Epidemiological impact of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* screening in men having sex with men: a modelling study

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ABSTRACT

Objectives The impact of the systematic screening of *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) in men having sex with men (MSM) on these pathogens' epidemiology remains unclear. We conducted a modelling study to analyse this impact in French MSM.

Methods We modelled NG and CT transmission using a site-specific deterministic compartmental model. We calibrated NG and CT prevalence at baseline using results from MSM enrolled in the Dat'AIDS cohort. The baseline scenario was based on 1 million MSM, 40 000 of whom were tested every 90 days and 960 000 every 200 days. Incidence rate ratios (IRRs) at steady state were simulated for NG, CT, NG and/or CT infections, for different combinations of tested sites, testing frequency and numbers of frequently tested patients.

Results The observed prevalence rate was 11.0%, 10.5% and 19.1% for NG, CT and NG and/or CT infections. The baseline incidence rate was estimated at 138.2 per year per 100 individuals (/100PY), 86.8/100PY and 225.0/100PY for NG, CT and NG and/or CT infections. Systematically testing anal, pharyngeal and urethral sites at the same time reduced incidence by 14%, 23% and 18% (IRR: 0.86, 0.77 and 0.82) for NG, CT and NG and/or CT infections. Reducing the screening interval to 60 days in frequently tested patients reduced incidence by 20%, 29% and 24% (IRR: 0.80, 0.71 and 0.76) for NG, CT and NG and/or CT infections. Increasing the number of frequently tested patients to 200 000 reduced incidence by 29%, 40% and 33% (IRR: 0.71, 0.60 and 0.67) for NG, CT and NG and/or CT infections. No realistic scenario could decrease pathogens' incidence by more than 50%.

Conclusions To curb the epidemic of NG and CT in MSM, it would not only be necessary to drastically increase screening, but also to add other combined interventions.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Intuitively, systematic screening for *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) infections should reduce their transmission in men having sex with men (MSM). However, epidemiological data do not support this assumption.

WHAT THIS STUDY ADDS

⇒ This modelling study, based on real-world data from a French cohort, indicates that neither increasing the screening frequency nor increasing the number of frequently screened patients could reduce NG and/or CT incidence by more than 50% in French MSM at steady state.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our results suggest that to curb the NG and CT epidemic, it is required to drastically increase screening and to combine it with other prevention interventions.

INTRODUCTION

Neisseria gonorrhoeae (NG) and *Chlamydia trachomatis* (CT) infections are highly prevalent sexually transmitted infections (STIs) in men who have sex with men (MSM). Both infections can lead either to symptomatic diseases or to an asymptomatic carriage. While symptomatic diseases are usually rapidly diagnosed, treated and thus cured, asymptomatic infections may persist for months and therefore, could contribute to the spread of pathogens. International guidelines recommend both NG and CT systematic screening in sexually active MSM at genital and extragenital (usually anal and pharyngeal) sites.[1–5] This screening policy is expected to have a positive impact on transmission dynamics by reducing the number of infected people (symptomatic or not) and the duration during which these infected people can transmit the pathogens. Actually, several modelling studies predicted that increasing screening would eventually decrease NG and/or CT incidence in the general population[6 7] and in MSM.[8–11] However, epidemiological data do not confirm yet these predictions. Indeed, NG and CT testing increased sharply in France between 2014 and 2021, reaching 25 per 1000 men over 15 years for NG (+200%) and 26 per 1000 for CT in 2021 (+106%).[12] In the meantime, the positivity rate for NG infections in men attending sexual health centres increased from 4.2% to 5.4% (8.4% in MSM) from 2016 to 2021, while the positivity rate for CT infections decreased from 9.0% to 6.5% in men (6.3% in MSM). A marked increase in NG and/or CT diagnosis has also been reported in the recent years in Europe,[13] in the UK,[14] in the USA[15]

or in Australia.[16] Thus, the relationship between an increasing testing and decreasing infections' incidence remains unclear until now, notably in MSM.

