitted to YBMSM from older BMSM, assumed to be between 50% and 80%. Thus, the lower bound for a total number of infections incident externally among YBMSM in the model was 28%×50%×5 per 100 py = 0.70 per 100 py, and the upper bound was 28%×80%×7 = 1.60 per 100 py. The daily probability for each HIV-negative person to get externally infected thus ranged between and Thus, this probability was used to conduct a Bernoulli trial for simulating an externally incident infection for each HIV-negative person at each time step. It was also assumed that the risk of getting externally infected was uniformly distributed with respect to age because this assumption produced simulated outcomes that were most consistent with empirical data.

Based on sensitivity analyses, we assumed that the risk of getting externally infected was uniformly distributed with respect to age because it produced the most consistent outcomes with the empirical data. External infections from women [31] and non-Black MSM [30] were not included due to evidence that very few infections among YBMSM are linked to either of these populations [31].

A.4.10. Transmission of HIV infection: Transmission of HIV infections through anal intercourse between HIV-infected and HIV-uninfected individuals within main and casual partnerships was modeled at each time step of the simulation. The probability of transmission during each sex act was derived using a number of different attributes, including stage of infection (determined by time since seroconversion) and viral load (in turn determined by the ART status of the infected partner) of the infected individuals, PrEP use by the uninfected partner, condom use at the time of intercourse (which reduced probability of transmission by 80%), and circumcision status of the uninfected partner.

Three stages of HIV infection were considered: acute, defined as lasting for 90 days from the onset of infection [21]; chronic infection that lasts for 3460 days [22]; and late-stage infection for 728 days [22]. Two widely varying estimates of the relationship between chronic stage infectivity and viral load were used in a sensitivity analysis (described in Section A.5 below) to determine the precise relationship between viral load and infectivity (defined as the probability of transmission during per act of condomless anal intercourse). The base infectivity during chronic HIV infection and additional multipliers for heightened infectivity during acute and late-stage infection are derived in Section A.5 below. The model included a 2.89-fold increase in infectivity corresponding to a unit increase in log viral load RNA [32].

# A.5 Sensitivity Analysis of Key Model Parameters

There were a few parameters for which there are wide variations in published estimates, and a few others that were estimated using secondary data analysis but the estimates might have been biased. For these parameters – listed in Table A.3 – sets of discrete values that spanned the uncertain ranges were considered. The model was simulated over the 100 year burn-in length with 30 repetitions of each parameter combination, and key model outputs, including model prevalence and annualized incidence rates, were analyzed.

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| **Table A.3: Parameters with uncertain estimates used for sensitivity analysis to obtain reasonable values.** | | |
| **Parameter** | **Range of possible estimates or reason for uncertainty** | **Discrete values taken for experimentation** |
| Infectivity multiplier for acute infection | A wide range of estimates has been published, ranging from 4.98 [33] to 26 [34]. | 5, 10 |
| Infectivity multiplier for late-stage infection | A wide range of estimates has been published, ranging from 3.49 [33] to 7 [34]. | 1, 3 |
| Infectivity during chronic stage of infection (per condomless anal sex act) | 0.00017 [32] and 0.0061795 [35] (averaged over insertive and receptive transmission probabilities). | Ten points at equal intervals between the estimates provided in [32] and [35]. |
| Frequency of sex in main partnerships (per condomless anal sex act) | The estimate of 0.093/week (from secondary analysis of data in [15]) appeared low. A maximum of 2 acts/week was considered in accordance with [26]. | Lower bound of 0.093 acts/week, upper bound of 2 acts/week, and the mean of the two extremities. |
| Frequency of sex in casual partnerships | The estimate of 0.053/week (from secondary analysis of data in [15]) appeared low. A maximum of 1 act/week was considered [26]. | Lower bound of 0.053 acts/week, upper bound of 1 act/week, and the mean of the two extremities |
| Reduction in transmissibility of HIV infection due to circumcision of uninfected partner | A maximum of 60% reduction has been estimated through studies of heterosexual couples [36–38], but studies in MSM have found negligible effect [39,40]. | Three discrete values were considered: one that assumed 60% protection, consistent with heterosexual studies [36–38], one that assumed 0% protection, and a protective effect halfway between (30%). |

