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

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Abstract

Objective(s): “Getting to Zero” (GTZ) initiatives aim to eliminate new HIV infections over a projected time frame. Increased PrEP uptake among populations with the highest HIV incidence, such as young black men who have sex with men (YBMSM), is necessary to accomplish this aim. Agent-based network models (ABNMs) can help guide policymakers on strategies to increase PrEP uptake.

Design: Effective PrEP implementation requires a model that incorporates the dynamics of interventions and dynamic feedbacks across multiple levels including virus, host, behavior, networks and population. ABNMs are a powerful tool to incorporate these processes.

Methods: An ABNM, designed for and parameterized using data for YBMSM in Illinois, was used to compare the impact of PrEP initiation and retention interventions on HIV incidence after 10 years, consistent with GTZ timelines. Initiation interventions selected individuals in

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AUTHOR CONTRIBUTIONS
John Schneider, Kayo Fujimoto, Nina Harawa, William Cunningham, Charles Hilliard, and Aditya Khanna conceptualized the study design. Aditya Khanna led the modeling team, consisting of Nicholson Collier, Jonathan Ozik, Abigail Skwara, and Arthi Ramachandran. The modeling team coded the model, generated data, analyzed simulated data, and produced the figures and tables. Input data were analyzed by Aditya Khanna, Angela Di Paola, and Rodal Issema. Aditya Khanna and John Schneider wrote the first draft of the manuscript. All authors contributed to the study design, data interpretation, writing and revision of the manuscript and the Appendix. All authors have read and approved the text as submitted to AIDS.
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serodiscordant partnerships, or in critical sexual network positions, and compared to a controlled setting where PrEP initiators were randomly selected. Retention interventions increased the mean duration of PrEP use. A combination intervention modeled concurrent increases in PrEP initiation and retention.

Results: Selecting HIV negative individuals for PrEP initiation in serodiscordant partnerships resulted in the largest HIV incidence declines, relative to other interventions. For a given PrEP uptake level, distributing effort between increasing PrEP initiation and retention in combination was approximately as effective as increasing only one exclusively.

Conclusions: Simulation results indicate that expanded PrEP interventions alone may not accomplish GTZ goals within a decade, and integrated scale-up of PrEP, ART and other interventions might be necessary.

Keywords

HIV infections; pre-exposure prophylaxis; computer simulation; data mining; sexual and gender minorities; preventive medicine

INTRODUCTION

Getting to Zero (GTZ) and other HIV elimination initiatives have gained momentum in the United States following the UNAIDS strategic plan in 2010 [1]. At least 14 jurisdictions are developing GTZ plans, and others are reporting new initiatives [2]. These initiatives, which typically focus on HIV elimination within local jurisdictions, have been driven by a plateauing domestic HIV incidence combined with the growing use of biomedical prevention modalities such as Treatment as Prevention (TasP), and especially, pre-exposure prophylaxis (PrEP). The majority of initiatives have established HIV incidence reduction targets and action plans that highlight specific strategies to be implemented within a defined period.

GTZ Illinois was conceptualized in 2016 by a group of 12 organizational partners from health departments, advocacy groups, academia, service providers, and community organizations. Following the presentation of a simpler incidence forecasting model [3,4], a major theme emerging from GTZ Illinois assessments is that the overall declines in HIV incidence in Illinois have not been experienced equally by sub-populations; younger (18-34 years) Black gay, bisexual and other MSM (YBMSM) have experienced relatively stable incidence rates [5,6]. These observations support the development of a model that focuses on YBMSM. Emerging phylogenetic evidence also indicates that YBMSM are involved in ongoing HIV transmission in other sociodemographic groups, including cis- and transgender women of color [7,8]. A successful PrEP intervention modeled with YBMSM would, therefore, indicate a greater likelihood for a successful wider statewide GTZ strategy.

Based on preliminary modeling work, GTZ Illinois set benchmarks of a 20% increase in PrEP and ART initiation by 2030 to achieve a “functional zero”, i.e., getting to fewer than 200 new infections annually [3]. These benchmarks were primarily based on simple forecasting models that analyzed trends in incidence data [3,4]. PrEP implementation at the population level, however, is complicated and requires systematic strategy development that employs several facets of implementation science [9,10]. These include “scaling out” specific PrEP implementation strategies, focusing on specific populations and synthesizing locally sourced data to parameterize complex forecasting models [11]. PrEP implementation decisionmaking for actual programs and policies, therefore, requires: (1) a model that can incorporate the dynamics of standalone interventions or combinations of distinct interventions; (2) an assessment of candidate PrEP implementation interventions, informed by input from expert stakeholders, and examination of the impact of such interventions on HIV incidence. Increasing PrEP uptake is a complex goal, and requires attention to PrEP continuum components, such as initiation and retention. Local couples-based testing initiatives [12] and social network awareness programs [13] for instance, are examples of strategies supported by local health departments that can be considered for identifying serodiscordant partnerships or influential people who can convince their social network members to initiate PrEP.

