

Epidemiology of gonorrhoea: a global perspective

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Abstract. Although understanding the local epidemiology of gonorrhoea is critical for local efforts, understanding the multinational epidemiology may support development of national and international prevention and control policies and strategies. In this paper, current epidemiology of gonorrhoea is reviewed through an international lens and with a focus on selected populations. The World Health Organization (WHO) estimates that ~87 million new gonococcal infections occurred among people aged 15–49 years in 2016. Gonorrhoea rates are rising in many countries. Gay, bisexual and other men who have sex with men, racial or ethnic minorities, Indigenous populations and sex workers appear to bear disproportionate burdens of gonorrhoea. International travel can facilitate spread of gonorrhoea, including resistant strains, across international borders. Critical gaps in epidemiological knowledge are highlighted, including data on gonorrhoea among transgender persons and the burden of extragenital gonorrhoea. Even as further data are gathered, action — informed by currently available data — is needed now to confront this growing international threat.

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Introduction

Gonorrhoea is a sexually transmissible infection (STI) caused by the bacterium *Neisseria gonorrhoeae*. Following transmission, *N. gonorrhoeae* infects mucosa of exposed anatomic sites, such as the urogenital tract, rectum, pharynx and conjunctivae. *N. gonorrhoeae* is fairly easily transmitted; the estimated probability of penile-to-vaginal transmission is ~50% per sex act, and vaginal-to-penile transmission is ~20% per act.^{1–3} Probabilities of per-condomless act transmission during oral (63% urethral-to-pharyngeal and 9% pharyngeal-to-urethral) and anal sex (84% urethral-to-rectal and 2% rectal-to-urethral) have been estimated from mathematical models.⁴

Urethral infections in cisgender men and other people with penises provide a useful marker of incident infection because symptoms generally develop within a week of exposure and — in areas where health care is available — the symptoms of gonococcal urethritis (e.g. profuse purulent discharge and painful urination) prompt people to seek care, diagnosis and treatment in a timely manner. In contrast, rectal, pharyngeal and cervical infections are often asymptomatic and most often detected through screening. As a result, case rates of infections at these anatomic sites are likely to be heavily influenced by screening practices. In populations in which oral or anal sex is common, asymptomatic infections at these anatomic

sites might be more likely to be prevalent at a given point in time than urethral infections (which may be promptly treated if symptomatic). In the absence of screening for asymptomatic infections, undetected gonococcal infections may be considerable.

If not treated in a timely manner, cervical gonorrhoea can lead to severe reproductive health complications, such as pelvic inflammatory disease (PID), chronic pelvic pain, ectopic pregnancies and tubal factor infertility. Gonococcal infections during pregnancy have been associated with chorioamnionitis, premature rupture of membranes (PROM), preterm birth, low birthweight and spontaneous abortions.^{5–8} Infants born to mothers with untreated cervical gonorrhoea can develop hyperacute conjunctivitis (neonatal ophthalmia), which can rapidly lead to corneal perforation and blindness if not rapidly treated. Infrequently, gonorrhoea can progress to bacteremia and systemic involvement (disseminated gonococcal infection), leading to septic arthritis, endocarditis and, rarely, meningitis. Gonorrhoea is also associated with heightened risk of HIV acquisition and transmission.^{9–11}

Particularly in countries where diagnostic testing and screening for gonorrhoea are readily available, prompt detection and effective treatment prevent sequelae and further transmission. However, provision of effective

treatment is under threat, as *N. gonorrhoeae* has successively acquired antimicrobial resistance to each antimicrobial agent used and recommended for treatment.¹² The confluence of emerging resistance to cephalosporins and macrolides and a dwindling antimicrobial development pipeline threatens to undermine gonorrhoea control and worsen ongoing management challenges.

To address the threat of gonorrhoea globally, prevention and control programs need to be strengthened and novel prevention approaches are needed. A robust and current understanding of the epidemiology of gonorrhoea can inform these efforts. Although understanding the local epidemiology of gonorrhoea is critical for local efforts, understanding the multinational epidemiology may inform national and international prevention and control policies and approaches. In this paper, we review the current epidemiology of gonorrhoea through an international lens and with a focus on selected populations.