In France, NG and CT screening is recommended every 3 months (ie, approximately every 90 days) in MSM.[17] This screening strategy is particularly well followed in pre-exposure prophylaxis (PrEP) users who undergo regular follow-up every 3 months. However, this is not the case for most MSM, as demonstrated by the small number of reimbursed tests that represented one per patient per year in 2021.[12] In order to better understand the impact of frequent screening on NG and CT epidemiology in French MSM, we initiated a modelling study that was calibrated with the data from the large prospective Dat'AIDS cohort.[18]

MATERIALS AND METHODS

We adapted our previous model of NG and CT transmission among MSM, using a site-specific deterministic compartmental model at anal (A), pharyngeal (P) and urethral (U) sites.[19] Following previously published modelling studies, we assumed that the transmission of NG and CT was independent (ie, no interaction between the two pathogens at the intrahost level). We considered in the model both symptomatic infections, for whom patients are usually seeking rapid treatment and asymptomatic infections, detected only through systematic screening. We assumed infectiousness to be the same for all infected individuals, irrespective of infection outcome (symptom onset and treatment, or spontaneous clearance). We did not model sexual practices explicitly and did not consider site-specific contact rates. However, we assumed that some sites are more at risk of infection than others and we included site-specific susceptibility and clearance rates. The model also included information on NG and CT spontaneous clearance, the proportion of symptomatic cases for each site, and assay sensitivity and specificity, all of which were assumed to be constant during the study period. The total MSM population in France N was estimated from available public health data to 1 million persons.[20 21] We defined two subpopulations: N_0, benefiting from frequent NG and CT testing and N_1, undergoing less frequent testing, with $N=N_0+N_1$. Newly sexually active individuals enter the susceptible compartment at the rate ν, and individuals exit all compartments at the rate $\mu = \nu/N$. Multisite NG and/or CT infections are represented by (A,P,U) triplets where A, P and U denote the infection status of the anal, pharyngeal and urethral sites, respectively, 0 meaning not infected and 1 meaning infected. Thus, eight sets of results combinations per site can be modelled: from set 0 ($A_0P_0U_0$) to set 7 ($A_1P_1U_1$). A summary of the model is presented in figure 1, and the model is fully described in online supplemental file 1.

We used NG and CT screening data from MSM enrolled in the Dat'AIDS cohort between 2010 and 2020 to determine prior distributions. In this cohort, data from persons living with HIV (PLWH) and from individuals attending sexual health centres were prospectively collected. We fitted our model to the anatomical site-specific prevalence using test results posterior to 2016 for which the three sites were tested. The site-specific positive rates remained stable over the period, so we assumed a steady state, then computed the average rates, and multiplied them by $N = 10^6$ to obtain site-specific absolute prevalence. We used a Metropolis-Hastings algorithm to fit our model, and used the same prior distributions for NG and CT. The parameter prior and posterior distributions for NG and CT are reported in online supplemental tables 1–8.