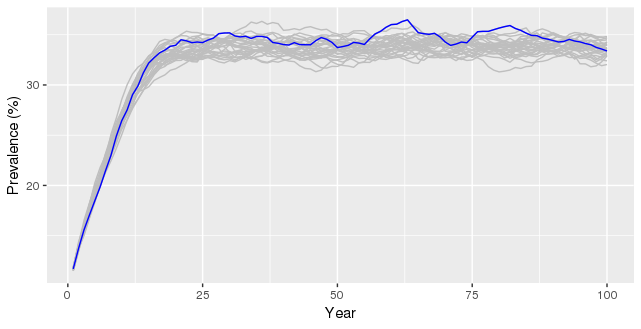
Given the number of discrete values listed above for each of these parameters, 1080 combinations of these parameters were generated. Each parameter combination was simulated 30 times, simulated in parallel using the “Extreme-Scale Model Exploration with Swift” framework [41], to provide a measure of statistical variation between stochastic model runs, and the overall prevalence and annual incidence rates in the population were analyzed. Parameter sets that produced final prevalence in the 33%-37% rage and annual incidence in the 5-7 per 100 person years range, as has been estimated from population-based cohort data collected in two different studies for Chicago YBMSM from 2013-2016 [16,28,29], were considered for further analysis. The parameter estimates that produced reasonable outcomes as defined above are given in Table A.4.

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| **Table A.4: Estimates found to give reasonable model outputs for uncertain parameters identified above.** | |
| **Parameter** | **Estimate** |
| Multiplier for acute infection | 5 |
| Multiplier for late-stage infection | 1 |
| Infectivity during chronic stage of infection (per condomless anal sex act) | 0.00092 |
| Frequency of sex in main partnerships (number of acts/day) | 0.189 |
| Frequency of sex in casual partnerships (number of acts/day) | 0.053 |
| Reduction in transmissibility of HIV infection due to circumcision of uninfected partner | 0 |

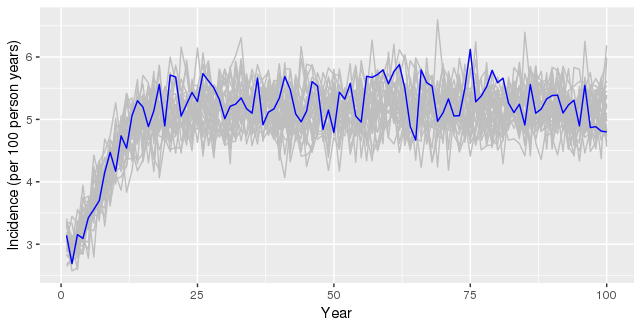
Figure A.2 shows the prevalence and incidence trajectories of 30 stochastic model runs with the parameter estimates provided in Table A.4 (and other input parameters described in Table 1 in the main body of the manuscript). Table A.5 displays key model outcomes averaged over the last 10 years of the baseline simulation. The prevalence and incidence data are averaged over the last ten years of the simulation. The averaged outcomes over the last 10 years were used to calibrate the baseline model because, as per the experimental design, that is the length of time that the interventions were going to be run over.

**Figure A.2: Prevalence (A) and incidence (B) trajectories over thirty baseline model runs with the parameters listed in Tables 1 and A.4. interventions.\***

1. **Prevalence trajectories**

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1. **Incidence trajectories**

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\* The blue curve denotes the one instance that was selected for the intervention analyses presented in the main text; the gray lines represent the other 29 instances. The x-axis shows HIV prevalence at a given time, and the y-axis shows the given year.

