

BMJ Open Gonorrhoea and chlamydia diagnosis as an entry point for HIV pre-exposure prophylaxis: a modelling study

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ABSTRACT

Objectives *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) increase the risk of HIV transmission among men who have sex with men (MSM). Diagnosis of NG/CT may provide an efficient entry point for prevention of HIV through the delivery of pre-exposure prophylaxis (PrEP); however, the additional population-level impact of targeting PrEP to MSM diagnosed with NG/CT is unknown.

Design An agent-based simulation model of NG/CT and HIV cocirculation among MSM calibrated against census data, disease surveillance reports and the US National HIV Behavioral Surveillance study.

Setting Baltimore City, Maryland, USA.

Interventions PrEP implementation was modelled under three alternative scenarios: (1) PrEP delivery at NG/CT diagnosis (targeted delivery), (2) PrEP evaluation at NG/CT screening/testing and (3) PrEP evaluation in the general community (untargeted).

Main outcome The projected incidence of HIV after 20 years of PrEP delivery under two alternatives: when equal numbers of MSM are (1) screened for PrEP or (2) receive PrEP in each year.

Results Assuming 60% uptake and 60% adherence, targeting PrEP to MSM diagnosed with NG/CT could reduce HIV incidence among MSM in Baltimore City by 12.4% (95% uncertainty range (UR) 10.3% to 14.4%) in 20 years, relative to no PrEP. Expanding the coverage of NG/CT screening (such that individuals experience a 50% annual probability of NG/CT screening and evaluation for PrEP on NG/CT diagnosis) can further increase the impact of targeted PrEP to generate a 22.0% (95% UR 20.1% to 23.9%) reduction in HIV incidence within 20 years. When compared with alternative implementation scenarios, PrEP evaluation at NG/CT diagnosis increased impact of PrEP on HIV incidence by 1.5(95% UR 1.1 to 1.9) times relative to a scenario in which PrEP evaluation happened at the time of NG/CT screening/testing and by 1.6 (95% UR 1.2 to 2.2) times relative to evaluating random MSM from the community.

Conclusions Targeting MSM infected with NG/CT increases the efficiency and effectiveness of PrEP delivery. If high levels of sexually transmitted infection screening can be achieved at the community level, NG/CT diagnosis may be a highly effective entry point for PrEP initialisation.

Strengths and limitations of this study

- This study helps to quantify the added value of targeting pre-exposure prophylaxis (PrEP) to men who have sex with men (MSM) diagnosed with *Neisseria gonorrhoeae/Chlamydia trachomatis* (NG/CT), in terms of population-level impact on disease incidence over time.
- The model is calibrated to a wide array of data including census data, disease surveillance reports and a nationally representative survey of HIV-related behaviours.
- This model offers policy-makers a support tool to estimate and compare the population-level impact of various prevention/control programmes.
- Study findings are limited by simplifying assumptions including (but not limited to) exclusion of other sexually transmitted infections such as syphilis, simplified representation of NG/CT natural history, simplification of sexual networks for NG/CT and HIV transmission, exclusion of HIV transmission through injection drugs or heterosexual sex and exclusion of transgender and bisexual individuals from the simulated population.
- Due to limited data as to whether MSM change their behaviour while taking PrEP, behavioural disinhibition was excluded from this analysis.

BACKGROUND

Infection with *Neisseria gonorrhoeae* (NG) and/or *Chlamydia trachomatis* (CT) may impact HIV transmission in multiple ways, particularly among men who have sex with men (MSM). From a biological standpoint, NG/CT infection may increase one's susceptibility to HIV acquisition: rectal infection, in particular, has been linked to an increased risk of HIV acquisition.^{1 2} HIV and NG/CT also share many risk factors at the individual level (eg, condomless sex) and network level (eg, having sex within a high-prevalence network), such that the three conditions are often epidemiologically linked.³ Additionally, HIV-negative men have an increased risk of

HIV acquisition when in partnership with an HIV-positive partner who is also coinfecting with NG/CT.^{4,5} As a result, better diagnosis and treatment of NG/CT can potentially reduce HIV incidence,⁶ and help to identify individuals at high risk of future HIV infection.

Pre-exposure prophylaxis (PrEP) is part of comprehensive HIV prevention services in which HIV-negative people take daily antiretroviral medication to lower risk of HIV transmission on exposure. The US Centers for Disease Control and Prevention (CDC) has recommended PrEP for HIV-negative individuals at substantial risk of infection.⁷ Among MSM, this includes HIV-negative men who are either diagnosed with a sexually transmitted infection (STI) in the last 6 months, are in an HIV discordant partnership or report a condomless sex act in the last 6 months. Despite this broad recommendation, the potential population-level impact of PrEP remains uncertain. Several barriers exist to the successful implementation of PrEP, including providers' perceived inability to deliver PrEP in primary care settings,⁸ individuals' limited knowledge of PrEP effectiveness,⁹ low self-perceived risk for HIV infection,¹⁰ patients' difficulty in maintaining adherence¹¹ and high costs (at over US\$10 000 per person-year for those without insurance or access to a medication assistance plan).^{12,13}

Given these challenges, optimising the efficiency of PrEP delivery is a public health priority. Specifically, it is important to tailor PrEP delivery to those who stand to gain the most from its preventive efficacy. Given the epidemiological link between NG/CT infection and HIV among MSM, new NG/CT diagnoses may serve as a useful means to identify high-risk MSM for PrEP evaluation and delivery.⁷ At present, the impact of such a strategy—in terms of reducing HIV and NG/CT incidence at a population level—is not clear. To address this question, we used surveillance data from Baltimore City (Maryland, USA) to construct an agent-based simulation model of the cotransmission of HIV and NG/CT among MSM,¹⁴ and applied this model to study the added value of targeting PrEP to MSM diagnosed with NG/CT, in terms of population-level impact on HIV incidence over time.