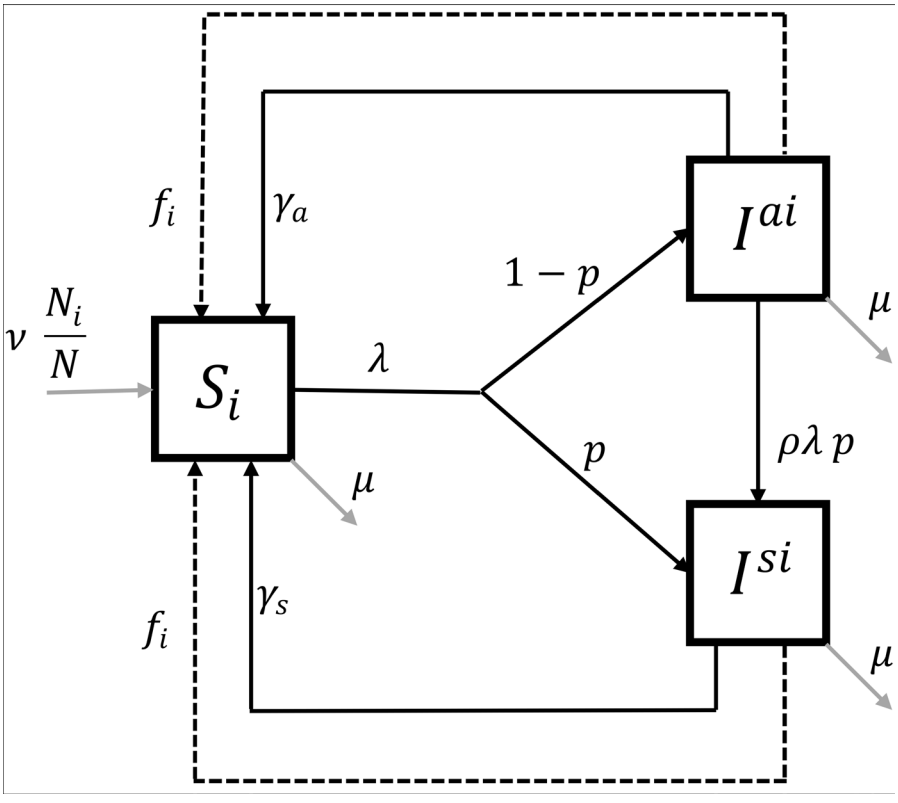

Figure 1 Summary of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* transmission model in men having sex with men. N, total population; N_i, subpopulations; I^a, asymptomatically infected compartment; I^s, symptomatically infected compartment; S_i susceptible compartment. The model is fully described in online supplemental file 1.

We ran simulations for 100 sets of parameter values randomly drawn in the posterior distribution. Scenarios' simulations were performed for these sets of parameter values, in order to estimate the mean steady-state incidences of NG and CT infection (that is, at the asymptote).

We assumed that the testing frequency of the frequently tested population could be controlled, with the testing frequency of the less frequently tested population remaining to its baseline value. In different scenarios, we varied the testing frequency of the frequently tested population between one test every 200 days to the extreme value of one test every 10 days and the size of the frequently tested population from 40 000 to 1 million (all MSM). We assumed that patients from both the frequently tested and the less frequently tested populations were all tested at the same sites. We simulated scenarios in which 100% of tests were performed at specified sites. Incidence rates were determined for NG, CT and NG and/or CT infections, with different combinations of tested sites, testing frequency and size of the frequently tested population. Incidence rate ratios were determined by dividing the result of a given incidence rate by the incidence rate of the baseline reference case.

The Dat'AIDS cohort is registered on ClinicalTrials.gov (NCT02898987 and 03795376).

RESULTS

The observed dataset was based on 202 026 A, P or U samples collected between 2010 and 2020 from 12 557 MSM enrolled in 25 centres participating in the Dat'AIDS cohort. The observed prevalence at the different sites was determined from 22 738 NG and CT APU triplet samples collected in 8254 MSM enrolled in the Dat'AIDS cohort from 2016 to 2020 (the distribution of positive NG, CT, and NG and/or CT samples among the different sites is given in figure 2). Overall, the prevalence rate at any site was 11.0%, 10.5% and 19.1% for NG, CT and NG and/or CT infections, respectively. The prevalence rate per site was 7.3%, 5.6% and 1.6% for NG infections, 8.5%, 1.5% and 2.1% for CT infections and 14.1%, 6.9% and 3.4% for NG and/or CT infections at A, P and U sites, respectively.

The observed mean testing frequency in our dataset was one test every 200 days. The baseline incidence rate was estimated at 138.2 per year per 100 individuals (/100PY) (95% CI 138.0 to 138.4), 86.8/100PY (95% CI 86.7 to 86.9) and 225.0/100PY (95% CI 224.8 to 225.2)) for NG, CT and NG and/or CT infections, respectively. By keeping the same testing frequency (every 200 days), systematically testing all three A, P and U sites resulted in the lowest incidence at steady state (incidence rate 118.4/100PY (95% CI 118.1 to 118.7), 66.6/100PY (95% CI 66.3 to 66.8) and 185.0/100PY (95% CI 184.6 to 185.4) for NG, CT and NG and/or CT, respectively). The corresponding incidence rate ratios were 0.86, 0.77 and 0.82 for NG, CT and NG and/or CT infections, respectively, meaning that, as compared with usual practice, systematically testing all APU sites would decrease NG, CT and NG and/or CT incidence by 14%, 23% and 18%, respectively. Testing only A and P sites gave close results to the baseline incidence. All other testing scenarios gave worst results than those at baseline. Figure 3 illustrates the incidence ratio for these different testing strategies.