In this paper, we introduce an agent-based network model (ABNM) [14–16] – parameterized with data largely collected in Illinois – designed to inform GTZ efforts, that examines the effectiveness of PrEP initiation and retention interventions for YBMSM. We focus on YBMSM exclusively, in contrast to models that have focused on addressing racial disparities [17–19], because of feedback from GTZ stakeholders on the importance of developing interventions for YBMSM, a population that represents a unique mix of intersectional identities. The ABNM approach used here addresses the limitations of simpler forecasting approaches considered thus far by GTZ Illinois [3,4] and has the flexibility to be applied to other jurisdictions where initiatives are being developed.

METHODS

Agent-Based Network Model (ABNM) Development

The ABNMs presented in this study were designed to examine PrEP interventions for YBMSM in Illinois. These ABNMs combined sexual network structure with a number of processes that impact HIV transmission (described below). The sexual network structure was estimated using exponential random graph models (ERGMs) [20]; this approach is consistent with the methodology developed in previous work [15,21–23]. The ABNMs presented here were implemented using the *statnet* [24] suite of packages in the R programming language to simulate dynamic networks. The ABM components were developed with the C++-based Repast HPC ABM toolkit [25,26]. Parameters and computer code to reproduce results are available in a public GitHub repository [27].

Demographic, Network, Behavioral and Biological Data

Data sources used to parameterize the ABNM were selected based upon a hierarchy of quality with a focus on systematically sampled data that were representative of YBMSM in Illinois. Local data sources included cohort data on Chicago YBMSM from “uConnect” [28,29] and the Young Men’s Affiliation Project (YMAP) [30]; both studies recruited participants in Chicago from 2013-2016 using systematic sampling schemes. Additional data on YBMSM were obtained from the 2014 cycle of the National HIV Behavioral Surveillance survey [31] in the Chicago Metropolitan Statistical Area. Other local and national sources, described below, were included where representative data from Illinois were not available. All procedures and protocols were approved by relevant institutional review boards.

Baseline Model

Baseline HIV transmission was simulated to capture existing epidemic features among adolescents and young adults (age 18 to 34 years), populated with 10,000 individuals at the start of the dynamic simulations. The model was calibrated using published HIV incidence and prevalence estimates. Simulations proceeded in daily time steps. The key model parameters are listed in Table 1. The substantive model components included arrivals, departures, dynamic sexual network structure, the temporal evolution of CD4 counts and HIV RNA ("viral load"), HIV testing and diagnosis, dynamics of ART and PrEP use, external HIV infections, and HIV transmission dynamics. These processes are described in greater detail in Section A.4 of the Appendix and represent the control setting without specific GTZ interventions.

Modeling Candidate PrEP interventions

Candidate PrEP implementation 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). For Axis I, the focus is on PrEP initiation and retention. PrEP initiation was modeled by scaling up the proportion of HIV-negative YBMSM initiating PrEP. PrEP retention interventions were modeled by increasing the mean duration of PrEP use. For PrEP initiation, HIV-negative individuals not on PrEP were randomly selected to initiate PrEP until the target scale-up was achieved. PrEP initiation probabilities were set to achieve uptake levels of approximately 20%, 30%, 40%, 50%, and 60%, measured in terms of percent of HIV-negatives on PrEP; the scenario corresponding to each PrEP initiation probability is labeled with the corresponding approximate uptake level that the probability is set to achieve. At baseline, PrEP uptake was set to 13%, consistent with empirical data [28,29]. Average PrEP retention was varied between our base assumption (1 year on average) and an average retention of 4 years, at six-month increments.

Axis II interventions were motivated by the importance of incorporating factors that move beyond the individual, such as social network structure, that are important drivers of HIV [14,32,33]. Two network-based interventions are considered here, one that prioritized more proximal network components such as HIV-negative individuals within serodiscordant partnerships, given the success of serodiscordant targeting through couples testing and partner services type interventions [34,35]. A second Axis II intervention that considered larger network structures was also modeled. In this intervention, HIV-negative individuals who were in critical network positions were selected [13,36]. (Background details behind the selection of these specific interventions is provided in Section A.7.1 in the Appendix.)

For serodiscordant partner interventions, HIV-negative main partners of HIV-positive individuals were selected for PrEP initiation, beyond the number that would be selected as per the baseline rate. A variant of this intervention where main and casual seronegative partners were selected was also modeled. This selection mechanism was implemented by computing a selection probability for HIV-negative persons in serodiscordant partnerships, calculated as the number of individuals required to make up the difference between baseline and the target PrEP uptake divided by the total number of HIV-negative individuals. Thus, HIV-negative individuals in serodiscordant partnerships had an additional selection probability over and above the selection probability determined by the baseline rates.