METHODS

We base our depiction of HIV on a published agent-based model of HIV transmission among MSM in Baltimore City¹⁴ (figure 1-top panel), and we extend this model to include coinfection of HIV with NG and CT infections (see section 1 of the online supplementary material).

NG/CT infection

NG and CT share similarities in natural history, including their acute nature, symptomatology, frequent codiagnosis and cotreatment.¹⁵ Given these similarities, and for simplicity of modelling, we model NG/CT as a single biological entity. We assume that NG/CT infection may occur at the urethral, rectal or pharyngeal site—each with different probabilities of symptomatic presentation,

diagnosis and treatment, and effects on HIV transmission, as shown in table 1. We include both asymptomatic and symptomatic infection and fit the model to the annual number of diagnoses at each clinical site (urethral, rectal or pharyngeal) among MSM in Baltimore City (see section 2 of the online supplementary material).

STI screening

In addition to testing of symptomatic NG/CT diagnosis, we also assume screening of asymptomatic individuals as follows (figure 1-bottom panel):

- ▶ Guidelines-based screening for HIV and NG/CT: MSM may present to HIV/STI care providers (eg, STI clinics, community health centres, HIV counselling programmes) 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 and sexual activity such that younger MSM with higher propensity of partnerships experience a higher likelihood of visits.^{16,17} We further assume that NG/CT is always screened at the urethral site, and a proportion of patients are also screened at the rectal and pharyngeal sites (calibrated to match the reported level of NG/CT infections diagnosis at each site among MSM in Baltimore City, as shown in table 1).
- ▶ NG/CT screening for HIV-positive MSM in care: Based on CDC recommendations, most MSM who are continuously engaged in HIV care should undergo repeated NG/CT screening at least annually.¹⁵ More frequent screening, such as screening every 3–6 months, is recommended for high-risk MSM, including those with an NG/CT diagnosis in the last year. Based on data from Baltimore City and a conservative estimate, we assume 40% adherence to these guidelines.^{18,19}

HIV testing

In addition to combined HIV/STI testing that takes place as part of STI screening, we assume that all MSM experience an additional probability of HIV testing (in excess of testing through the STI programme) and calibrate this probability to match the reported level of HIV diagnosis among MSM in Baltimore City.

Calibration

The model was calibrated against aggregate estimates of HIV and NG/CT incidence and prevalence, as well as the estimated continuum of HIV care, in Baltimore City. Calibration targets pertaining to NG/CT epidemiology are derived from data on gonorrhoea surveillance and STI clinic visits collected by the Baltimore City Health Department as part of the STD Surveillance Network Project (see section 2 of the online supplementary material).

Pre-exposure prophylaxis

Our primary outcome for this analysis is the projected incidence of HIV after 20 years of delivering PrEP to MSM. We measure this outcome in three different PrEP delivery scenarios, selected for purposes of evaluating the

