Estimated costs and quality-adjusted life-years lost due to N. gonorrhoeae infections acquired in 2015 in the United States: A modelling study of overall burden and disparities by age, race/ethnicity, and other factors

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Summary

Background Disparities in the health and economic burden of gonorrhoea have not been systematically quantified. We estimated population-level health losses and costs associated with gonococcal infection and sequelae in the United States.

Methods We used probability-tree models to capture gonorrhoea sequelae and to estimate attributable disease burden in terms of the discounted lifetime costs and quality-adjusted life-years (QALYs) lost due to incident infections acquired during 2015 from the healthcare system perspective. Numbers of infections in 2015 were obtained from a published gonorrhoea transmission model. We evaluated population-level disease burden, disaggregated by sex, age, race/ethnicity, and for men who have sex with men (MSM). We conducted a multivariate sensitivity analysis for key parameters.

Findings Discounted lifetime QALYs lost per incident gonococcal infection were estimated as 0.093 (95% uncertainty interval [UI] 0.022-0.22) for women, 0.0020 (0.0015-0.0024) for heterosexual men, and 0.0015 (0.00070-0.0021) for MSM. Discounted lifetime costs per incident infection were USD 261 (109-480), 169 (88-263), and 133 (50-239), respectively. At the population level, total discounted lifetime QALYs lost due to infections acquired during 2015 were 53,293 (12,326-125,366) for women, 621 (430-872) for heterosexual men, and 1,078 (427-1,870) for MSM. Total discounted lifetime costs were USD 150 million (64-277 million), 54 million (25-92 million), and 97 million (34-197 million), respectively. The highest total burden of both QALYs and costs at the population-level was observed in Non-Hispanic Black women, and highest burden per 1,000 person-years was identified in MSM among men and American Indian/Alaska Native among women.

Interpretation Gonorrhoea causes substantial health losses and costs in the United States. These results can inform planning and prioritization of prevention services.

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Keywords: Sexually transmitted infections; Gonorrhoea; Disparities; Quality-adjusted life-years lost; Costs

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Research in context

Evidence before this study

We searched PubMed without language or date restrictions for all records matching "(neisseria gonorrhoeae or gonorrhoea or gonorrh*) and (inequalit* or unequal or disparit*) and (quality-adjusted life-years or burden or cost* or health expenditure* or incidence or prevalence or rate*)" in any field, returning 114 records. Of these studies, 49 estimated burden of gonorrhoea and other sexually transmitted infections (STIs). Racial and ethnic disparities in gonorrhoea have been measured using epidemiological metrics including notification rate of diagnoses, prevalence, incidence, and other summary measures of infectious disease rates such as Black-to-White rate ratio and population attributable proportion. Studies done in the United States found that the rate of reported gonorrhoea cases was highest among Non-Hispanic Black people and lowest among Non-Hispanic White people. Racial and ethnic disparities in reported rates of gonorrhoea diagnoses in United States decreased from 1993 to 2013 but increased after 2013. Men who have sex with men (MSM) have carried a substantially higher burden of gonorrhoea compared to other populations. Few studies have measured both short- and long-term consequences of gonorrhoea, such as infertility, ectopic pregnancy, and chronic pelvic pain. There have been studies estimating overall health and economic impacts of gonorrhoea and complications. A few studies have investigated quality-adjusted life-years (QALYs) lost for chlamydia but not for gonorrhoea. Notably, there have been no studies evaluating racial and ethnic disparities in gonorrhoea using QALYs lost and costs. This presents a research gap in health metrics related to racial and ethnic inequities, which limits the ability to quantify the extend of the disparities and measure progress in reducing inequities.

Added value of this study

By using life course perspective, we synthesized evidence describing health and economic outcomes and costs during and following gonococcal infection. We estimated discounted lifetime QALYs lost and costs due to incident infection acquired during 2015 in the United States, by sex, age, race/ethnicity and for men who have sex with men (MSM). We estimated total QALYs lost of 53,293 and costs of 150 million for women. Of this estimated burden 44.9% occurred among Non-Hispanic Black women. The highest per-capita burden occurred among MSM and among American Indian/Alaska Native women. The per-capita burden among MSM was 45.1 times of that among heterosexual men. The per-capita burden among American Indian/Alaska Native women was 4.42 times of that among Non-Hispanic White women. For women, we found that QALYs lost (98.8%) and costs (65.4%) result primarily from sequelae of gonorrhoea, while for men the main source of these losses were symptomatic gonococcal infections (94.7% for QALYs lost and 65.7% for costs). As composite measures of lifetime burden of gonorrhoea and its sequelae, our results can serve as metrics to evaluate progress in reducing racial/ethnic disparities in gonorrhoea.

Implications of all the available evidence

Although gonorrhoea is a short-term infection, it causes longer term health losses and associated costs with substantive disparities in burden of disease by race/ethnicity and for MSM within the United States. Quantifying the broader health losses more accurately reflects the total magnitude of racial/ethnic inequities related to gonococcal infection. The QALYs lost and costs associated with gonococcal infection may increase in the future with rising antibiotic resistance highlighting the importance of understanding the consequences of untreated infection. Non-Hispanic Black women and American Indian/Alaska Native women experience worse reproductive health outcomes compared to Non-Hispanic White women and gonorrhoea associated disparities in QALYs lost are another manifestation of the underlying inequities. Our estimates of QALYs lost per infection can be used to measure benefits of interventions that can reduce development of gonorrhoea associated sequelae. Our work provides a comprehensive framework for evaluating gonorrhoea associated health outcomes and disparities.

Introduction

In the United States, there were 583,405 gonorrhoea diagnoses reported in 2018, making *Neisseria gonorrhoeae* the second most common cause of notifiable infections.[1] Reported gonorrhoea rates have increased since 2009,[1–4] particularly among men who have sex with men (MSM).[1,5–7] Along with chlamydia, gonorrhoea is an important cause of pelvic inflammatory disease (PID), chronic pelvic pain (CPP), ectopic pregnancy (EP), and tubal infertility (TI) in women and epididymitis in men.[8–10] Gonococcal infection may also increase the risk of human immunodeficiency virus (HIV) acquisition and transmission.[11,12]

The aim of this study is to present a comprehensive analysis of gonorrhoea burden and disparities by race/ethnicity and other factors in the context of current prevention efforts, based in part on published estimates of gonorrhoea incidence. Recent studies estimated that there were 1.57 million incident gonococcal infections among adults aged 15 to 39 years in the United States in 2018,[13] with expected lifetime medical costs of $271 million.[14,15] Although the 2018 incidence estimates by Kreisel and colleagues are the most recent available, those estimates were not stratified by race/ethnicity and did not explicitly account for men who have sex with men (MSM).[13] Therefore, we used estimates of incidence in 2015 by race/ethnicity and for MSM from the Tuite et al. gonorrhoea transmission model[16] in this study.