The second Axis II intervention type – network interventions – was modeled by selecting individuals who were in critical network positions, as measured by their degree centrality and eigenvector centrality computed on the sex network. Degree is a count of the number of sexual partnerships, and eigenvector centrality indicates individuals who are influential in a given network [37] (technical definitions of the two network position algorithms are provided in Appendix Section A.7.2.) Both measures were computed daily for each individual in the simulated population and included both main and casual partnerships. The HIV-negative individuals with the top 10% degree scores and the HIV-negative individuals with the top 10% eigenvector scores were selected for PrEP initiation. These individuals are selected by defining a selection probability which is calculated as the number of individuals required to make up the difference in the target and baseline levels of PrEP uptake divided by the total number of HIV-negative individuals. Thus, HIV-negative individuals with the top 10% degree and eigenvector scores had an additional selection probability over and above the selection probability determined by the baseline. (Sensitivity analyses that varied the proportion of top scorers are described in Section A.7.3 of the Appendix.)

Finally, a combination scenario where initiation probability under random selection and mean retention period were simultaneously increased was also considered. All Axis I and II interventions were simulated for ten years. PrEP initiation probabilities were uniformly increased over the first five years, and held constant for the next five, to achieve the uptake levels described above. ThePrEP inititation probabilities were gradually scaled up to better approximate real world implementation.

Outcomes

The control setting and intervention were each simulated 30 times. The primary outcome was the HIV incidence rate ten years after the start of implementation, averaged over the 30 model simulations. The annual incidence rate in the tenth year for the serodiscordant couples' and network interventions were compared with the random scale-up scenario, which served as a "control" setting.

RESULTS

Tables 2 and 3 provide the mean 10th year incidence rate (per 100 person years) and the mean number of HIV infections in the 10th year, at the target levels of initiation and retention periods described above. Figure 1 displays the average annual incidence rates, with color bands that demonstrate the standard deviation across the 30 simulations for a given set of parameters, for each of the scenarios. The top and bottom panels of Figure 1 display simulated data for interventions that increase PrEP initiation and retention respectively.

HIV incidence at 10 years declined considerably as PrEP uptake increased across all intervention scenarios. Prioritizing HIV-negative YBMSM in serodiscordant main and serodiscordant main and casual partnerships resulted in the largest declines in the 10th year incidence rate, relative to other interventions. In early intervention years, HIV incidence declines were most noticeable when those in serodiscordant main partnerships were selected (2.75 per 100 person years at 30% PrEP initiation) with target levels of PrEP initiation set to 30% or below. As PrEP initiation increased to 40% (or above), HIV incidence declined more rapidly in the scenario where PrEP was provided to MSM in serodiscordant main and casual partnerships. Note also that when PrEP initiation probabilities were set to achieve uptake of 30% (or more) of HIV-negatives, the pool of available main serodiscordant partners was exhausted, and the final PrEP uptake achieved was about 25% (see Figure 1). This "saturation" effect was not seen when both main and casual serodiscordant partners were selected for the intervention. Even with 25% uptake, selecting main serodiscordant couples produced consistently lower incidences than other interventions which did not saturate. It should also be noted that even in scenarios without such a saturation effect, the attrition of PrEP users due to age-specific mortality and imperfect adherence, resulted in simulated uptake levels that were close, but not equal, to the uptake levels defined in the six PrEP initiation scenarios.

A visualization of the YBMSM sexual network at time 0, prior to the start of the interventions, is given in Figure 2. Note that this cross-sectional network on a given day is mostly composed of distinct small clusters. The sexual network-based interventions that utilized this network structure also had substantial, though, smaller impact on HIV incidence than interventions that focused on serodiscordant partners. Selecting HIV-negative YBMSM with more sex partners, as measured by degree centrality, generally outperformed selecting individuals based upon influence (as measured by eigenvector centrality).

Table 3 provides the 10th year incidence for the intervention where PrEP retention was increased. Increasing PrEP retention also demonstrated substantial reductions, with increasing duration from 12 to 24 months having similar HIV incidence reduction as increasing PrEP initiation by approximately 20% (Tables 1 and 2). Even under the most effective interventions, however, the annual number of new HIV infections after ten years was close to 200. At a given level of PrEP uptake, increasing PrEP initiation and retention in combination produced a similar incidence decline as increasing either alone (see Appendix Section A.7.4). Note that when PrEP initiation and retention are simultaneously increased, under some conditions, PrEP uptake can rise to levels that might be unrealistically high; our interpretation, however, was based on combination interventions that produced the uptake levels close to those described above.