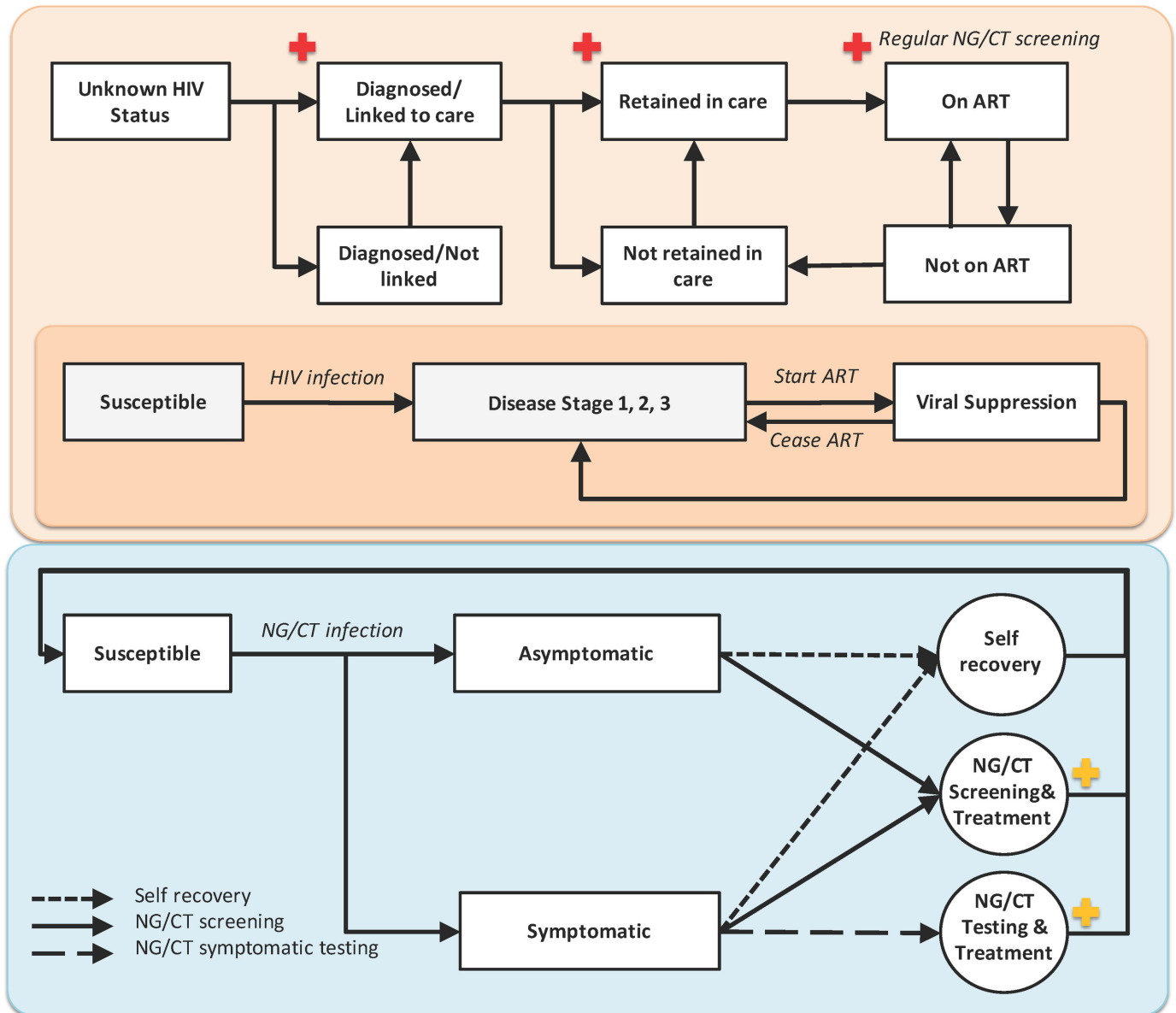


Figure 1 An agent-based model of *Neisseria gonorrhoea/Chlamydia trachomatis* (NG/CT) and HIV cotransmission. The top panel represents the HIV care continuum and natural history: On infection with HIV, individuals serially progress through three disease stages over time; this progression can be halted by initiation of antiretroviral therapy (ART), which is assumed to result –if taken– in viral suppression within 4–24 weeks (see table 1).²⁹ We assume, for simplicity, that engagement in care involves initiation of ART (as episodes of care engagement not resulting in ART initiation do not affect HIV transmission in the model). HIV-positive individuals in care are assumed to undergo regular screening for NG/CT (marked in red) subject to patients presenting for scheduled visits and clinician decision to screen. The bottom panel represents the natural history of NG/CT: infection may be symptomatic or asymptomatic, individuals remain infectious until diagnosis and treatment (which can occur either through symptomatic presentation to care or routine screening of asymptomatic individuals) or spontaneous resolution. On diagnosis with incident NG/CT, we assume that individuals are also screened for HIV infection (marked in yellow); if HIV-negative, we consider the possibility of PrEP delivery in this analysis. PrEP, pre-exposure prophylaxis.

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 and Baltimore City PrEP guidelines²⁰ (see section 1 of the online supplementary material) and includes HIV-negative individuals 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. The three scenarios are thus:

- ▶ PrEP delivery at NG/CT diagnosis ('targeted' strategy and primary analysis): all MSM diagnosed with NG/CT are offered PrEP at the time of diagnosis.
- ▶ PrEP evaluation at NG/CT screening/testing ('at-testing'): PrEP eligibility is evaluated at the time