Although disparities in gonorrhoea and other STIs by race/ethnicity, age, sex and other factors have been well documented, these disparities typically have been measured based on reported case numbers and rates,[2,3,5,8] whereas diagnosed infections represent only a subset of all infections. To date, the population-level disparities in quality-adjusted life-years (QALYs) lost and costs of gonococcal infection and short- and long-term sequelae have not been systematically quantified, reflecting a knowledge gap in our understanding of gonorrhoea burden in the United States. The key contribution of this study was to quantify the population burden of gonorrhoea in terms of health impact and cost. Specifically, we estimated the lifetime number of QALYs lost and healthcare costs associated with gonococcal infections acquired in 2015 by age, sex, race/ethnicity, and for MSM in the United States.

Methods

Analytic overview

We estimated costs and health losses attributable to gonorrhoea among ages 15–39 years, separately for women, men who have sex with women (MSW) and MSM, summarized as expected discounted lifetime QALYs lost and expected discounted lifetime costs per incident gonococcal infection. We combined these estimates with the total numbers of estimated incident infections acquired in 2015 (the most recent available year for input estimates) by age, sex and race/ethnicity to estimate overall population-level health and economic disease burden and disparities. Model inputs and parameter values were derived from a variety of sources, including: (1) estimates of gonorrhoea incidence, and probabilities of symptomatic infection, testing and treatment from the Tuite et al. gonorrhoea transmission model[16]; and (2) probabilities, durations, quality of life impact, and costs of gonorrhoea sequelae from synthesis of published literature. An important feature of the Tuite et al. estimates is that they are stratified by age, sex, race/ethnicity and MSM, which allowed us to calculate disparities across these strata. Analyses were undertaken in R version 3.5.2 (R Foundation for Statistical Computing, Vienna, AUT).

Model structure and probabilities of key clinical outcomes

We developed probability trees to model clinical outcomes following gonococcal infection, adapted from prior decision analysis studies.[17–19] Separate models were specified for women, men who have sex with women (MSW), and MSM (Figures 1 and 2).

For women, gonococcal infections were categorized as symptomatic or asymptomatic with different durations of infection, leading to distinct probabilities of developing PID and subsequent complications (Figure 1).[17] Our analysis included only urogenital infections in women under the presumption this captures the dominant site of the infection. Although treatment for gonorrhoea is not explicitly distinguished as a separate branch in Figure 1, the estimated durations of infection accounted for the fraction of cases treated. The possible complications following PID were CPP, EP, and TI (Figure 1B). Although we included disseminated gonococcal infection (DGI) as a sequela for men (see below), we excluded this sequela for women in the interest of parsimony, given that it occurs with lower probability than the other included sequelae. The probability of symptoms given infection and the durations of either symptomatic or asymptomatic infection were derived from the Tuite et al. gonorrhoea transmission model.[16] Duration of asymptomatic infection differed across age groups due to differences in screening rates.[16] For the probability of developing PID, we synthesized data from previously published studies[20–25] on rates of developing PID secondary to chlamydial infection using a

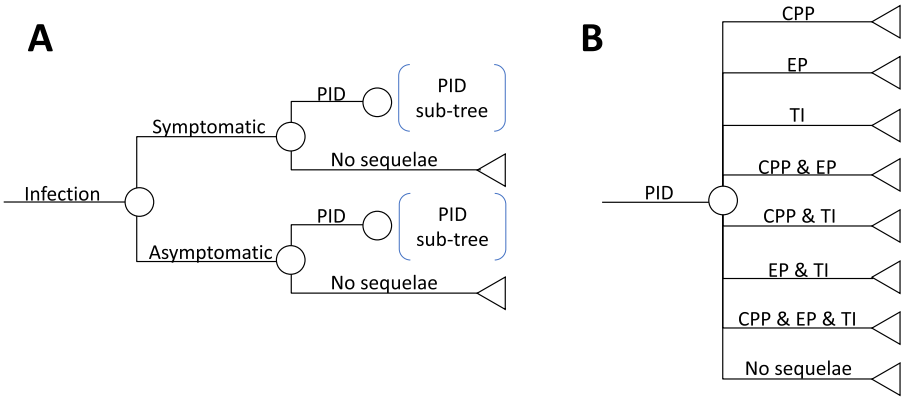

Figure 1. Probability tree for sequelae following gonococcal infection among women (Panel A), with complications of PID shown in Panel B.

*Abbreviations: PID = pelvic inflammatory disease, CPP = chronic pelvic pain, EP = ectopic pregnancy, TI = tubal infertility.