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| **Table A.5: Key model outputs produced with baseline model run for 100 years.** | | |
| **Simulation number** | **Overall prevalence (%)** | **Overall incidence rate (per 100 py)** |
| 1 | 33.90 | 5.46 |
| 2 | 32.55 | 5.62 |
| 3 | 33.95 | 4.81 |
| 4 | 33.62 | 4.85 |
| 5 | 34.31 | 5.54 |
| 6 | 33.95 | 5.91 |
| 7 | 33.10 | 5.05 |
| 8 | 34.06 | 4.80 |
| 9 | 34.43 | 5.22 |
| 10 | 34.16 | 4.74 |
| 11 | 34.06 | 4.91 |
| 12 | 34.80 | 4.97 |
| 13 | 33.85 | 6.19 |
| 14 | 33.04 | 5.21 |
| 15 | 34.82 | 4.80 |
| 16 | 33.42 | 4.80 |
| 17 | 34.24 | 5.20 |
| 18 | 33.85 | 4.64 |
| 19 | 32.68 | 4.65 |
| 20 | 34.13 | 5.24 |
| 21 | 33.97 | 5.20 |
| 22 | 33.94 | 5.39 |
| 23 | 34.11 | 5.19 |
| 24 | 32.90 | 5.37 |
| 25 | 34.78 | 4.56 |
| 26 | 33.15 | 5.11 |
| 27 | 33.70 | 5.34 |
| 28 | 33.53 | 4.73 |
| 29 | 33.34 | 5.99 |
| 30 | 34.20 | 4.84 |

Since all of the above instances showed a reasonable match with our target statistics, one instance was randomly chosen (simulation number 8 from Table A.5) for further intervention analysis.

# A.6 Model Diagnostics

A number of model outputs, described in the table below, from the selected simulation above were compared to empirically derived target values to verify that the model outputs provided a reasonable approximation of the processes included here.

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| **Table A.6: Comparison of simulated and target values for key model inputs.** | | | |
| **Parameter** | **Simulated statistics** | **Target statistics** | **References (for target statistics)** |
| Mean number of main partnerships | 0.39 | 0.38 | [15,16] |
| Mean number of casual partnerships | 0.46 | 0.46 | [15,16] |
| Degree distribution for main partnerships | Degrees 0, 1, 2: 62%, 37%, 1% | Degrees 0, 1, 2: 64%, 34% 2% | [15,16] |
| Degree distribution for casual partnerships | Degrees 0, 1, 2: 60%, 33%, 7% | Degrees 0, 1, 2: 59%, 32%, 7% | [15,16] |
| Mean duration of main partnerships | 522 days | 512 days | [18] |
| Mean duration of casual partnerships | 161 days | 160 days | [18] |
| Per cent HIV-negatives on PrEP | 12.8% | 13.2% | [15,16] |

# A.7 Simulating Interventions

A.7.1 Candidate PrEP intervention design: Candidate PrEP intervention strategies were selected from ongoing interventions supported by health departments and organized across two axes: (I) PrEP continuum stage (initiation and retention); and (II) sex network targeted (serodiscordant partners and network position). These specific interventions were considered given input from GTZ Illinois. Early discussions within GTZ Illinois considered adherence interventions which are commonly modeled; however, given that rates of initiation and retention in care are low and are a requirement for downstream adherence, the focus in this paper was shifted to PrEP initiation and retention.

PrEP use among YBMSM in Chicago was estimated at approximately 13% in 2016 [15], and has been found to be comparably low in other studies across the U.S. [42,43]. Evidence for low PrEP retention among YBMSM (and other MSM) in Chicago is also available, and half of the PrEP initiators discontinue within 12 months [27]. These interventions that accounted for larger networks were motivated by the evidence for network change agent type of interventions [44]. Importantly, interventions that prioritize serodiscordant partners and network position are also funded by health departments (details follow), making them candidates for implementation. For instance, the Chicago Department of Public Health funds “PrEP Chicago” – a network intervention that focuses on individuals in key network positions [45], and partner services interventions that focus on initiating PrEP for HIV seronegative partners of HIV/STI infected individuals [46]. Evidence for network interventions [47,48] and interventions for serodiscordant partners [49] in international contexts is also emerging. Modeling such interventions alone or in combination allows informed consideration of a spectrum of candidate PrEP implementation strategies, without the need for costly and research trials that may be difficult to implement.