DISCUSSION

Primary findings

In this paper, ABNMs revealed findings about several GTZ PrEP implementation interventions. First, increasing PrEP initiation by 20% from baseline uptake modestly decreased HIV incidence and is unlikely to have a major impact on GTZ goals. Second, increasing PrEP initiation and retention had similar effects on HIV incidence; increasing

PrEP retention threefold from baseline to 36 months produced a similar average 10th year incidence as increasing initiation roughly three-fold from baseline to 40%. Third, PrEP interventions that prioritized HIV-negative YBMSM in serodiscordant partnerships could be highly effective in decreasing HIV incidence. Fourth, among interventions that leverage network structure information, prioritizing individuals with more sex partners performed better than interventions targeting persons in influential positions. Finally, results indicate that increasing both initiation and retention is comparable to increasing either one exclusively to the same PrEP uptake level; no synergistic effect between retention and initiation was observed.

Interpretation of primary findings

The conclusions presented here are consistent with previous modeling studies that have suggested the effectiveness of PrEP scale-up in reducing HIV incidence worldwide [38–43]. Targeted PrEP initiation approaches, that prioritize individuals for PrEP based on their partner characteristics, have been modeled before [44–46]. Among studies that focus on MSM, however, ours is one of the first that considers YBMSM exclusively – a population that represents a unique mix of intersectional identities that include age, race and sexual minority statuses. This is in contrast to recent modeling work that has focused on addressing racial disparities [17–19] in the PrEP continuum among MSM in the United States. The dynamics of PrEP initiation and retention modeled here were in response to the expressed needs of GTZ Illinois stakeholders, who have found it necessary to increase both; whereas models examining novel technologies for PrEP delivery [47] and the impact of increasing adherence [48,49] have been developed, models for increasing initiation and retention have received less attention. Our finding that increasing PrEP initiation by 20% would have limited impact among YBMSM was likely driven by low PrEP retention [50]; even the highest PrEP initiation scenarios considered here with random selection did not reduce the number of new HIV infections annually below 200. It is worth noting that initiation and retention represent critically different interventions and may not be equivalent in terms of implementation complexity or cost. While increasing retention three-fold would require intensive peri-clinic interventions, increasing PrEP initiation would require making PrEP broadly accessible and easy to initiate. Substantial HIV incidence reduction was observed in the serodiscordant couple intervention; PrEP scale-up to at least 50% uptake achieved the GTZ target of a functional zero HIV incidence. Serodiscordant interventions that included main partners only had larger HIV incidence reduction effects with modest scale-up, which is unsurprising given the higher frequencies of condomless anal sex within these partnerships [51]. As PrEP for serodiscordant couples was scaled up, however, initiating PrEP within both main and casual partnerships was important in incidence reduction. This finding is reasonable given that the pool of HIV-negative individuals in main serodiscordant partnerships are quickly saturated at the population level as PrEP scale-up targets were increased.

Our finding that that of the two network interventions considered here, degree outperformed eigenvector centrality, is not surprising because degree directly measures the number of sexual partnerships on any given day, and would be expected to have a greater protective effect. Eigenvector centrality, which reflects larger network structures, provides a measure of social influence [37]. It is likely that the sparse, disconnected structure of the cross-sectional sexual network (Figure 2) was another reason why degree centrality was generally more effective than eigenvector centrality. A previous modeling study has found a similarly high impact of prioritizing individuals with a high number of sexual partners for PrEP [52]. Regardless, neither network intervention had as large an impact as prioritizing serodiscordant partners. Both network and serodiscordant partner interventions have received public health support in the form of diffusion-of-information type interventions that utilize social network structure [13], and partner services interventions that focus on initiating PrEP for HIV-negative individuals in serodiscordant partnerships [53].

Limitations

There are several limitations in this study. A major limitation in the study is that HIV infections among YBMSM, attributable to Black MSM older than 35 years of age and other populations, were not explicitly modeled, but computed as a proportion of the overall HIV incidence among YBMSM. The model design thus treated transmission among YBMSM as primary effects and transmission attributable to non-YBMSM as secondary. The model was designed as such because YBMSM have experienced relatively stable HIV incidence rates [5,6], even as overall HIV incidence in Illinois has declined, and a systematic strategy focused on reducing new HIV infections among YBMSM is needed. Moreover, external infections from women [7] and non-Black MSM [54] were not included due to evidence that very few infections among YBMSM come from either of these populations [7]. This model design, however, limits its generalizability to broader populations. Explicitly including a broader age range of Black MSM and other populations would be a useful next step to aid the design of comprehensive GTZ strategies. Additionally, modeled interventions for serodiscordant couples did not account for possible misclassification of HIV serostatus, which can occur during acute infection or when HIV test results are unknown to either partner. Conversations on HIV testing and status disclosure within main and casual partnerships are also necessary to make this model more realistic. Finally, while our baseline model did include treatment-as-prevention as a consequence of adherence to ART regimens, we did not explicitly consider interventions that expand treatment-as-prevention. Modeling combination ART and PrEP interventions is an important next step that may be needed to achieve GTZ targets.