We searched for research articles published between 2009 and 2019 in PubMed® without language restrictions, using PubMed Medical subject heading (MeSH) terms in the following literature search strategy: ('*Neisseria gonorrhoeae*' OR gonorrhoea OR gonococcal OR gonococci OR gonococcus OR STI or 'sexually transmitted infection' OR STD OR 'sexually transmitted diseases') AND (Epidemiolog* OR epidemic* OR outbreak OR sexual network* OR risk* OR behaviour* OR trend* OR prevalence OR incidence OR phylogeny*) AND ('Men who have sex with men' OR MSM OR gay OR bisexual OR transgender* OR black OR African* OR Caribbean* OR indigenous OR aborigin* OR 'first nation' OR 'native American' OR 'American Indian' OR race OR ethnic* OR 'sex work' OR 'sex workers' OR 'sex worker' OR travel* OR 'sex abroad' OR disparities OR 'health inequity' OR 'health inequity' OR 'health inequality' OR 'Health Status Disparities'). We reviewed the generated list of 6496 articles for relevance and hand searched bibliographies.

International overview

The World Health Organization (WHO) estimated the pooled 2016 global prevalence of urogenital gonorrhoea (the proportion of the world's population with gonorrhoea in a given year) to be 0.9% in women and 0.7% in men, corresponding to a total of 30.6 million gonorrhoea cases worldwide.¹³ By region, prevalence among women was highest in the WHO African region (1.9%), the region of the Americas (0.9%) and the Western Pacific region (0.9%), and were lowest in the European region (0.3%). Similarly, among men, prevalence was highest in the African region (1.6%), the Americas (0.8%) and Western Pacific (0.7), and lowest in Europe (0.3%). Likely owing to differences in healthcare infrastructure and availability of screening and treatment, countries categorised as low-income by World Bank criteria had higher prevalences than those categorised as high-income.¹³ Prevalence estimates from specific countries further highlight heterogeneity across geographic areas. From 1999–2008, the overall prevalence of urogenital gonorrhoea in the USA was 0.3%; during 2010–12, the gonorrhoea prevalence was <0.1% in Great Britain.^{14,15} Among young adults in Peru,

the prevalence was similarly low (0.1%) in 2002.¹⁶ In contrast, the pooled prevalence across studies of people aged 15–24 years in South Africa was 4.6%, and across studies of higher-risk people aged 15–24 years in the region of East Africa, the prevalence was 8.2%.¹⁷

Incidence rate, a measure of new infections or diagnoses in a specific time period, was 20 per 1000 women and 26 per 1000 men globally in 2016, translating into 86.9 million new cases. Incidence was highest in the WHO African Region, the Americas and Western Pacific, and lowest in the European region.¹³

National case report data complement WHO estimates and allow interpretation of trends. Reliable case report data are generally available only from high-income countries, as systematic, representative and timely collection and submission of case reports to national public health agencies require well-functioning clinical, laboratory and public health infrastructures. Importantly, gonorrhoea case rates are influenced not only by incidence of infection, but also by factors such as screening and testing practices and completeness of case reporting. In many countries, gonorrhoea case rates have increased recently. In the USA, case rates increased 75.2% from 2009 (98.1 per 100 000) to 2017 (171.9 per 100 000).¹⁸ Similarly, case rates increased in Australia (65.5 per 100 000 in 2013 to 118.0 per 100 000 in 2017) and Canada (33.5 per 100 000 in 2010 to 55.4 per 100 000 in 2015).^{19,20} Although case rates did not increase in all countries in the European Union (EU)/European Economic Area (EEA), the overall gonorrhoea notification rate in the EU/EEA increased during 2012–16 with a few fluctuations.²¹ The largest relative increases in rates within the EU/EEA during 2015–16 were observed in Iceland (108.7% increase: 13.7 – 28.6), Ireland (49.1% increase: 27.7 – 41.3), Finland (49.0% increase: 5.1 – 7.6) and Spain (36.1% increase: 10.8 – 14.7).²¹ The rate of gonorrhoea diagnoses in England rose steadily from 2008 (28.9 per 100 000) to 2018 (101.1 per 100 000), with a momentary decline in 2016.²² In the USA, England, Australia, Canada and nearly all EU/EEA countries, rates were often highest among adolescents and young adults, and were higher (and increasing more rapidly) among men than women.^{18–22}

Selected populations

Some populations have historically been disproportionately affected by gonorrhoea, marginalised and at greater risk for poor sexual health outcomes, or might play important roles in transmission. In this section, we summarise epidemiological data published during the past decade on gonorrhoea in several of these populations, the epidemiological importance of these populations and the factors likely contributing to disease acquisition or transmission within each population.