The modeled interventions are summarized in Table A.7 below.

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| **Table A.7: Modeled PrEP interventions.** | | | | |
| **Intervention name** | **Intervention type** | **Selection of New Agents to achieve target PrEP levels** | **Rationale for Intervention** | **Results** |
| PrEP initiation | Random Selection | All HIV-negative individuals are equally likely for PrEP initiation. | This scenario provides a controlled setting to measure the efficacy of specialized PrEP interventions. | Table 2, Figure 1A |
| Main serodiscordant partners | HIV-negative individuals in main serodiscordant partnerships are selected. | Initiating PrEP for HIV-negative individuals whose main partner(s) are HIV-infected may substantially increase the number of new infections prevented at the population level. | Table 2, Figure 1A |
| Main and casual serodiscordant partners | HIV-negative individuals in main and casual serodiscordant partnerships are selected. | Initiating PrEP for HIV-negative individuals whose main or casual partner(s) are HIV-infected may have a substantial population-level effect on preventing new infections. | Table 2, Figure 1A |
| Network position: Degree centrality | HIV-negative individuals with top 10% of degree centrality scores are selected. | Initiating PrEP for individuals with the highest number of main and casual sexual partners may prevent downstream transmission of new HIV infections. | Table 2, Figure 1A |
| Network position: Eigenvector centrality | HIV-negative individuals with top 10% of highest eigenvector centrality scores are selected. | Initiating PrEP for individuals who have sexual partnerships with other individuals with high number of sexual partnerships may prevent downstream transmission of new HIV infections. | Table 2, Figure 1A |
| PrEP retention | Mean duration of PrEP use is increased | N/A | Overall PrEP uptake can be increased by increasing retention. | Table 3, Figure 1C |
| Combination  (initiation & retention) | PrEP initiation rates and duration of use are simultaneously increased | N/A | To assess if increasing initiation and retention rates simultaneously (with overall PrEP uptake held constant) is more effective at preventing new infections than increasing either initiation or retention exclusively. | Appendix Table A.9, Figure A.3 |

A.7.2 Mathematical definitions of the network position measures: The degree centrality of an individual is equal to where is a distinct node in the network from , and is the adjacency matrix where if and are connected by an edge, and otherwise [50]. The eigenvector centrality score of a node in a network is defined as the eigenvalue corresponding to the principal eigenvector of the adjacency matrix defining the network, as given by where is the adjacency matrix of the network, is the constant eigenvalue, and is theeigenvector [51].Each individual receives a score that is equal to the th component of the principal eigenvector. Highscoring nodes are those that are connected to others that are themselves high scorers [52]. The eigenvector centrality score is based on the assumption that the flow process of interest on the network diffuses via unrestricted walks. This measure is best suited for mechanisms where one node can impact all of its neighbors simultaneously [52], and has therefore been used in public health applications that utilize peer influence [53–55].