Table 1 List of selected simulation parameters and calibration targets

<i>Neisseria gonorrhoeae</i> (NG) and <i>Chlamydia trachomatis</i> (CT) parameters	Value	Reference
Proportion of cases symptomatic*		
Urethral	0.74	30
Rectal	0.20	31 32
Pharyngeal	0.10	32 33
Duration of infection (at each site) in the absence of treatment	(3–12) months†	4 34–47
Coefficient of NG/CT transmission per week	0.294	Calibrated to provide the incidence of NG/CT
Proportion of NG/CT infections occurring at each site		Calibrated to provide the site-specific incidence of NG/CT
Urethral	0.35	
Rectal	0.49	
Pharyngeal	0.16	
Increase in HIV transmissibility (for those with urethral or rectal infection)	(1.5–2) fold*	5 48–51
Increase in HIV susceptibility (for those with urethral or rectal infection)	(1–2.5) fold*	33 34 51 52
NG/CT calibration targets	Mean‡ (Range)	
Number of annual NG/CT diagnosis among MSM in Baltimore City		Values estimated from local data on gonorrhoea surveillance and STI clinic visits in Baltimore City (see section 2 in the online supplementary material)
Urethral	337 (269–405)	
Rectal	25 (18–33)	
Pharyngeal	42 (23–60)	
Site-specific annual number of incident NG/CT cases among MSM in Baltimore City		
Urethral	944 (753 – 1135)	
Rectal	1251 (998 – 1505)	
Pharyngeal	409 (326 – 492)	
HIV parameters		
Disease duration		
Acute	(6–9) weeks*	53 54
Chronic	(8–10) years*	55 56
Late stage§	(1–3) years*	55–57
Mortality rate‡		
Acute and chronic, no ART	5 per 1000 person-years	58–60
Late stage, no ART	1/duration of late stage	
Reduction in mortality due to ART	0.58	
Time from ART discontinuation to pre-ART CD4 nadir¶	ART treatment duration up to 1 year	61–64
Time from ART initiation to full viral suppression	(4–24) weeks*	29
Average viral load (log ₁₀ copies/mL)		55
Acute, no ART	6.5	
Chronic, no ART	4.5	
Late stage, no ART	5	
On ART, partially suppressed	3.5	
On ART, fully suppressed	1.5	

Continued

Table 1 Continued

HIV parameters		
Infectiousness per sexual contact	2.45 ^{(log(VL)-4.5)}	55
Weekly probability of engagement in HIV care	0.006	65–67
Weekly probability of ART discontinuation	0.015	68
Gap in care after ART discontinuation	26 weeks	69
Relative probability of accessing HIV care among black MSM compared with white MSM	0.5	70
HIV calibration targets		
HIV prevalence	0.22 per 100 000 person-year	71
HIV continuum of care: proportion of cases		
Diagnosed	0.86	
Linked to care	0.62	
Engaged in care	0.5	
On ART	0.39	
Virally suppressed	0.27	

*Values represent a pooled estimate of the reported measures for NG and CT infections.

†Values are selected over uniform distributions across the ranges presented.

‡Values represent the reported levels of NG/CT diagnosis among Baltimore City's MSM, and they are likely to underestimate the proportion of ongoing rectal and pharyngeal infections. We, therefore, consider such potential underestimation in estimating the annual incidence of NG/CT (see section 2 of the online supplementary material) and have calibrated the model to represent realistic levels of prevalence (see the section on population overview in the main text).

§Mortality rate in late stage is defined as 1/(duration of late-stage disease).

¶Infectiousness assumed equal to that of the chronic disease.

ART, antiretroviral therapy; MSM, men who have sex with men; STI, sexually transmitted infection.

of screening/testing for NG/CT, and all eligible individuals are offered PrEP.

- ▶ **Untargeted PrEP:** PrEP eligibility is evaluated at random, and all eligible MSM are offered PrEP.

All else being equal, increasing the number of MSM on PrEP will result in larger effects on HIV incidence (as more people are protected from HIV transmission). However, for a given number of MSM screened—or a given number of MSM on PrEP (eg, if resource constraints are such that not all MSM meeting the criteria for PrEP can be placed/maintained on PrEP)—targeting PrEP to those screened for/diagnosed with NG/CT may be more efficient. Our primary aim was to quantify the extent of this gain in efficiency; thus, we compared scenarios in which the same number of MSM would be evaluated for PrEP, or alternatively the same number of MSM would be maintained on PrEP. Furthermore, to illustrate the potential impact of reaching highly ambitious targets for improved STI screening, we considered a hypothetical scenario for improving the underlying level of NG/CT screening (such that individual MSM not on PrEP experience a 50% annual probability of NG/CT screening and evaluation for PrEP on NG/CT diagnosis), and studied the additional gain in effectiveness of NG/CT-targeted PrEP under this assumption.

In all scenarios, we assume that PrEP eligibility is reassessed every 3 months among patients receiving PrEP, and

those who remain eligible for PrEP continue to receive it over time. Furthermore, we assume that in each scenario, a given proportion of eligible MSM who are offered PrEP will initiate prophylaxis (PrEP uptake ranging (0%–100%)) and adhere to it (PrEP adherence ranging (0%–100%)), with adherence defined as taking a sufficient number of doses to protect against HIV transmission in the specified percentage of potential transmission events.²¹ As a criterion for initiation of PrEP, all eligible MSM are also screened and treated for NG/CT infection before starting PrEP.

Sensitivity analysis

A variety of sensitivity analyses were performed with the model. Using the HIV incidence at 10 years in the absence and presence of PrEP (via all three scenarios) as the main output of interest, one-way sensitivity analyses were performed to the variation of all model parameters to $\pm 25\%$ of their original value. We also varied condom usage among MSM on PrEP to model behavioural disinhibition (section 3 of the online supplementary material).

Patient and public involvement

Patients and/or public were not involved in this study.