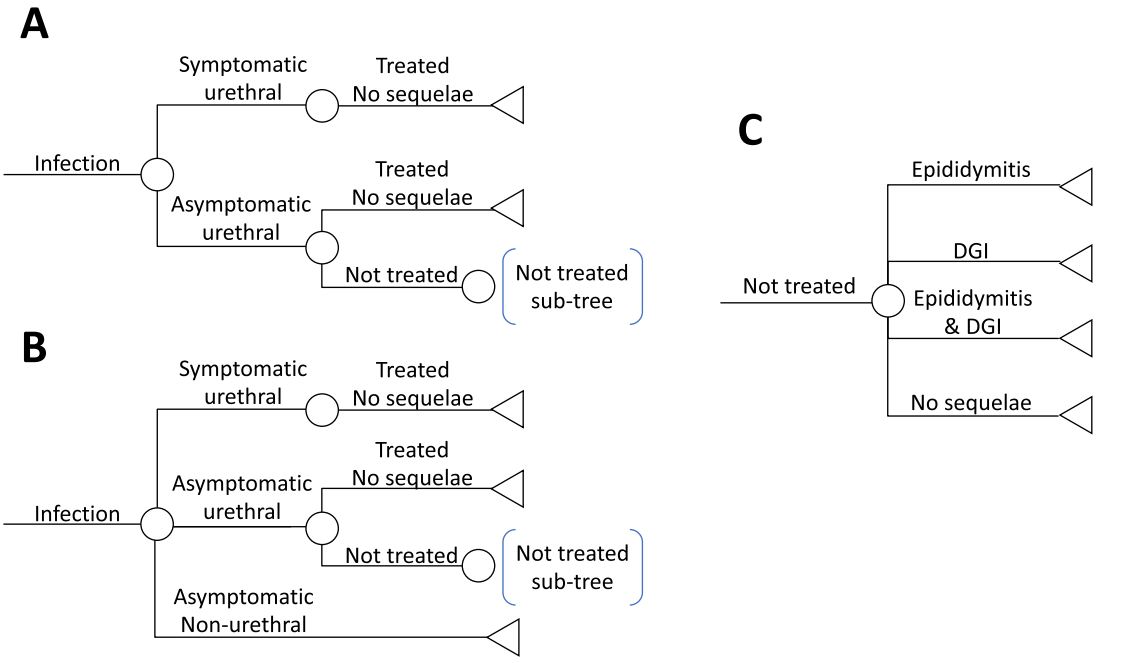

Figure 2. Probability tree for sequelae following gonococcal infection among MSW (Panel A) and MSM (Panel B), with complications of untreated urethral infections shown in Panel C.

*Abbreviations: DGI = disseminated gonococcal infection.

continuous-time Markov model implemented in the JAGS modelling language,[26] and translated the rates into associated probabilities of PID given durations of symptomatic or asymptomatic gonococcal infection. The conditional probabilities of CPP, EP, and TI given PID were derived by pooling estimates from previous longitudinal studies on sequelae among women with chlamydia.[27–33]

For MSW, infections were categorized as symptomatic or asymptomatic urethral gonococcal infections (Figure 2A), followed by possible sequelae of epididymitis and DGI (Figure 2C). We assumed that all symptomatic infections are diagnosed and successfully treated, and that treatment prevents any further complications in men; this simplifying assumption implies that epididymitis and DGI occur only among untreated asymptomatic cases. There is sparse evidence on the relationship between duration of infection and sequelae development for men, and epididymitis and DGI were modelled as probabilities that were independent of duration. The probability of symptoms given gonococcal infection was obtained from the Tuite et al. gonorrhoea transmission model.[16] We estimated the probability of epididymitis among untreated asymptomatic infections based on pooled estimates from longitudinal studies on sequelae among men with chlamydia.[34,35] The probability of DGI was derived from a previous Institute of Medicine (IOM) study.[19]

For MSM, the model depicted urethral infections as described for MSW (Figures 2B and 2C). In addition, rectal and pharyngeal infections, which are typically asymptomatic, were assumed to impose no direct health utility losses, consistent with assumptions made in a study on rectal chlamydia.[36] This was a simplifying assumption that also implied that only urethral infections lead to epididymitis and DGI. The proportion of gonococcal infections that are urethral in MSM was obtained from synthesis of the published literature.[37,38] We assumed that the probability of symptoms given urethral infection among MSM was the same as that of MSW, obtained from the Tuite et al. gonorrhoea transmission model.[16]

Diverging from the approach taken in prior related studies using probability trees, we have explicitly modelled both independent sequelae and combinations of sequelae following PID for women and following urethral infections for MSW and MSM, whereas prior studies have assumed that all complications were independent and additive.[16,18,19] Further details on the values, ranges, distributions, and sources of probabilities for key clinical outcomes can be found in Table 1 and in the Supplement. In addition to the pathways of clinical outcomes shown in Figures 1 and 2, we further stratified some health states by treatment status for the purpose of computing costs and utility losses. For gonococcal infections, we distinguished treated and untreated infections; for sequelae following infection, we assumed that all cases are treated and distinguished inpatient from outpatient treatment for PID, EP, epididymitis and DGI. Probabilities, utilities, durations and

Parameter	Mean estimate	Uncertainty interval[a]	Reference
Outcome probabilities (women)			
Proportion of infections that are symptomatic	0.37	0.27 to 0.47	16
Probability of PID given symptomatic infection	0.0025	0.00092 to 0.0055	16,20–26
Probability of PID given asymptomatic infection (age 15-24y)	0.075	0.031 to 0.13	16,20–26
Probability of PID given asymptomatic infection (age 25-39y)	0.091	0.037 to 0.16	16,20–26
Probability of CPP given PID	0.26	0.23 to 0.29	27,28
Probability of EP given PID	0.071	0.049 to 0.098	28–30,32
Probability of TI given PID	0.17	0.12 to 0.23	28,29,31–33
Outcome probabilities (men)			
Proportion of infections that are urethral (MSW)	1	Fixed	
Probability of symptoms given urethral infection (MSW)	0.72	0.60 to 0.84	16
Proportion of infections that are urethral (MSM)[b]	0.76	0.38 to 0.99	37,38
Probability of symptoms given urethral infection (MSM)	0.72	0.60 to 0.84	16
Probability of diagnosis and treatment for symptomatic urethral infection (MSW and MSM)	1	Fixed	16
Probability of diagnosis and treatment for asymptomatic urethral infection (MSW and MSM)	Table A1-5-(b)		16
Probability of epididymitis given untreated urethral infection	0.042	0.0012 to 0.14	34,35
Probability of DGI given untreated urethral infection	0.010	0.0075 to 0.013	19,52
Durations (years)			
Gonococcal infection (women, symptomatic)[c]	0.017	0.0099 to 0.031	16
Gonococcal infection (women, asymptomatic, ages 15-24y)[c]	0.53	0.39 to 0.66	16
Gonococcal infection (women, asymptomatic, ages 25-39y)[c]	0.65	0.47 to 0.83	16
Gonococcal urethral infection (Men, symptomatic)[f]	0.019	0.010 to 0.028	19
PID[e]	0.028	0.015 to 0.042	19
CPP	[d]	5 to lifetime	19,43,53
EP[e]	0.078	0.040 to 0.12	19
TI	[d]	5 to lifetime	19,43,53
Epididymitis[e]	0.019	0.0099 to 0.028	19
DGI[e]	0.024	0.013 to 0.036	19
State-specific utilities			
Symptomatic gonococcal infection (women)	0.85	0.78 to 0.92	19
Symptomatic gonococcal urethral infection (men)[f]	0.84	0.76 to 0.92	19
PID[e]	0.65	0.48 to 0.82	19
CPP	0.60	0.41 to 0.79	19
EP[e]	0.58	0.39 to 0.79	19
TI	0.82	0.73 to 0.91	19
Epididymitis[e]	0.46	0.20 to 0.72	19
DGI[e]	0.63	0.45 to 0.81	19
Costs (in 2020 US$)			
Diagnosis costs			
Urine nucleic acid amplification and diagnosis procedure	63	33 to 94	18,19,54–56
Treatment of gonorrhoea			
Women	103	54 to 154	18,55–59
Men, symptomatic urethral gonococcal infection[f]	151	80 to 224	18,55–61
Men, asymptomatic urethral gonococcal infection	103	54 to 154	18,55–59