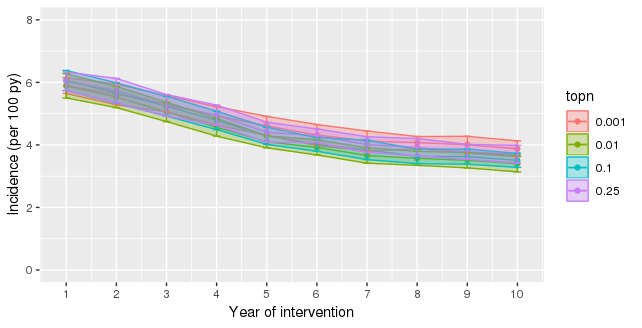
A.7.3 Revisiting key assumptions behind the network position measures: The network interventions described in the main body were implemented under the assumption that target PrEP uptake was achieved by initiating the top 10% of the two network position scorers to make up the difference between the base and target levels of PrEP uptake. The proportion of HIV-negative individuals with the highest eigenvector centrality and degree centrality scores, which defined the pool of eligible individuals from which new PrEP initiators could be selected beyond the baseline uptake levels (called the “topn” parameter), was varied in a sensitivity analysis.

Table A.6 below shows that only the smallest topn value considered here prevents the target PrEP scaleup level from being achieved; any reasonable value of the topn parameter has no impact on the PrEP uptake level at the end of the simulation. This is because too few agents are eligible to increase their PrEP initiation probability. Because of attrition of PrEP users due to age-specific mortality and imperfect PrEP adherence, as mentioned in the main body of the paper, the simulated PrEP uptake is expected to be close, but not equal, to uptake levels that the PrEP initiation probabilities were selected to achieve. Figure A.1 below shows that the incidence rate trajectories show a large degree of overlap (i.e., the uncertainty regions around the incidence curve trajectories for different scenarios) intersect for all reasonable topn values, implying that the topn parameter had little impact on the PrEP uptake levels achieved in the simulations.

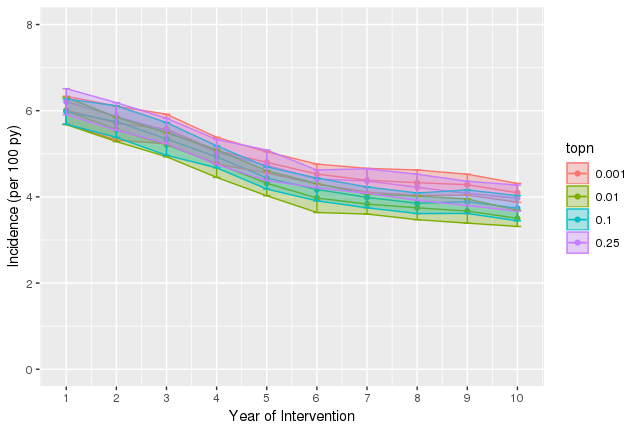
|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table A.8: PrEP uptake levels achieved at the end of the 10-year intervention run when different values of the top degree centrality and eigenvector centrality position scorers (“topn” parameter) were eligible for PrEP initiation beyond the baseline PrEP uptake levels.** | | | | | |
|  | topn: Proportion of top network position scorers prioritized for PrEP initiation. | | | | | |
| Target PrEP uptake | 0.1% | 1% | 10% | 25% | 50% | |
| 20% | 18% | 19% | 19% | 19% | 19% | |
| 30% | 25% | 29% | 29% | 29% | 29% | |
| 40% | 31% | 38% | 39% | 39% | 39% | |
| 50% | 31% | 48% | 49% | 49% | 48% | |
| 60% | 31% | 57% | 58% | 58% | 58% | |

**Figure A.3: Incidence trajectories for cases when different values of the top network position scorers (“topn” parameter) were eligible to initiate PrEP.\***