RESULTS

Population overview

The simulation models a population of 15 000 MSM in Baltimore City, projecting an average of 215 (95%

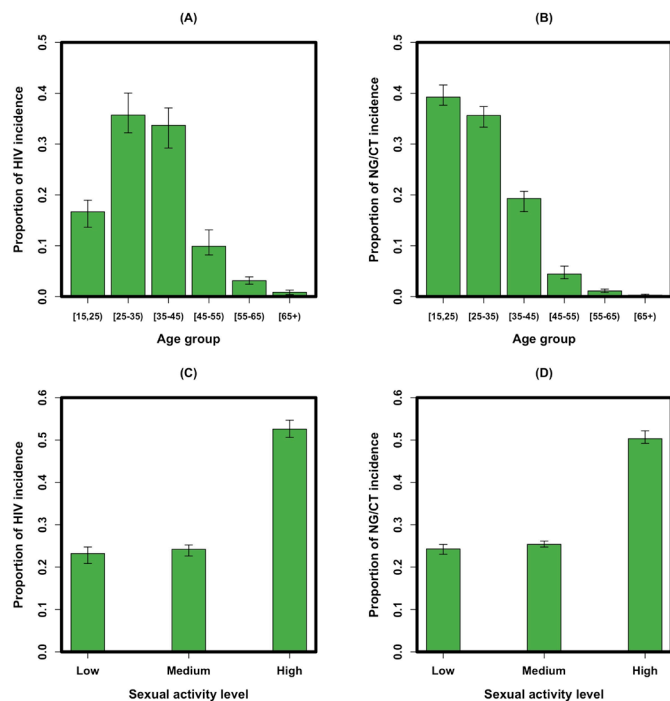


Figure 2 Model projections of the distribution of new infections by age and sexual activity level. Shown on the y-axes are the distribution of HIV (A) and NG/CT (B) incidence by age group and the distribution of HIV (C) and NG/CT (D) incidence by the sexual activity level. Bars represent the mean values of simulations (in green) with error bars representing the 95% uncertainty range of observations around each simulated measure. NG/CT, *Neisseria gonorrhoeae/Chlamydia trachomatis*.

uncertainty range (UR): 181 to 251) incident HIV cases per year. Within this population, the coepidemic of NG/CT was calibrated to 2598 (2204–2996) incident cases annually among which 35.0% (33.4% to 36.5%) of cases appear with urethral infection, 49.0% (47.4% to 50.6%) with non-urethral/rectal infection and 16.0% (14.8% to 17.2%) with pharyngeal-only infection. Point prevalence of NG/CT infection was estimated as 9.9% (8.4% to 11.5%), with 68.0% (63.5% to 72.5%) of infections occurring among black MSM (accounting for 58% of the MSM population). New infections occurred primarily in younger individuals, with 74% (72% to 78%) of new NG/CT infections occurring in MSM younger than 35 years old, and 69% (66% to 72%) of new HIV infections occurring among MSM between the ages of 25 and 45 (figure 2A,B). Over half of new HIV and NG/CT infections occurred among MSM in the high sexual activity class, which accounted for 33% of the simulated population (figure 2C,D). Overall, 81.5% (81.0% to 82.1%) of MSM diagnosed with NG/CT in the model were tested on the basis of symptomatic presentation (rather than asymptomatic screening), and 20% (18.0% to 22.0%) of incident NG/CT cases were coinfecting with HIV.

Epidemiological impact of PrEP at NG/CT diagnosis

At baseline and in the absence of PrEP (steady-state equilibrium), 361 (95% UR 298 to 427) MSM were annually

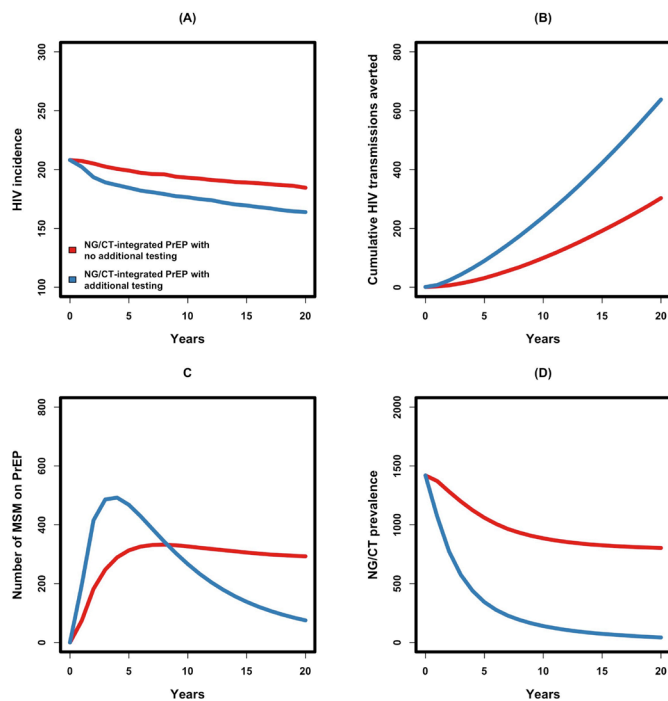


Figure 3 Impact of NG/CT-integrated PrEP, according to frequency of NG/CT screening/testing. Shown on the y-axes are the annual incidence of HIV (A), cumulative number of HIV transmissions averted (B), number of MSM on PrEP (C) and NG/CT prevalence (D). The red line depicts a scenario in which all MSM 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 blue line shows a hypothetical scenario in which 50% of MSM are additionally screened for NG/CT every year, with those testing positive for NG/CT also offered PrEP. MSM, men who have sex with men; NG/CT, *Neisseria gonorrhoeae/Chlamydia trachomatis*; PrEP, pre-exposure prophylaxis.