Table 1 *(Continued)*

Parameter	Mean estimate	Uncertainty interval[a]	Reference
Treatment of sequelae			
PID[e]	1,723	901 to 2,575	18,19,39,57–60,62,63
CPP	1,260	657 to 1,871	19,39,57
EP[e]	4,818	2,511 to 7,241	19,39,57
TI	6,567	3,423 to 9,758	19,39,57,58,60,62,63
Epididymitis[e]	487	252 to 731	19,40,57–60,62
DGI[e]	2,495	1,090 to 4,387	19

***Table 1*: Model input parameters describing gonorrhoea and sequelae probabilities, durations, utilities, costs, and probabilities of diagnosis and treatment for gonorrhoea.**

[a] Uncertainty intervals given as 95% uncertainty intervals for probabilities and durations of gonococcal infections based on results from the Tuite et al. gonorrhoea transmission model,[16] for probabilities of sequelae based on beta distributions, and for all other parameters based on uniform distributions (see the Supplement for details).

[b] We pooled the study subjects with gonococcal infections at any anatomic sites (rectal, urethral, and pharyngeal) from the two studies.[37,38] The mean of the proportion of infections that are urethral was estimated as the number of subjects with urethral infections (urethral only, rectal and urethral, pharyngeal and urethral, all three sites) divided by the number of subjects with gonococcal infections at any anatomic sites in the pooled population. We estimated the variance of the proportion under the simplifying assumption that the mean estimates in the two studies spanned the 95% uncertainty intervals about the mean. For the range, we defined a beta distribution with the estimated mean (0.76) and variance (0.17) as described here.

[c] The Tuite et al. transmission model was used to estimate duration of asymptomatic infection, which varies in relation to the fraction of infections that are diagnosed. Differences between different race/ethnicity groups were relatively small, while differences between age groups were larger. For parsimony, we therefore allowed durations to vary by age but not by year and race/ethnicity group. Symptomatic infection was assumed to have a 100% probability of being diagnosed and treated, with a much shorter duration of infection.

[d] Mean duration taken from uniform distribution between 5 years and lifetime duration. While one study applied a lifetime duration of these conditions based on expert opinion,[19] previous analyses have assumed much shorter durations based on unspecified evidence.[53] Details on life table calculations used to compute discounted QALY losses for lifetime duration are provided in the Supplement.

[e] We distinguished inpatient from outpatient treatment for PID, EP, epididymitis and DGI. Estimates of probabilities of inpatient (vs. outpatient) treatment for these four sequelae are reported in Supplement table A1-3-(a). Durations, utilities, and treatment costs for each of these four sequelae are summarized as probability-weighted combinations of the inpatient and outpatient treatment. Details of calculations are described in Table A1-3-(a) and Table A1-3-(b).

[f] Durations and utilities of symptomatic urethral infection for men were driven by urethritis, which was assumed to occur in all male individuals with symptomatic gonorrhoea.[64] For men, costs of treatment for symptomatic infections were assumed to be higher than for men with asymptomatic infections, because men with symptomatic gonococcal infection were more likely to seek treatment in a higher cost setting such as an emergency department.[66] However, we did not vary the input parameters defining costs of treatment for symptomatic versus asymptomatic gonococcal infections for women. Our rational for including a slightly higher cost for symptomatic infections (vs. asymptomatic) infections in men but not for women is that evidence suggests that emergency department visits by women with gonorrhoea are relatively more likely to be attributable to chlamydia and gonococcal co-infection rather than attributable solely to gonorrhoea.[65] Details are reported and discussed in Supplement Section 7 and Table A1-6.

PID = pelvic inflammatory disease; CPP = chronic pelvic pain; EP = ectopic pregnancy; TI = tubal infertility; DGI = disseminated gonococcal infection; MSM = men who have sex with men; MSW= men who have sex with women.

costs of inpatient and outpatient treatment for the four sequelae are reported in Supplement Table A1-3-(a) and Table A1-3-(b). Probabilities of testing and treatment for gonococcal infections for women, MSW and MSM in 2015 were obtained from the Tuite et al. gonorrhoea transmission model,[16] and were stratified by age and race/ethnicity (Table A1-5-(a) and Table A1-5-(b) in the Supplement). Of patients treated for PID, EP, epididymitis and DGI, we assumed 0.10, 0.15, 0.0054 and 0.29 were treated on an inpatient basis, respectively (Table A1-3-(a)).[19,39–41]

Lifetime QALYs lost and costs per incident infection

Utilities and durations for clinical outcomes related to gonorrhoea and sequelae were derived from the prior IOM study, which used an expert panel to estimate durations of sequelae and health-state weights measured via the Health Utilities Index (HUI).[19] The utility weights for gonorrhoea and sequelae were multiplied by background utilities reflecting chronic comorbidities by age, based on nationally representative EQ-5D index scores.[42] CPP and TI were treated as chronic sequelae, and durations were estimated using a life table approach. Age-specific mortality rates for women were derived from National Centre for Health Statistics (NCHS) data.[43] Costs were estimated from the healthcare perspective and included all direct medical costs regardless of payer. All costs were inflated to 2020 U.S. dollars using the medical care component of the consumer price index.[44] Costs and QALYs incurred in years after the incidence of infection were discounted to the year of infection, using a discount rate of 3% per year.[45] Further details can be found in Table 1 and the Supplement.

Based on the probability-tree models in Figures 1 and 2, discounted lifetime QALYs lost per incident infection were estimated by summing the expected losses for each unique sequela or sequelae combination (the product of the probability, duration, and disutility). Lifetime costs per incident infection were estimated analogously for diagnosis and treatment of symptomatic cases and asymptomatic cases. For symptomatic infection, we assumed the costs of diagnosis and treatment applied to

all symptomatic cases. For asymptomatic infection, costs only applied to the proportion of cases diagnosed and treated as listed in Table 1 and Supplement Table A1-5. Details on the discounted costs of diagnosis and treatment for gonorrhoea and sequelae can be found in Table 1.