Simulations were then computed, varying the testing frequency and the size of the frequently tested population in the simulated population of 1 million MSM. Testing every 2 months a frequently tested population of 40 000 MSM (similar to PrEP intake in French MSM in 2022) resulted in incidence rates

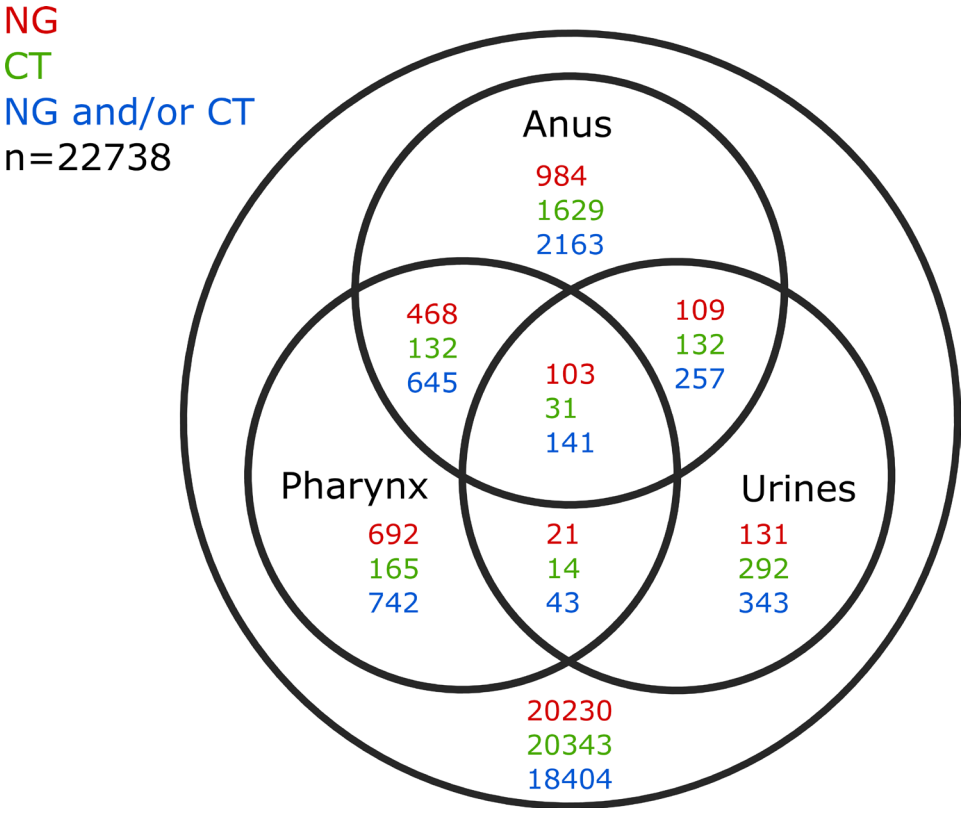

Figure 2 *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) tests collected in 22 738 anal/pharyngeal/urethral (APU) triplet samples from 8254 men who have sex with men enrolled in the Dat'AIDS cohort from 2016 to 2020. Positive tests are shown within the APU circles and their intersections; negative tests are shown within the larger circle and outside the APU circles. Red: NG; green: CT; blue: NG and/or CT.