1. **Degree centrality**



1. **Eigenvector centrality**



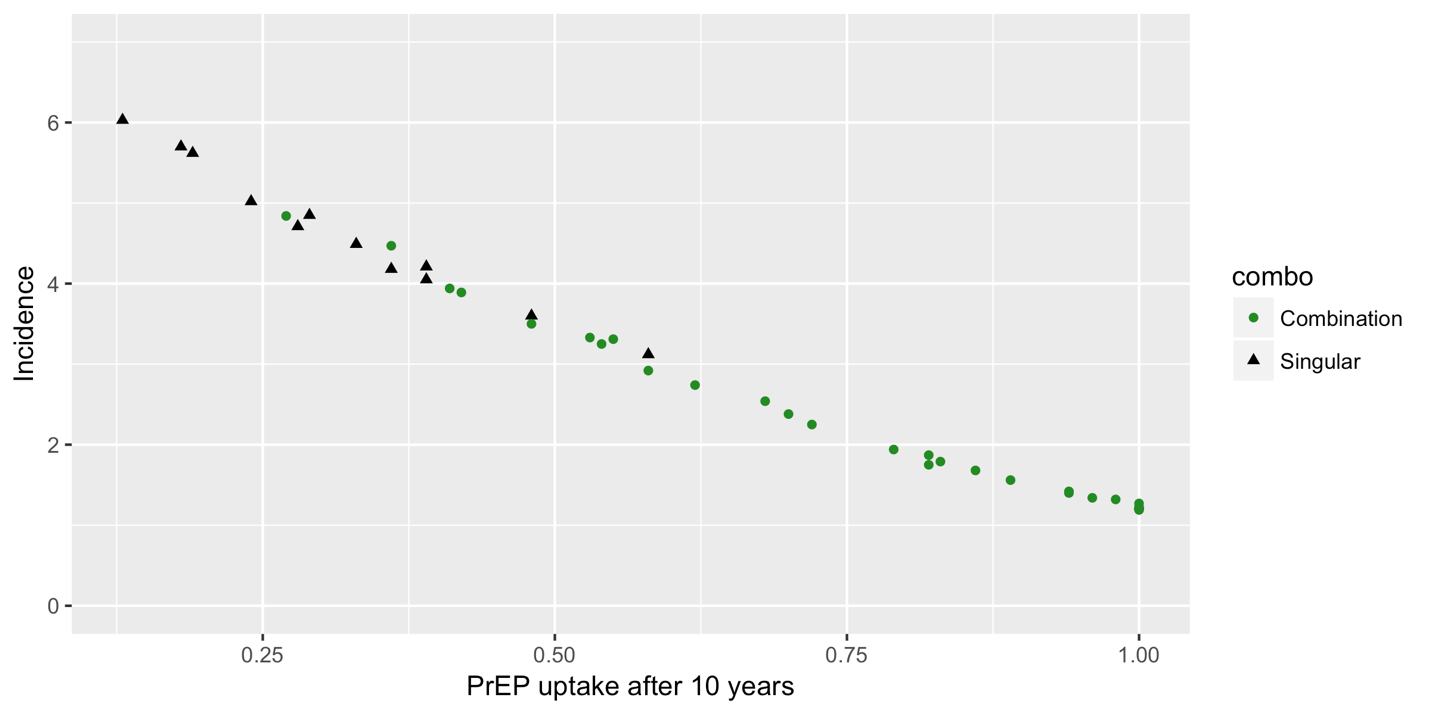
\* The y-axis shows annual HIV incidence (per 100 person years) and the x-axis represents intervention year. Each curve corresponds to a scenario with a different proportion of highest scoring HIV-negative individuals.

A.7.4 Data from combination interventions: As mentioned in the main body of the manuscript, at a given level of achieved PrEP uptake, increasing PrEP initiation and retention in combination produced a similar incidence decline as increasing either initiation or retention alone. Data supporting this conclusion are provided in Table A.9 and Figure A.4.