diagnosed and treated for NG/CT infection (calibrated). If 60% of MSM diagnosed with NG/CT could be started on PrEP (ie, uptake=60%) and maintained at a degree to which 60% of subsequent HIV infections were averted (ie, adherence=60%), HIV incidence was estimated to decline by 12.4% (10.3% to 14.4%) over 20 years (figure 3A). This corresponds to averting 318 (253–385) potential HIV transmissions through 5808 (5730–5886) person-years of PrEP delivered or 5479 (4330–6632) infections averted per 100 000 person-years of PrEP (figure 3B). Under the current level of NG/CT diagnosis, the number of MSM receiving PrEP is projected to increase through the first 8 years of the programme (reaching a total of 332 (327–338) MSM on PrEP) and to fall afterwards with a declining incidence of NG/CT (figure 3C). Due to the increased level of NG/CT screening/treatment among those on PrEP (through reassessment every 3 months), the prevalence of NG/CT was estimated to decline by 43.3% (41.6% to 44.9%) over 20 years of PrEP implementation (figure 3D).

The impact of PrEP on HIV incidence can be further increased by expanding the coverage of NG/CT screening at the community level. In our baseline model,

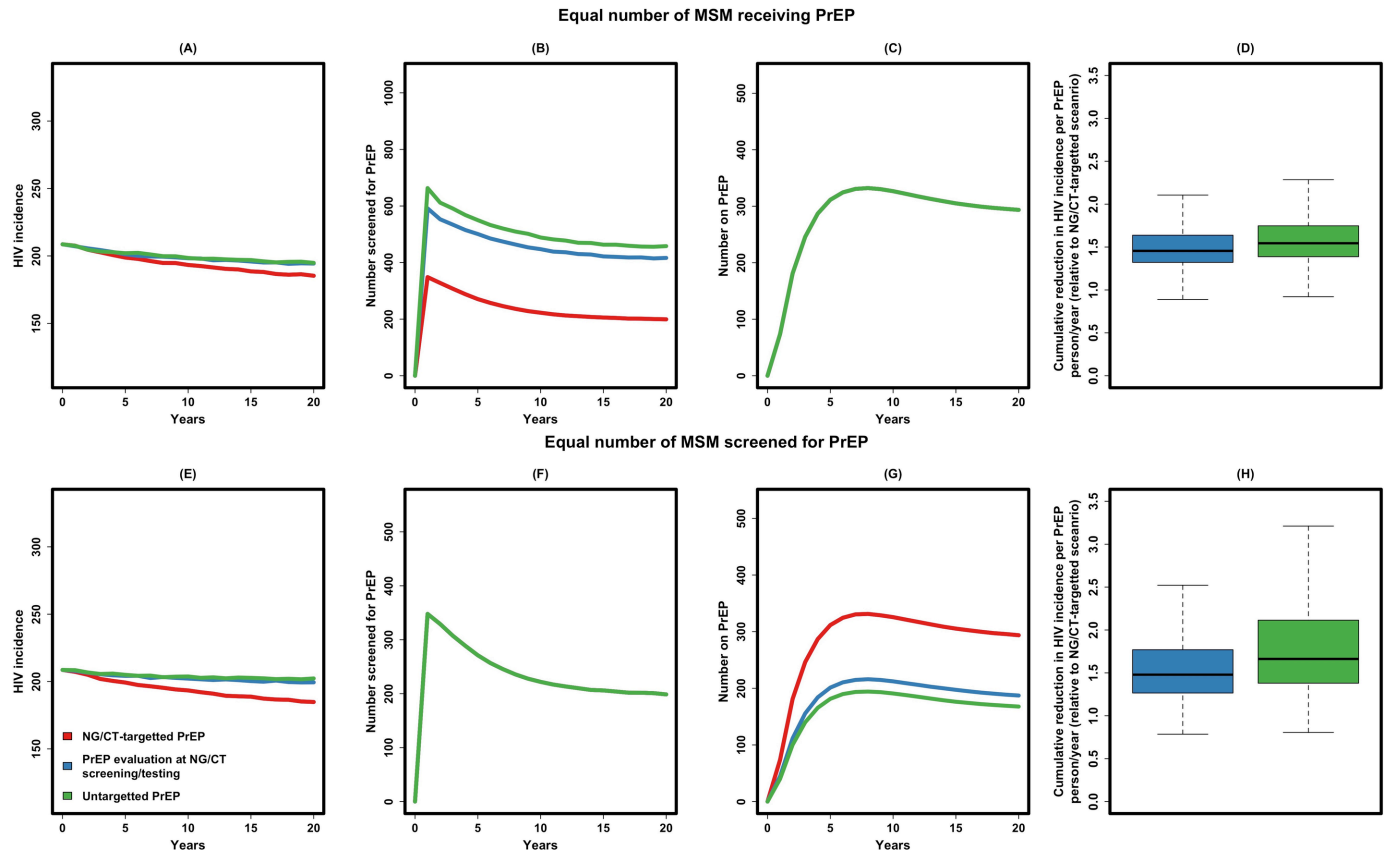


Figure 4 Relative impact of NG/CT-integrated PrEP. Shown in this figure is the relative impact of NG/CT-integrated PrEP (in red, also corresponding to the red line in figure 3), compared against PrEP evaluation at NG/CT screening/testing (in blue) and untargeted PrEP (in green), with full description 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 (panel A to D), or the same number of MSM would be screened for PrEP (panel E to 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 scenario (similar pattern in panel E through H). MSM, men who have sex with men; NG/CT, *Neisseria gonorrhoeae/Chlamydia trachomatis*; PrEP, pre-exposure prophylaxis.

25.0% (95% UR 24.0% to 26.0%) of MSM undergo NG/CT screening/testing at least once annually (CDC recommendation). In an expanded-screening scenario in which all MSM experienced a 50% probability of screening for NG/CT annually, we projected a 180% increase in the baseline estimate of 4033 (3883–4182) annual NG/CT testing/screening events. Offering PrEP to those testing positive for NG/CT subsequently generated a 22.0% (20.1% to 23.9%) decline in HIV incidence over 20 years, corresponding to 648 (589–710) potential HIV transmissions averted. For further information on levels of uncertainty in these results, see section 4 of the online supplementary material.

Relative impact of targeted versus untargeted PrEP

NG/CT-integrated PrEP increased the efficiency of PrEP delivery in at least two ways (figure 4A). First, a higher percentage of MSM were eligible for PrEP among those evaluated for PrEP (figure 4B, C). In our model, 71.1% (95% UR 65.0% to 77.2%) of all MSM diagnosed with NG/CT were eligible to receive PrEP (as 29% of this population is HIV-positive), compared with 45.2% (43.2% to

48.2%) of MSM screened for NG/CT and 41.3% (39.1% to 43.5%) of randomly selected MSM. Second, providing PrEP to MSM diagnosed with NG/CT targets individuals at higher risk of potential HIV infection (due to both biological factors and high-risk behaviour), such that—under the baseline assumption of equal numbers of people receiving PrEP—the impact of NG/CT-targeted PrEP on HIV incidence was greater than the other two scenarios (figure 4D). Specifically, over 20 years of implementation, targeting PrEP to MSM diagnosed with NG/CT infection increased the impact of PrEP by 1.5 (1.1–1.9) times relative to PrEP evaluation at NG/CT screening/testing, and by 1.6 (1.2–2.2) times relative to untargeted PrEP. In another comparison, if the same number of individuals were evaluated for PrEP, the efficacy of NG/CT-integrated PrEP was increased even further relative to other scenarios (figure 4E through 4H).