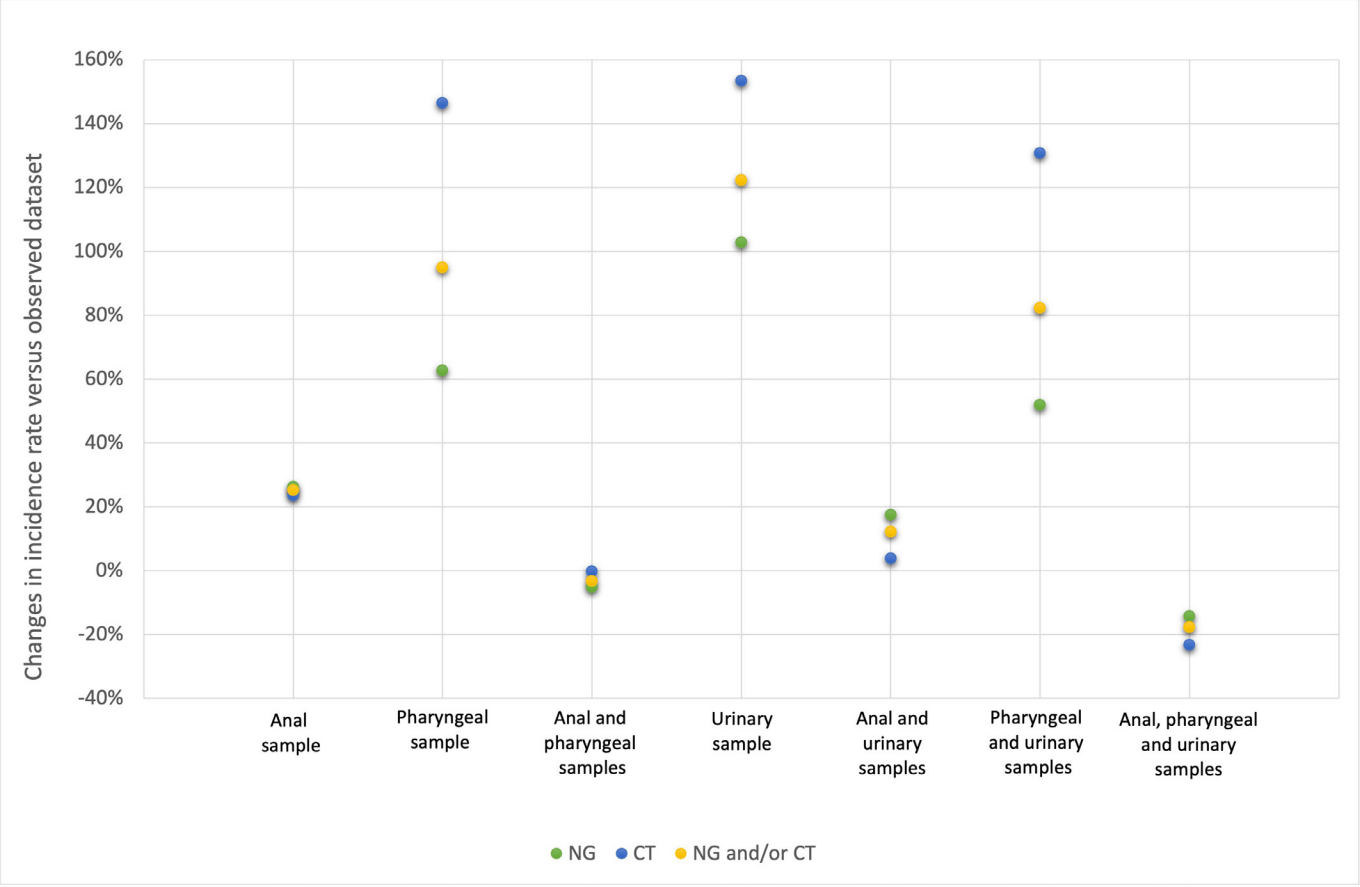

Figure 3 Changes in incidence rate for *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and NG and/or CT infections according to various sites' screening strategies as compared with the respective NG, CT and NG and/or CT baseline incidences (in the observed dataset, where patients were tested every 200 days).