In addition, we note several real-world implementation challenges. First, the random implementation of PrEP served as a “control” scenario, which allowed us to assess the decline in incidence attributable to a specific serodiscordant partnership or network intervention. We considered a random implementation of PrEP as the control, and not specific PrEP use guidelines (which have been modeled previously [16]), because of evidence on the limited utility of such guidelines for PrEP provision among Black MSM [55,56]. Expanding serodiscordant partner interventions in the real world is challenging given complexities around the determination of serodiscordance within casual or exchange partnerships. Serodiscordant interventions may thus require the use of digital extraction and analyses from hook-up apps or other social media, which could also be challenging to implement. Third, among the two network interventions considered here, degree interventions might be easier to implement, since they directly measure the number of sexual partnerships, whereas eigenvector centrality measures influence, and is harder to determine. Fourth, combination PrEP initiation and retention interventions are likely more feasible given lower levels of increase required in each and should be further explored. Finally, explicit considerations of implementation costs in future work may be helpful to GTZ stakeholders.

Conclusion

In sum, comprehensive models that have the capacity to include multiple biological, social, and network interventions are needed to inform GTZ decision making for the development of systematic HIV elimination initiatives [16,17,57]. We present an agent-based network model with the goal of developing an implementation science framework to inform GTZ initiatives in the United States, which require examination of downstream intervention effects, and may therefore be less amenable to empirical trials. We found that the goal of fewer than 200 new infections annually – i.e., a "functional zero" – was achieved in a decade by increasing PrEP uptake to at least 50% of HIV-negatives when new initiators were selected from HIV-negative individuals in serodiscordant partnerships. Rolling out a PrEP intervention targeted towards serodiscordant couples, however, might face implementation impediments that prevent scale-up to sufficiently high levels. Thus, to accomplish GTZ targets, other synergistic interventions, particularly scaling up ART use, and addressing psychosocial and structural barriers, will need to be considered. Our group, and others, are conducting modeling and empirical studies to design such interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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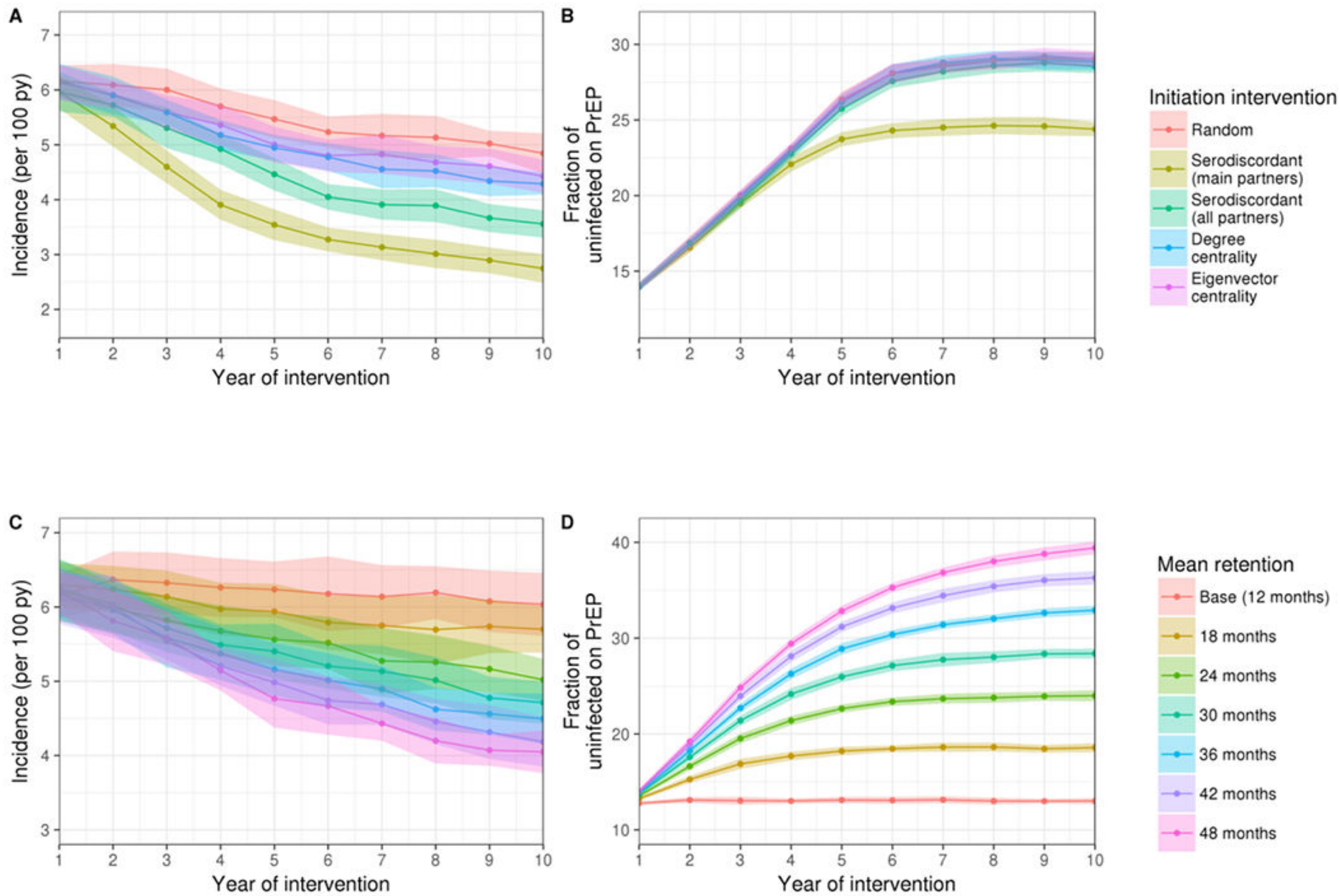