In Table A.9, the “PrEP initiation” scenario represents the six unique target PrEP uptake scenarios that were considered in the main analyses. To model a combination intervention, we combined the six PrEP initiation scenarios and seven retention periods described in the main body of the manuscript. Thus, a total of 42 unique combination scenarios were considered. The “achieved PrEP uptake” column shows data for the mean PrEP uptake (averaged over 30 simulations) that was achieved in a given combination scenario. The primary outcome is the mean HIV incidence in the tenth year in each of these 42 scenarios, summarized in “mean 10th year population incidence”.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table A.9: 10th year incidence rates produced when a combination PrEP initiation and retention interventions are considered simultaneously. Colors are used to group similar Archived PrEP uptake % values in the same range intervals:** 10-19%,20-29%**,** 30-39%**,** 40-49%**,** 50-59%**,** 60-69%**,** 70-79%**,** 80-89%**,** 90-100% | | | | | |
| **Parameter set ID** | **PrEP initiation scenarios** | **Mean PrEP retention** | **Achieved PrEP uptake (%)** | **Mean 10th year population incidence** | **Std. error** |
| 1 | Base | 12 months | 13 | 6.03 | 0.08 |
| 2 | 20% | 12 months | 19 | 5.62 | 0.06 |
| 3 | 30% | 12 months | 29 | 4.85 | 0.07 |
| 4 | 40% | 12 months | 39 | 4.21 | 0.05 |
| 5 | 50% | 12 months | 48 | 3.6 | 0.05 |
| 6 | 60% | 12 months | 58 | 3.12 | 0.03 |
| 7 | Base | 18 months | 18 | 5.7 | 0.06 |
| 8 | 20% | 18 months | 27 | 4.84 | 0.06 |
| 9 | 30% | 18 months | 41 | 3.94 | 0.05 |
| 10 | 40% | 18 months | 55 | 3.31 | 0.04 |
| 11 | 50% | 18 months | 68 | 2.54 | 0.04 |
| 12 | 60% | 18 months | 82 | 1.87 | 0.04 |
| 13 | Base | 24 months | 24 | 5.02 | 0.05 |
| 14 | 20% | 24 months | 36 | 4.47 | 0.04 |
| 15 | 30% | 24 months | 53 | 3.33 | 0.05 |
| 16 | 40% | 24 months | 70 | 2.38 | 0.03 |
| 17 | 50% | 24 months | 86 | 1.68 | 0.03 |
| 18 | 60% | 24 months | 96 | 1.34 | 0.03 |
| 19 | Base | 30 months | 28 | 4.71 | 0.05 |
| 20 | 20% | 30 months | 42 | 3.89 | 0.06 |
| 21 | 30% | 30 months | 62 | 2.74 | 0.04 |
| 22 | 40% | 30 months | 82 | 1.75 | 0.04 |
| 23 | 50% | 30 months | 94 | 1.42 | 0.02 |
| 24 | 60% | 30 months | 100 | 1.2 | 0.02 |
| 25 | Base | 36 months | 33 | 4.49 | 0.06 |
| 26 | 20% | 36 months | 48 | 3.5 | 0.05 |
| 27 | 30% | 36 months | 72 | 2.25 | 0.03 |
| 28 | 40% | 36 months | 89 | 1.56 | 0.02 |
| 29 | 50% | 36 months | 100 | 1.27 | 0.02 |
| 30 | 60% | 36 months | 100 | 1.2 | 0.02 |
| 31 | Base | 42 months | 36 | 4.18 | 0.06 |
| 32 | 20% | 42 months | 54 | 3.25 | 0.05 |
| 33 | 30% | 42 months | 79 | 1.94 | 0.04 |
| 34 | 40% | 42 months | 94 | 1.4 | 0.03 |
| 35 | 50% | 42 months | 100 | 1.23 | 0.03 |
| 36 | 60% | 42 months | 100 | 1.21 | 0.02 |
| 37 | Base | 48 months | 39 | 4.05 | 0.05 |
| 38 | 20% | 48 months | 58 | 2.92 | 0.03 |
| 39 | 30% | 48 months | 83 | 1.79 | 0.03 |
| 40 | 40% | 48 months | 98 | 1.32 | 0.02 |
| 41 | 50% | 48 months | 100 | 1.19 | 0.02 |
| 42 | 60% | 48 months | 100 | 1.2 | 0.02 |

**Figure A.4: 10th year incidence rates produced when combination PrEP initiation and retention interventions are considered simultaneously.**

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