In one-way sensitivity analyses, the projected HIV incidence at 10 years in the absence of PrEP was sensitive to parameters relating to HIV and NG/CT transmission (including level of HIV viral load, condom use and

condom effectiveness) and parameters describing overall sexual activity (including the probabilities of starting new partnerships and the level of sexual activity in the most sexually active class). A similar variation in HIV incidence was observed in scenarios modelling PrEP evaluation at the time of NG/CT diagnosis, NG/CT screening or at random. Impact of PrEP in terms of reduction in HIV incidence in all scenarios relative to baseline was robust to reasonable variation of most model parameters (section 3 of the online supplementary material).

DISCUSSION

This agent-based simulation of HIV transmission among MSM suggests that screening for NG/CT may be an important and efficient entry point for PrEP evaluation and delivery. Specifically, if all MSM who currently test positive for NG/CT could be offered PrEP—assuming 60% uptake and sufficient adherence to maintain 60% protection—HIV incidence could be reduced by approximately 12%, averting one HIV infection annually per 1000 MSM population, with fewer than 20 per 1000 taking PrEP every year. On the basis of infections averted per PrEP dose delivered, providing PrEP to MSM with NG/CT diagnosis is nearly twice as efficient as providing PrEP randomly among eligible MSM. Thus, the use of NG/CT diagnosis as an entry point is a highly efficient and feasible mechanism for PrEP delivery. If NG/CT screening could be expanded to 50% of MSM every year (with PrEP offered only to those testing positive), this impact could be more than doubled. Given this substantial potential impact, it will be important to assess willingness and uptake and identify best practices to support PrEP uptake and adherence among MSM diagnosed with NG/CT.

These findings are consistent with other studies of PrEP delivery among MSM.^{22 23} Previous studies have shown that the population-level impact of PrEP depends strongly on PrEP uptake and adherence,^{14 22} as suggested in our study as well. Importantly, NG/CT diagnosis may be useful in this regard, as MSM who have recently been diagnosed with an STI may be more aware of their HIV risk and more likely to accept and initiate PrEP. Past research has shown that HIV interventions may be more effective when they are conducted or initiated at the time of an STI diagnosis.²⁴ Initiation of PrEP simultaneously with NG/CT diagnosis may also be a clinically feasible approach—as an STI diagnosis is already likely to prompt an HIV test (if not already performed), and MSM who are diagnosed with NG/CT have at least some level of health-care access. Unlike performing detailed sexual histories, offering PrEP to all HIV-negative MSM diagnosed with NG/CT is a simple guideline that is easy for most clinicians to follow.^{25 26} Further research is needed to assess the feasibility of this approach in the field, especially in ascertaining the degree to which the continuum of PrEP care (including linkage to care and longer term maintenance on PrEP) can be maintained in this population.