Figure 1: Simulated annual mean incidence rates and PrEP uptake levels, under several intervention strategies to increase PrEP initiation (Panels A and B) to 30% while PrEP retention is held at base levels*, and increasing PrEP retention to a range of levels (Panels C and D), while PrEP initiation is held constant at base levels.**

* In the base case, PrEP retention is 12 months on average.

** In the base case, PrEP initiation is 12.7% of HIV-negatives for persons <=26 years old and 14.7% of HIV-negatives for persons > 26 years old.

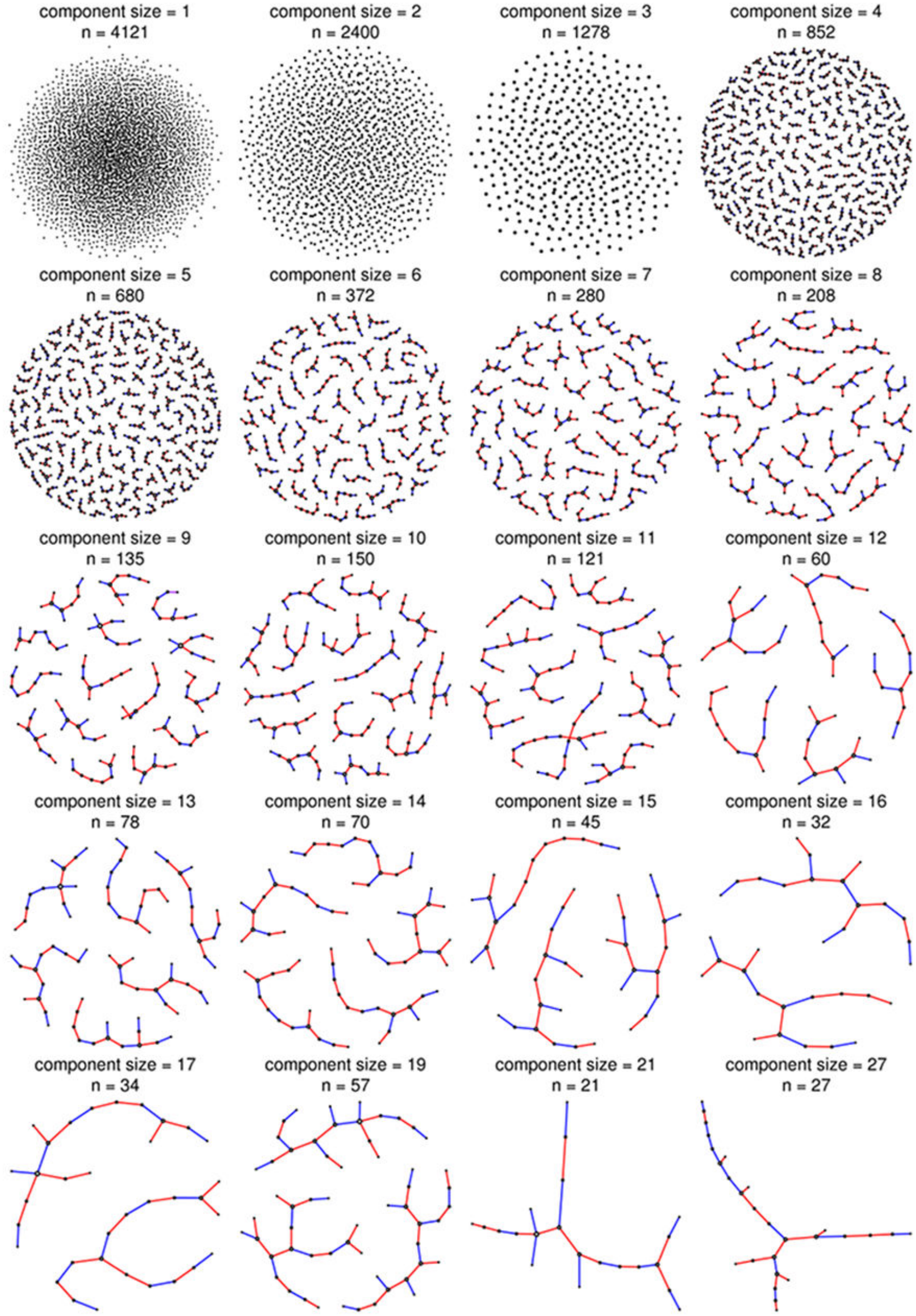

Figure 2:

Composition of steady state sexual network clusters at t=0. Main partnerships are displayed in blue, and casual partnerships are displayed in red.

Table 1:

Parameters to Model HIV Transmission among young Black men who have sex with men (YBMSM), Illinois.

Demography		
Parameter	**Estimate**	**Source**
Age range	[18 – 34) years	Defined population of interest
HIV prevalence among 18-year olds at entry into the model	1%	[58]
Mortality for uninfected individuals	Age-specific mortality rates for Chicago; achieving age >34 years	[59]
Sexual Behavior		
Mean partnership duration	Main: 512 days. Casual: 160 days.	[31]
Mean number of partnerships (per person) on any given day.	Main: 0.378. Casual: 0.458.	[28,29]
Frequency of sex (per partnership per day)	Main: 0.189. Casual: 0.053.	See Appendix Section A.5.
Proportion of acts where condoms are used in serodiscordant partnerships	Main: never: 26.1%; rarely: 4.7%; sometimes: 8.1%; usually: 8.7%; always: 52.3%. Casual: never: 28.1%; rarely:1.4%; sometimes: 4.3%; usually: 5.4%; always: 60.7%	[28,29]