Disease burden and disparities at population level

Estimates for the incidence of gonococcal infection were obtained from the Tuite et al. gonorrhoea transmission model.[16] The study used a model that was calibrated using a Bayesian approach to synthesize information from several large national datasets over the period 2000-2015, including reported gonorrhoea diagnoses, prevalence estimates from the National Health and Nutrition Examination Survey, and other sources.[16] This national-level gonorrhoea meta-population model described a population aged 15-24 and 25-39 years, with the heterosexual population of men and women stratified into the following three race/ethnicity groups: Non-Hispanic Black, Hispanic, and Non-Hispanic White and Other. The population of MSM was stratified by age, but not by race/ethnicity due to limited data available at the national level.

In our model, the population was stratified by age and sex, and men were further stratified into MSW and MSM. Among the heterosexual population (women and MSW), the population in the present study was additionally divided into five categories indicating both ethnicity (Hispanic or non-Hispanic) and race, following the classification of the NCHS bridged-race categories: Hispanic, Non-Hispanic Black (hereafter, "Black"), Non-Hispanic White (hereafter, "White"), (Non-Hispanic) American Indian or Alaska Native (AI/AN), and (Non-Hispanic) Asian, Native Hawaiian or Other Pacific Islander (A/NH/OPI).[46,47] To compute incidence of gonococcal infection among heterosexual AI/AN, A/NH/OPI and White persons as sub-populations of incidence estimated among Non-Hispanic White and Other, we assumed that incidence rates for these three racial/ethnic groups followed the same relative reported gonorrhoea case rates in these groups, which were obtained from CDC's NCHHSTP AtlasPlus data.[48]

To estimate the population size in the United States by sex, age, and race/ethnicity, we used Bridged-Race Population Estimates from CDC WONDER.[49]

Outcome measures

The health and economic burden of disease associated with gonorrhoea was measured as the numbers of discounted lifetime QALYs lost and costs in 2015 and beyond due to gonococcal infections that were acquired in 2015, by age and race/ethnicity for women and MSW, and by age for MSM. These aggregate costs and QALYs were computed as the product of population size, incidence rates per population, and QALYs lost and costs per incident infection. Our population size and incidence rate assumptions corresponded to an estimated 575,809 (465,189 to 717,787), 316,890 (236,676 to 420,051), 727,386 (442,858 to 1,078,093) incident infections for women, MSW and MSM, respectively. Estimates of QALYs lost and costs are summarized in terms of aggregate population-level counts, as well as per 1,000 person-years.

Multivariate sensitivity analysis

We performed multivariate sensitivity analyses including uncertainty in (i) incidence of gonorrhoea in each sub-population, (ii) proportion of infected persons within each sub-population receiving diagnosis and treatment; (iii) sequelae probabilities, and (iv) utilities, durations, and costs. 1,000 samples were used in the sensitivity analyses. The five groups of input parameters were drawn from the posterior distributions estimated by the Tuite et al. gonorrhoea transmission model[16] (for input categories i and ii above) or from specified distributions describing uncertainty in sequelae probabilities (for input categories iii and iv above) (Table 1). We report all outcomes using the mean and 95% uncertainty intervals (95% UI).

The reporting in this study follows Consolidated Health Economic Evaluation Reporting Standards (CHEERS),[50] and Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER)[51] as applicable.

Role of the funding source

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Results

Lifetime QALYs lost and costs per gonococcal infection

The average number of discounted lifetime QALYs lost per incident gonococcal infection in 2015 was estimated as 0.093 (95% UI 0.022-0.22) for women, 0.0020 (0.0015-0.0024) for MSW, and 0.0015 (0.00070-0.0021) for MSM in (Table 2). The QALYs lost per incident infection were highest for women aged 25-39 years and were higher for women than for MSW and MSM. QALYs lost from gonococcal infection in women were predominantly from long-term chronic sequelae such as CPP and TI. QALYs lost in men were from short-

Sex and age-group	Mean	95% uncertainty interval
QALYs lost per infection		
Women		
Ages 15-24 years	0.089	(0.021 to 0.21)
Ages 25-39 years	0.11	(0.026 to 0.25)
Ages 15-39 years	0.093	(0.022 to 0.22)
MSW		
Ages 15-24 years	0.0020	(0.0015 to 0.0024)
Ages 25-39 years	0.0019	(0.0015 to 0.0024)
Ages 15-39 years	0.0020	(0.0015 to 0.0024)
MSM		
Ages 15-24 years	0.0015	(0.00070 to 0.0021)
Ages 25-39 years	0.0015	(0.00069 to 0.0021)
Ages 15-39 years	0.0015	(0.00070 to 0.0021)
Costs (2020 US dollars)		
Women		
Ages 15-24 years	255	(107 to 466)
Ages 25-39 years	287	(118 to 534)
Ages 15-39 years	261	(109 to 480)
MSW		
Ages 15-24 years	169	(88 to 263)
Ages 25-39 years	169	(88 to 263)
Ages 15-39 years	169	(88 to 263)
MSM		
Ages 15-24 years	134	(50 to 239)
Ages 25-39 years	133	(50 to 238)
Ages 15-39 years	133	(50 to 239)

***Table 2*: Estimated number of discounted lifetime QALYs lost and costs (in 2020 US dollars) associated with gonorrhoea, per incident gonococcal infection in 2015, by sex and age-group.**

term complications with durations of several days to weeks. QALYs lost per incident gonococcal infection were higher in MSW than in MSM, owing to our assumptions that all infections in MSW were urethral, and excluding QALYs lost from anal and oropharyngeal infections in MSM based on evidence that suggested most of these were asymptomatic.[36]

Estimated discounted lifetime costs per incident infection in 2015 were $261 (109-480) for women, $169 (88-263) for MSW, and $133 (50-239) for MSM (Table 2). The costs per incident infection in the 15-24 year population were lower than for the 25-39 year population, for women, which can be attributed to higher screening rates among younger women which reduces the probability of PID and sequelae given asymptomatic infection for the younger age group.