Furthermore, the potential trade-off between the positive impact of PrEP on STI prevalence through enhanced screening and its negative impact through behavioural disinhibition (if MSM on PrEP adopt riskier sexual behaviours) merits further investigation. Additional implementation research is also needed to identify effective mechanisms for improving adherence to CDC PrEP guidelines and overcoming barriers to acceptance and uptake of PrEP such as lack of awareness, lack of access, financial strain and stigma.^{11 27}

As with any modelling analysis, our findings are limited by necessary simplifying assumptions. Given the overlap in clinical practice for treating NG and CT and the substantial uncertainty regarding the natural history of the two infections (eg, duration of infectiousness, propensity toward asymptomatic infection), we have combined these infections as a single entity (NG/CT) and have used composite parameter values to describe the natural history of both diseases. However, there are still important differences between NG and CT, and to the extent that the natural history of each disease may differ, our findings may overestimate or underestimate the impact of PrEP targeted at these STIs. For example, an infection with a shorter infectious period and a higher transmission probability per sex act will concentrate more strongly on high-risk networks and may provide a more effective entry point for HIV PrEP. Further research can extend our analysis by considering the impact of each disease separately on HIV transmission dynamics. Furthermore, due to limited data on site-specific transmission dynamics (eg, relative frequency of oral-only vs oral-plus-anal vs anal-only sex among MSM in Baltimore), we adopted a simplified approach that does not fully capture the complete transmission dynamics but should result in the appropriate distributions of NG/CT infections at each anatomical site. Additional simplifying assumptions used in the underlying HIV simulation model include applying the same sexual network for NG/CT and HIV transmission; simplification of sexual networks as comprising only stable and casual partnerships; simplified definition of sexual activity classes as a lifetime attribute among MSM; exclusion of serosorting by HIV status, sexual activity class or PrEP; exclusion of HIV transmission through injection drugs or heterosexual sex and exclusion of transgender individuals from the simulated population. To the extent that these dynamics result in a higher concentration of NG/CT among MSM at high risk for HIV infection, our model may underestimate the impact of STI-targeted PrEP.

We excluded the potential existence of behavioural disinhibition for MSM on PrEP in the main analysis and applied a simplified approach for modelling the combined role of PrEP uptake/adherence for HIV protection. In additional sensitivity analyses, we studied the impact of decreased condom use among MSM on PrEP on the outcome of NG/CT-targeted PrEP, and the relative efficacy of STI-targeted scenario compared with the other comparators (see section 3 of the online supplementary

material). As expected, the projected impact of NG/CT-targeted PrEP on the incidence of HIV and NG/CT declined with reduced levels of condom use among PrEP users. This further highlights the need for additional behavioural surveillance data characterising changes in the level of condom use and risky behaviours among PrEP users in local settings. Despite this behaviour, the main outcome of our analysis (increased effectiveness of PrEP implementation through an NG/CT-targeted approach) remained robust to variation in the rate of condom use reduction.

There are strong racial disparities in HIV incidence and healthcare access in the USA, such that the highest risk populations may be the ones least likely to have access to PrEP²⁸; these disparities were not included in our simplified cascade of PrEP. Our model calibration was limited to the scope of local surveillance data, and available literature for values lacking direct empiric estimates from Baltimore City (eg, probability of symptomatic infection). We also assumed a future trajectory of HIV infection in the future that represents continuation of current trends; this trajectory is unlikely to remain constant for the next 20 years but may help to provide a useful conceptual construct for present-day decision-making, which is the ultimate goal of this analysis. Our results are further limited by exclusion of syphilis infection, another STI that is often transmitted in the same populations and may affect transmission and acquisition of HIV. Finally, we did not incorporate cost or other resource constraints into the present model; future analyses could evaluate the efficiency of NG/CT-targeted PrEP delivery from a cost-effectiveness or budget impact perspective.

In summary, this stochastic agent-based model representing the codynamics of NG/CT and HIV transmission among MSM suggests that NG/CT diagnosis may serve as an efficient and effective entry point for PrEP. If linkage between STI and HIV control programmes can be effectively developed, further investment in NG/CT screening (followed by PrEP initiation) can have major impact, on the incidence and prevalence of NG/CT, and on transmission of HIV—potentially averting up to 20% of all HIV infections through NG/CT-targeted PrEP alone. Future analyses could evaluate whether such approaches could even be cost saving in the long term. Ultimately, ending the HIV epidemic in MSM populations will require a combination of multiple activities, including strengthening the continuum of HIV care, ensuring continued access to clinical services and prevention through both behavioural approaches (eg, condom use) and PrEP. Using NG/CT diagnosis as an entry point for PrEP initiation may serve as an important component of such a combined prevention approach.

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