Distribution of number of sexual partnerships on any given day	Main: 0 (60%), 1 (38%), 2 (1%). Casual: 0 (61%), 1 (32%), 2 (7%)	[28,29]
Mean absolute value of difference in partner ages	Main: 2.9 years. Casual: 3.1 years.	[28,29]
Testing and Diagnosis		
Detection window of test	22 days	[60]
Testing among HIV-negative/undiagnosed individuals	For individuals <26 years, 7.8% never test. For individuals ≥ 26 years, 2.3% never test.	[28,29]
Linkage to Care and ART		
Time between diagnosis and ART initiation	For individuals <26 years: 0-1week (16.9%);1week-1month (31.4%); 1-3months (19.1%); 3-6 months(6.7%); 6months-1year (12.3%); 1-2years (8.9%); 2-5years (4.5%). For individuals ≥ 26 years: 0-1week (16.7%);1week-1month (26.2%); 1-3months (9.5%); 3-6 months(14.3%); 6months-1year (14.3%); 1-2years (7.1%); 2-5years (4.7%).	[28,29]
CD4 evolution for ART initiated	CD4 count recovers by 15 cells/μl every month until pre-infection level or for 3 years, whichever is first	[61,62]
Viral load evolution for ART initiated	Declines to 200 copies/ml in 30 days	[63]
Distribution of ART adherence	Never: 10%, Sometimes: 30%, Usually: 28%, Always: 32%	[28,29]
PrEP Use		
% of HIV-negatives who use PrEP	12.7% <26 years; 14.7% >= 26 years at a given time	[28,29]
Time that a PrEP user is retained on PrEP	1 year (on average)	[50] (and additional details in Appendix Section A.4.7.)
Adherence to PrEP, for those who have initiated	Non-adherence: 0 pills/week (21.1%); low adherence: <2 pills/week (7.0%), moderate adherence: 2–3 pills/week (10.0%), and high adherence: 4+ pills/week (61.9%)	[64,65]
Reduction in transmission associated with levels of PrEP adherence	Non-adherence: 0%; low: 31%; moderate: 81%; high: 95%	[65,66]
Biology		
CD4 in uninfected men	916 cells/μl	[67]