Population-level QALYs lost and costs due to gonococcal infections

The population-level discounted lifetime QALYs lost associated with gonococcal infections in 2015 were 53,293 (95% UI 12,326-125,366) for women, 621 (430-872) for MSW, and 1,078 (427-1,870) for MSM (Table A1-7). The total population-level discounted lifetime costs associated with gonococcal infections in 2015 were $150 million (64-277 million) for women, $54 million (25-92 million) for MSW, and $97 million (34-197 million) for MSM (Table A1-8). The total QALYs lost were highest for women aged 15-24 years and were higher for women than for MSW and MSM, which can be attributed to a higher number of QALYs lost per gonococcal infection for women than for men (Table 2, Figures 3–5). The total costs were higher for women than for MSW and MSM, primarily due to higher costs per gonococcal infection for women than men (Table 2). Although the QALYs lost and costs per gonococcal infection were lower for MSM than for MSW (Table 2), the total QALYs lost and total costs were higher for MSM than for MSW (Figures 4 and 5), primarily due to a much higher incidence of gonorrhoea in MSM (annual incidence rate of 316 per 1,000 MSM, 95% UI 190-475) than MSW (5.51 per 1,000 MSW, 95% UI 4.14-7.29) in 2015.[16]

Disparities in the total lifetime QALYs lost and costs reflect variation in the incidence of gonococcal infection across different populations, as well as different population sizes across groups. The total QALYs lost in 2015 were highest among Black persons and White persons, followed by Hispanic persons, AI/AN persons, and A/NH/OPI persons, for both women and heterosexual men. For example, among women aged 15-24 years the total QALYs lost in 2015 were 18,694 (4,437-44,119) for Black persons, 15,583 (3,447-37,711) for White persons, 4,074 (962-9,504) for Hispanic persons, 1,090 (241-2,638) for AI/AN persons, and 632 (140-1,529) for A/NH/OPI persons (Figure 3, Table A1-7). The total costs in 2015 were highest among Black and White for women. For men, the highest total costs were among MSM, Black, and White (Figures 4 and 5 and Table A1-8).

Disparities in lifetime QALYs lost and costs per 1,000 person-years reflect variation in incidence across different populations. For women, QALYs lost per 1,000 person-years were highest among AI/AN persons and Black persons, followed by White persons, Hispanic persons and A/NH/OPI persons. For men, the highest QALYs lost per 1,000 person-years were among MSM and Black persons (Figures 4 and 5 and Table A1-7). Costs per 1,000 person-years in 2015 were higher among MSM, at $45,282 (15,781-91,865) than MSW, at $1,014 (483-1,742) (Table A1-8).

Decomposition of lifetime QALYs lost and costs

QALYs lost were higher in women than in MSW for all race/ethnicity groups. The duration of chronic sequelae in women was estimated to be longer than the duration of sequelae in men. Among women, the composition of total QALYs lost was estimated to be 76% (95% UI 70%-82%) due to CPP and 22% (16%-28%) from TI

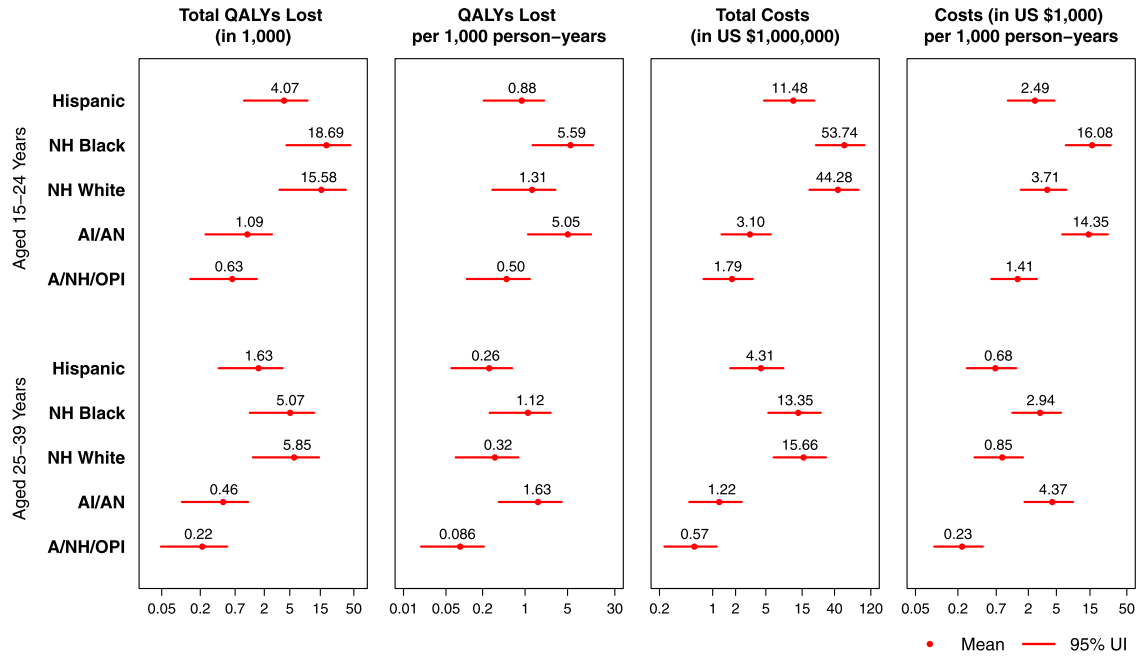

Figure 3. Population-level numbers of QALYs lost, QALYs lost per 1,000 person-years, total costs (US$), total costs per 1,000 person-years, for women, by age and race/ethnicity, in 2015.

NH White (Non-Hispanic White), A/NH/OPI (Asian or Native Hawaiian or Other Pacific Islander), AI/AN (American Indian or Alaska Native), NH Black (Non-Hispanic Black). Note that x-axis differs between the plots.