of 116.1/100PY (95% CI 115.8 to 116.4), 65.1/100PY (95% CI 66.8 to 65.4) and 181.2/100PY (95% CI 180.8 to 181.6) for NG, CT and NG and/or CT infections, respectively. The corresponding incidence rate ratios were 0.84, 0.75 and 0.81 for NG, CT and NG and/or CT infections, respectively. With a frequently tested population of 40 000 patients and testing three sites every 10 days, the minimum incidence rate ratio obtained by the model was 0.80, 0.71 and 0.76 for NG, CT and NG and/or CT infections, respectively. On the other hand, multiplying by five the size of the frequently tested population (200 000 over 1 million MSM) while keeping the same testing frequency every 3 months in this population resulted in incidence rates of 98.1/100PY (95% CI 97.6 to 98.6), 51.8/100PY (95% CI 51.4 to 52.2) and 149.9/100PY (95% CI 149.2 to 150.6) for NG, CT and NG and/or CT, respectively. The corresponding incidence rate ratios were 0.71, 0.60 and 0.67 for NG, CT and NG and/or CT infections, respectively. To decrease the incidence rate by half compared with baseline (eg, incidence rate ratio 0.50), it is required to test every 90 days for NG, CT and NG and/or CT infections 430 000, 300 000 and 380 000 MSM over the total population of 1 million MSM, respectively. Figure 4 illustrates the incidence rate ratios estimated by the model for NG (figure 4A), CT (figure 4B) and NG and/or CT (figure 4C) infections, respectively.

DISCUSSION

The rising epidemiology of NG and CT infections in MSM is challenging and measuring the impact of interventions remains difficult. In this modelling study, we demonstrate that increasing either the testing frequency or the number of frequently tested patients (such as PrEP-users) would have a limited impact on NG and CT incidence in the total French MSM population. In fact, increasing the testing frequency from every 3 months to every 2 months would only decrease NG, CT and NG and/or CT incidence by 16%, 25% and 19%, respectively, while increasing the number of tests (and their cost) by 33%. On the other hand, increasing the number of frequently tested MSM while keeping the current testing frequency every 3 months would have a greater but still limited impact. Indeed, multiplying by five the number of frequently tested MSM would only decrease NG, CT and NG and/or CT incidence by 29%, 40% and 33%, respectively. However, applying the current recommendations of systematically testing both extragenital sites (AP) and urines would decrease NG, CT and NG and/or CT incidence in MSM by 14%, 23% and 18%, respectively. In addition, screening every 3 months proved to be cost-effective (compared with screening every 6 months) in both the MSM population and the general population.[22 23] Consequently, our model predicted that no realistic scenario would drop either pathogens' incidence by more than 50% in this population, meaning that neither increasing the testing frequency, nor increasing the size of the frequently tested population would alone be enough to control NG and CT infections in this population. These results should in no way lead health professionals to abandon screening for NG and CT, as it provides an opportunity for access to care and enables simultaneous screening for other STIs, notably syphilis