Demography		
Parameter	**Estimate**	**Source**
CD4 Decline in HIV-infected but untreated individuals	As per a linear model	See Appendix Section 4.3.
Acute stage duration	Infection to peak viremia = 45 days; peak viremia to viral set point = 45 days	[68]
Chronic stage duration	3550 days	[69]
Late stage (AIDS) duration	728 days	[69]
Level of Peak Viremia	6.17 log	[70]
Viral set point	4.2 log	[70]
Max. late stage viremia	5.05 log	[70]
Infection Transmission		
Per act (chronic stage)	As per sensitivity analysis	See Appendix Section A.4.10.
Increase in infectivity corresponding to one unit increase in log viral RNA	2.89	[71]
Infectivity multiplier for acute infection	As per sensitivity analysis	See Appendix Section A.4.10.
Infectivity multiplier for late-stage infection	As per sensitivity analysis	See Appendix Section A.4.10.

Table 2

A: Mean (se) population HIV incidence at ten years among young Black MSM with varying PrEP initiation probabilities across several intervention scenarios					
		Serodiscordant partnerships		Sexual network position*	
PrEP initiation scenarios	**Random selection, mean (se)**	**Main partners, mean (se)**	**All partners, mean (se)**	**Degree, mean (se)**	**Eigenvector, mean (se)**
Base**	6.03 (0.08)	6.03 (0.08)	6.03 (0.08)	6.03 (0.08)	6.03 (0.08)
20	5.62 (0.06)	4.53 (0.04)	5.03 (0.07)	5.33 (0.06)	5.41 (0.07)
30	4.85 (0.07)	2.75 (0.05)	3.56 (0.05)	4.29 (0.04)	3.74 (0.06)
40	4.21 (0.05)	2.48 (0.04)	2.03 (0.04)	3.50 (0.04)	3.74 (0.05)
50	3.60 (0.05)	2.31 (0.04)	1.32 (0.02)	2.83 (0.05)	3.00 (0.04)
60	3.12 (0.03)	2.33 (0.04)	1.15 (0.02)	2.28 (0.04)	2.51 (0.04)
B: Mean (se) number of new HIV infections at ten years					
Base**	428 (5.1)	428 (5.1)	428 (5.1)	428 (5.1)	428 (5.1)
20	404 (4.3)	341 (3.2)	371 (4.8)	389 (4.1)	394 (4.9)
30	358 (4.5)	226 (3.8)	280 (3.4)	328 (2.8)	334 (4.1)
40	319 (3.7)	208 (3.3)	170 (2.9)	277 (3.2)	293 (3.8)
50	281 (3.6)	197 (3.2)	115 (1.8)	231 (3.5)	241 (3.3)
60	248 (2.5)	199 (3.4)	103 (1.9)	191 (3.1)	207 (2.9)
C: Mean PrEP uptake after ten years					
Base**	13.00 (0.07)	13.00 (0.07)	13 (0.07)	13 (0.07)	13 (0.07)
20	19.32 (0.10)	19 (0.11)	19.2 (0.11)	19.46 (0.07)	19.29 (0.08)
30	29.16 (0.10)	24.37 (0.09)	28.61 (0.08)	28.87 (0.10)	29.15 (0.12)
40	38.57 (0.12)	25.18 (0.07)	37.63 (0.12)	38.57 (0.12)	38.82 (0.12)
50	48.4 (0.14)	24.81 (0.10)	40.61 (0.12)	48.5 (0.14)	48.27 (0.17)
60	57.87 (0.19)	24.69 (0.08)	40.7 (0.14)	57.68 (0.14)	58.02 (0.13)

* Degree is a count of the number of main and casual partnerships of each person. Eigenvector is a measure of a person's influence based on their position in the sexual network.

** In the base case, PrEP initiation is 12.7% of HIV-negatives for persons <=26 years old and 14.7% of HIV-negatives for persons > 26 years old.

Table 3:

Mean population HIV incidence and number of new infections at ten years among YBMSM with increasing PrEP retention duration

PrEP Retention in Care (months*)	**Mean (se) population incidence in the 10^{th} year**	**Mean (se) number of new infections in the 10^{th} year**	**Mean (se) percent of HIV negative YBMSM using PrEP at intervention end**
12**	6.01 (0.05)	428 (5.1)	13.0 (0.07)
18	5.51 (0.06)	409 (3.8)	18.6 (0.10)
24	5.03 (0.07)	369 (3.9)	23.9 (0.13)
30	4.79 (0.08)	350 (3.7)	28.5 (0.14)
36	4.31 (0.05)	339 (4.5)	33.0 (0.07)
42	4.08 (0.05)	317 (4.3)	36.4 (0.15)
48	3.87 (0.05)	311 (3.8)	39.7 (0.14)

*Rounded from retention in care days

**Base case