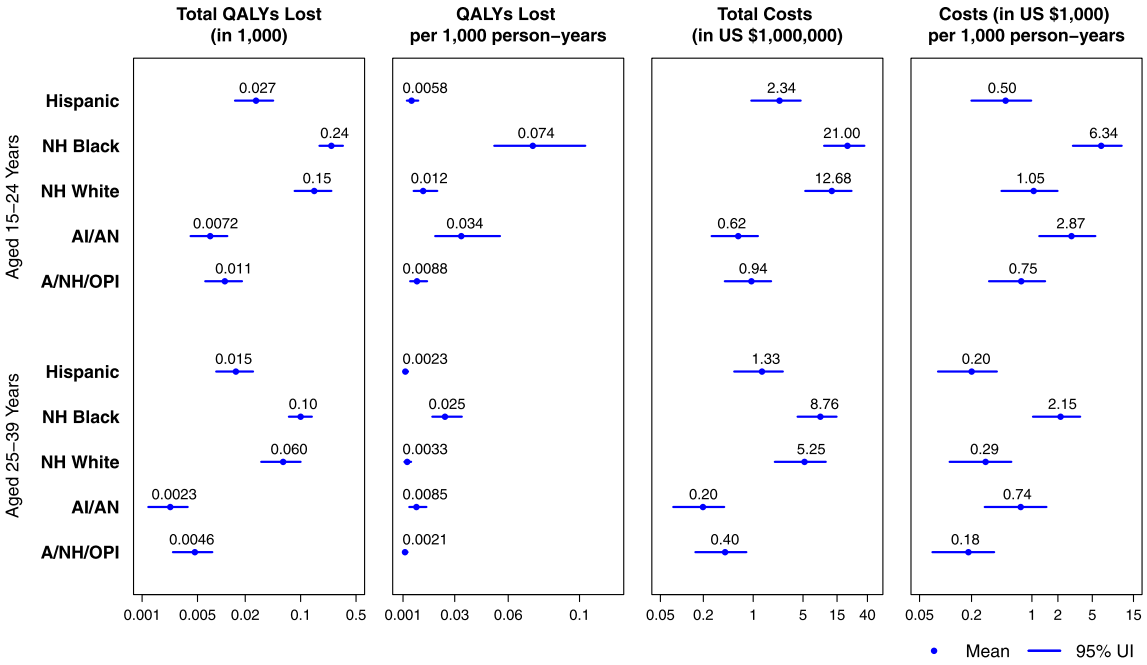

Figure 4. Population-level numbers of QALYs lost, QALYs lost per 1,000 person-years, total costs (US$), total costs per 1,000 person-years, for heterosexual men, by age and race/ethnicity, in 2015.

NH White (Non-Hispanic White), A/NH/OPI (Asian or Native Hawaiian or Other Pacific Islander), AI/AN (American Indian or Alaska Native), NH Black (Non-Hispanic Black). Note that x-axis differs between the plots.

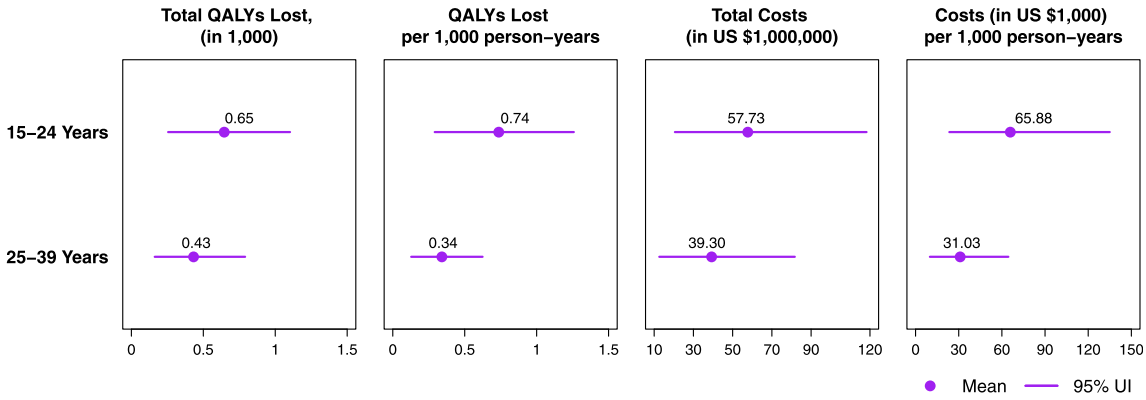

Figure 5. Population-level numbers of QALYs lost, QALYs lost per 1,000 person-years, total costs (US$), total costs per 1,000 person-years, for men who have sex with men (MSM), by age, in 2015.

Note that x-axis differs between the plots.

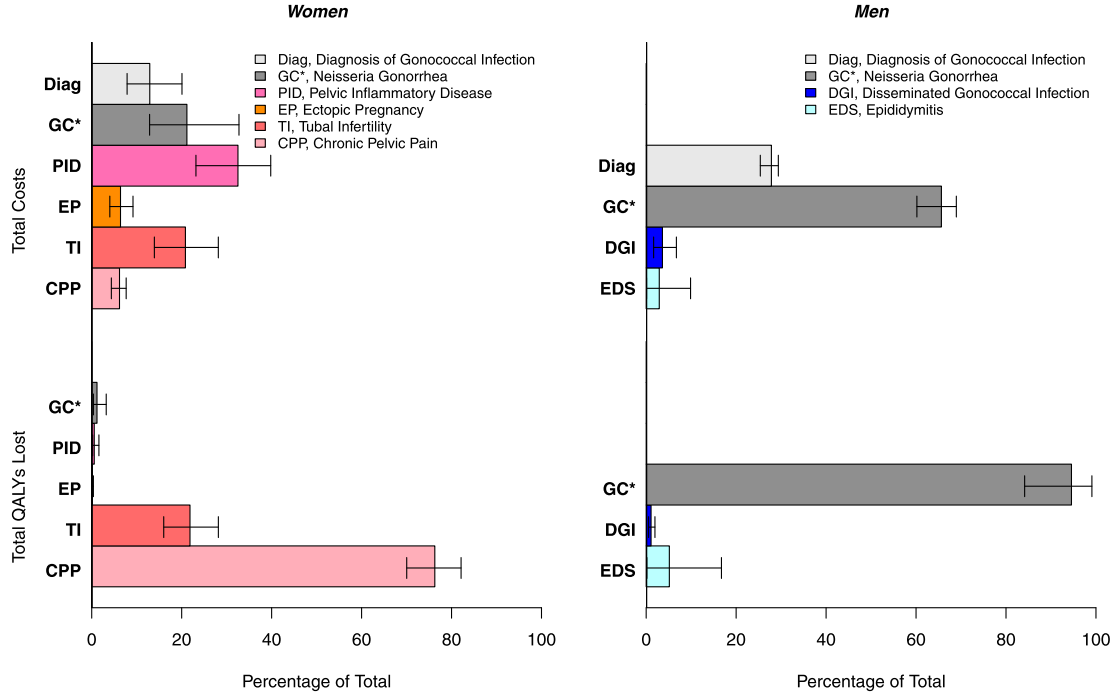

Figure 6. Decomposition of total lifetime QALYs lost and costs by main complications and broad cost categories.

Note in the total costs panel, GC represents the costs of treatment for gonococcal infections, not including the costs of treatment for gonorrhoea sequelae. In the total QALYs panel, GC represents the QALYs lost for gonococcal infections, not including the QALYs lost from gonorrhoea sequelae.