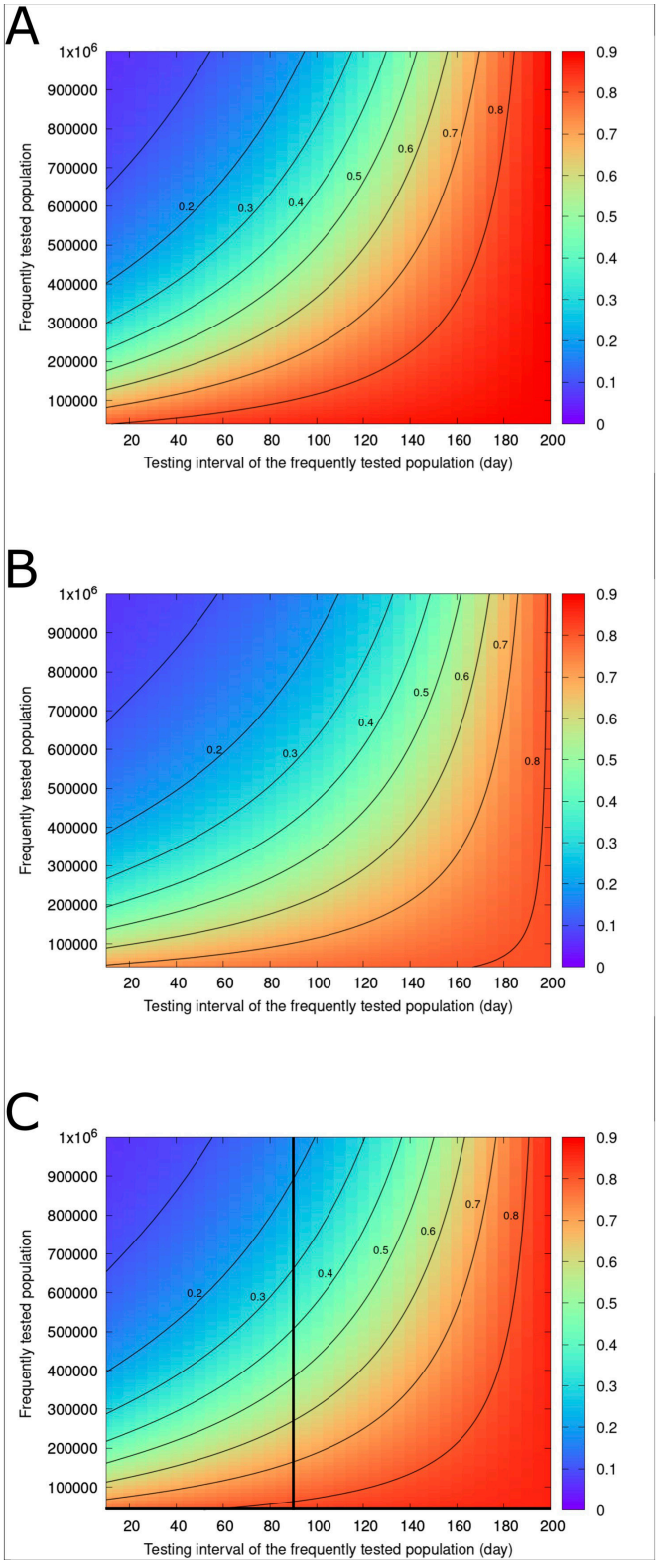

Figure 4 Incidence rate ratios for: (A) *Neisseria gonorrhoeae* (NG); (B) *Chlamydia trachomatis* (CT); and (C) NG and/or CT infections. Simulations are done in a simulated population of 1 million men who have sex with men (MSM) systematically tested at anal/pharyngeal/urethral sites, according to the number of frequently tested patients (vertical axis) and to the testing interval in frequently tested patients (horizontal axis). The black lines crossing indicate the current baseline case of 40 000 MSM tested every 90 days, corresponding to the pre-exposure prophylaxis uptake in French MSM in 2022.

and HIV. Reducing screening would therefore have deleterious consequences for all STIs.

These results have great potential implications. Despite the benefits of treating infected individuals and initiating the contact tracing of their sexual partners, the current test and treat approach of NG and CT infections is unlikely to have a significant epidemiological effect on the incidence of these infections in a high-risk transmission setting like MSM population. Consequently, if a population effect is expected, such results argue to combine different intervention strategies. Recent data suggested that doxycycline post-exposure therapy might reduce CT and syphilis incidence in high-risk MSM, while the effect on NG incidence remains controversial.[24 25] Similarly, the meningococcal serogroup B vaccine has been associated with a reduced NG prevalence and incidence in two cohort studies, while having no effect on CT infections.[26 27] A specific NG vaccine is also currently under study. The benefit of combining these different interventions remains unknown at this moment. Finally, adjusting these different interventions to risk profiles would probably increase their efficacy. For example, a recent modelling study found that a meningococcal serogroup B vaccination strategy depending on individual risk profile would be the most cost-effective approach to reduce NG infections in English MSM, over vaccination on attendance or over vaccination on diagnosis.[28] In any case, even if these complementary interventions had a beneficial impact on the incidence of NG and/or CT infections, our results strongly suggest that under no circumstances should the frequency of systematic screening for these STIs be reduced: all interventions must add up if there is to be any hope of controlling the epidemic.