(Figure 6), with negligible contributions from other outcomes. Although chronic complications of CPP and TI were the main source of total QALYs lost in women with gonococcal infection due to their long and lifetime durations, the direct costs from these two complications were smaller. TI was estimated to contribute 21% (14%-28%) of the total direct medical costs among women, with a further contribution of 6% (4%-8%) from CPP. The major contributor to the total costs were treatment of PID (32%, 23%-40%) and treatment of gonorrhoea (21%, 13%-33%). Among men, the major contributor to the total QALYs lost was symptomatic urethral infections (95%, 84%-99%). The cost of diagnosis for gonorrhoea was the smallest component, contributing 13% (8%-20%) of the total costs for women, and 28% (25%-29%) for men. The main costs for women were from treatment for gonorrhoea sequelae, which contributed 66% (47%-79%) of the total costs, while the main costs

for men were from treatment for gonococcal infections, which contributed and 66% (60%-69%) for men.

Discussion

In this study we quantified the burden of gonococcal infection in the United States using discounted lifetime QALYs lost and costs, and examined disparities in the population. Women were estimated to have higher QALYs lost and costs per incident gonococcal infection than men, and Black women had the largest burden of disease of all subpopulations examined. QALYs lost and costs per 1,000 person-years were the highest in MSM among men and Black among women, reflecting the significant burden of gonococcal infection in these populations. QALYs lost per 1,000 person-years for Black women were over 4 times those of White women, and for AI/AN women over 3 times as high as for White women. QALYs lost per 1,000 person-years for MSM (all racial/ethnic groups combined) were over 80 times those of White MSW.

Gonococcal infection has relatively short duration, but its longer-term consequences are captured in our estimates of QALYs lost. These estimates point to unmet sexual and reproductive health needs and wider inequities within the population, which place people at differential risk of infection and sequelae. Black persons and MSM also have been noted as key populations for gonorrhoea prevention by analyses of surveillance data.[3,8] The high relative burden of gonorrhoea among AI/AN persons has received less attention. Reports of a multi-state syphilis outbreak,[66] and high burden of chlamydia among young AI/AN persons,[67] signal that there are systemic disparities that need to be addressed. Racial/ethnic disparities in reported rates of sexually transmitted diseases cannot be explained by differences in individual-level sexual behaviour, but instead reflect differences in sexual networks and other social determinants of health.[68] Discrimination, socio-economic status, segregation, institutional racism, and access to and utilization of health care are among the factors contributing to racial/ethnic disparities.[68–70]

Availability of estimates based on a range of models rather than a single model can better characterize the range of uncertainties in the literature. We estimated the discounted lifetime cost per incident infection to be $261 (95% UI 109-480) for women infected in 2015, which is similar to a previous estimate of $254 (96-518) per incident infection in women.[15] Our estimated discounted lifetime costs per incident infection of $169 (88-263) for MSW and $133 (50-239) for MSM are higher than the corresponding estimates for all men ($78 [36-145]) in Kumar et al.[15] The difference is attributable to our using a lower probability of asymptomatic infection[16] and a higher probability of epididymitis[34,35] than those used in previous studies; and including disseminated gonococcal infection as a sequela and incorporating costs of treatment for side effects due to antibiotics, which were not considered in the Kumar study.[15]

Our study has a number of limitations. First, as with previous studies,[56,59,71] we have assumed that chlamydia and gonorrhoea are associated with similar probabilities of developing sequelae. However, gonococcal infection may result in more severe PID than chlamydia.[10] In that case, the assumption that sequelae probabilities are transferrable from studies of outcomes secondary to chlamydial infections may underestimate the costs and QALYs lost due to gonorrhoea. Second, costs in our study reflect average costs. There are undoubtedly variations in costs across geographical and other settings, and some costs may have changed over time. Further, we included only direct medical costs, and our estimates of the burden of gonorrhoea would be even greater had we included other costs, such as productivity costs associated with missing work to seek treatment.[56] Third, as an economic analysis of national disease burden, it would be more consistent with standard methodological recommendations to use community-based rather than expert-based utility measures;[72] however, we were not able to identify any existing studies that report community-based utilities for the range of outcomes associated with gonococcal infection among men. Finally, we did not include the potential increase for HIV acquisition or transmission in people with gonococcal infection. For example, an estimated 10.2% of HIV infections are attributable to gonorrhoea and chlamydia among MSM.[73] Including these HIV infections would result in larger total burden associated with gonococcal infection than our current model estimates.

Our analysis has important implications for addressing health disparities in STDs and other health outcomes. First, we have shown that metrics of burden of disease such as costs and QALYs lost can be used to assess health disparities. Second, using these metrics in conjunction with estimates of disease incidence and prevalence can provide a more detailed picture of the scope of these disparities than using disease incidence or prevalence alone. For example, we found that PID and sequelae contributed substantially to the cost and QALY burden of gonorrhoea. Therefore, strategies to reduce the risk of PID in non-Hispanic Black women with gonorrhoea could have a notable effect on reducing racial/ethnic disparities in the QALY burden of gonorrhoea, even if such efforts did not have a substantial effect on racial/ethnic disparities in the incidence of gonorrhoea. Third, our estimates of QALYs lost and costs per incident infection can serve as inputs for future studies of cost-effectiveness analysis of gonorrhoea interventions.

The findings in our study have important implications for resource prioritization and planning, and for informing control policies. They underscore the longer-term burden of a short-term infection, and the

continued disparities by race/ethnicity and for MSM within the United States. The QALYs lost and costs associated with gonococcal infection are likely to increase in the future with rising antibiotic resistance. Given the potential bridging from MSM to heterosexual women, reducing gonorrhoea in MSM might also reduce gonorrhoea in heterosexual populations.[74] Decreasing disparities by interventions focused on disproportionately affected populations would improve the overall health of the population. Measuring both short- and long-term consequences and costs of gonococcal infection provides a comprehensive framework for measuring and evaluating gonorrhoea associated health outcomes.

Contributors

YL, MMR and JAS conceptualized the study. YL, MMR, HWC, TLG, KH, NAM, and JAS contributed to study design. YL, MMR, ART, TAT, CT, MB curated data. YL, MMR, HWC, TLG, KH, NAM, and JAS contributed methodology, formal analysis, and validation. YL drafted the first version of the Article. YL, MMR, ART, HWC, TLG, TAT, CT, MB, KH, AAB, YM, NAM, and JAS reviewed and edited the manuscript. All authors read and met the ICMJE criteria for authorship and agree with the results and conclusions. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. YL and MMR verified the data.

Data sharing statement

All data used in this study are openly accessible and available through the sources listed in Table 1.

Declaration of interests

The authors declare no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2022.100364.

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