Our results may differ from previous modelling studies in several ways. Several previous studies attempted to predict the impact of NG and CT systematic screening in the general population and may not extrapolate to an MSM population.[6 7 29] Other studies were based on a theoretical MSM population without prior controls,[8 11] while others restricted the MSM population to those who visited a sexual health centre and who may not be fully representative of the whole MSM population.[9] Our study, based on real-world data and applied to a model covering MSM population at a country level, may lead to more realistic scenarios. Indeed, our results are partially confirmed by the increased prevalence of self-reported NG and/or CT infections in MSM from 2010 to 2017 found in two large European studies, which correlated with country-level screening rates.[30]

Our study has some limitations, among which is the representativeness of the studied population. The Dat'AIDS cohort covers about 25% of PLWH and of PrEP users in care in France and is well represented throughout the country, including overseas department. However, its representativeness is probably much lower regarding patients not living with HIV and not using PrEP. Consequently, our results based on an MSM population should not be extrapolated to the general population. Additionally, since the cohort is hospital based, it is possible that symptomatic patients are over-represented in our population, which could influence the distribution of NG and CT infections. However, most patients enrolled in the cohort were outpatients and were probably not different from other patients followed up in other sexual health centres. Another limitation lies in the fact that, while we could precisely identify most of PLWH or PrEP users, we could not be sure that other patients were indeed not living with HIV or using PrEP, since most of these patients had anonymous files. This means that a PLWH attending anonymously for STI screening could appear twice in the cohort, first in the infectious diseases unit as well as in the STI clinic. Since NG and

CT distribution was similar in PLWH and in PrEP users, we thus chose to consider the entire population for analysis. Additionally, symptomatic and asymptomatic patients could not be differentiated in our database. However, since symptomatic infections are usually rapidly treated, they probably contribute less to NG and CT epidemiology than asymptomatic infections and this point has been considered in our model. Another limitation must be mentioned: no data were available concerning sexual behaviour and behavioural changes, so there was no heterogeneity in our MSM population. We assume in our model that epidemiological parameters were the results of the overall behaviour of the population, which probably remained stable, since NG and CT prior distributions remained stable during the studied period. Thus, our results represent a steady-state situation. Only focusing on steady states is another limitation of the study. Yet, in our case, this approach provides informative upper bounds on the effect of policies. For this reason and for the sake of clarity, we left investigations of the transition to steady state for later studies. Also, we deliberately chose not to study the effect of behavioural changes, since we were not able to determine which intervention could influence behaviours at a population level. Our study was based on a clinical dataset obtained before the COVID-19 pandemic and the mpox epidemic, both periods during which French MSM may have changed their sexual practices. However, following the marked decrease from 2019 to 2020, the testing rates for all STIs including NG and CT increased in 2021 and achieved higher levels than those in 2019.[12] This indicates that the impact of the COVID-19 pandemic on sexual practices in France was probably limited in time.

Our study has also major strengths, including the prospective collection of data and the large number of patients included allowing for solid prior estimates. Additionally, we used in our model either documented data or conservative epidemiological hypothesis. Finally, we designed the model to be representative of a whole MSM population at the country level, meaning that patients travelling from one site to another would not result in them entering and leaving the model but remaining in it. Thus, we believe that the results obtained by this model will be of great applicability.

In conclusion, our study demonstrates that increasing the frequency of NG and CT systematic testing in MSM beyond every 3 months or increasing the number of frequently tested MSM, such as PrEP users, would have a limited efficacy in reducing NG and CT incidence in French MSM. Therefore, our results suggest that to curb the NG and CT epidemic, it is not only necessary to drastically increase screening but also to combine it with other prevention interventions, such as vaccination, post-exposure antibiotic prophylaxis and behavioural interventions.

Correction notice This article has been corrected since it was first published online. The Dat'AIDS Study Group has been added as an author.

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Contributors JF, LH, RP, LCu, OR, PP, CD, NV and LCo designed the study. LCo collected and prepared the data. JF, NV and LCo prepared the modelling study. JF and NV performed the modelling study. LCo and LH redacted the draft manuscript. JF, RP, LCu, LH, OR, PP, CD, NV and LCo revised the manuscript. JF accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants. The Dat'AIDS cohort was approved by the French National Commission on Informatics and Liberty (CNIL 2001/762876). All subjects included in the cohort gave written consent.

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