Gay, bisexual and other men who have sex with men

In many countries, data about gonorrhoea among gay, bisexual and other men who have sex with men (hereafter referred to as MSM) are limited by poor surveillance and lack of elicitation of gender of sex partners by healthcare providers or researchers (often owing to stigma and discrimination).^{21,23} Recent national

case-report data from high-income countries suggest that a disproportionately high percentage of gonococcal infections occur among MSM.^{18,21,24} In 15 EU/EEA countries that reported mode of transmission for at least 60% of all cases to the European Centre for Disease Prevention and Control (ECDC) in 2016, 46% of cases were among MSM.²¹ In England (where data on gender and gender of sex partners were available for nearly all cases), 51.6% of cases in 2014 were among MSM.²⁴ Because of widespread use of electronic laboratory reporting in the USA, gender of the sex partner(s) is not routinely collected in case reports in this country. Yet, the gonorrhoea male-to-female rate ratio increased from slightly less than 1.0 in 2012 to 1.4 in 2017, hinting that sex between men contributed to increasing rates.¹⁸ More compelling are supplemental data from the US-based sentinel surveillance system, the STD Surveillance Network; overall, 26.5% of gonococcal infections in participating jurisdictions were in MSM in 2017, with a range by jurisdiction of 20% in Florida to over 80% in San Francisco, California.¹⁸

Gonorrhoea prevalence or test positivity estimates from cross-sectional studies of MSM are more widely available, including from middle- and low-income countries. Prevalence or test positivity estimates were elevated across studies of MSM, but estimates varied substantially by the sampled population. As expected, test positivity was highest among MSM attending STI clinics: 35% among 229 STI clinic attendees in Guatemala and 22% among 463 men in Guangzhou, China (including 7.2% rectal positivity and 3.9% pharyngeal positivity).^{25,26} In over 10 000 MSM tested in 42 STI clinics in the USA during 2010–12, 11.1% tested positive for urethral gonorrhoea, 10.2% tested positive for rectal gonorrhoea and 7.9% tested positive for pharyngeal gonorrhoea.²⁷ Much lower test positivity was found among MSM who were enrolled in cohort studies or sampled through respondent-driven sampling in Brazil, Thailand, coastal Kenya and Uganda; 1.4–1.8% had urethral gonorrhoea, 1.8–9% had rectal gonorrhoea and 0.5% pharyngeal gonorrhoea at baseline.^{28–31} In one of the most robust estimates of community prevalence to date, a recently conducted multisite assessment of 2077 MSM attending community venues, such as bars and clubs, in the USA, demonstrated a 4.5% prevalence of rectal gonorrhoea and 4.6% prevalence of pharyngeal gonorrhoea.³²

Not only is gonorrhoea prevalent among MSM, but the incidence of gonococcal infections may be increasing among MSM, at least in high-income countries. In a retrospective cohort of MSM attending sexual health clinics in Australia, gonorrhoea incidence among MSM was calculated as having increased from 14.1 per 100 person-years (PY) in 2010 to 24.6 per 100 PY in 2017, with the greatest increases in incidence at oropharyngeal and rectal sites.³³ Similar trends have been observed in England, Ireland, Spain, the USA and Canada.^{22,34–38}

While some observed increases in gonorrhoea diagnoses among MSM may be due, in part, to expanded extragenital screening, routine screening as a component of HIV pre-exposure prophylaxis (PrEP), and high throughput screening clinics for MSM in many countries, changes in testing alone are unlikely to account for the entirety of the observed

increases.^{18,24,37} Gonorrhoea incidence among MSM appears to be increasing. These gonorrhoea increases parallel those of other STIs among MSM, including infectious syphilis, lymphogranuloma venereum and even sexually transmitted enteric infections.^{18,39,40} Gonorrhoea among MSM is likely associated with increased numbers of sexual partnerships, concurrency, heightened density of same-sex sexual networks and high underlying prevalence of gonorrhoea within sexual networks.^{41,42} In addition, condom use among MSM, including during anal sex, has declined.^{43–45} Increasing use of geospatial applications to find sex partners, use of HIV seroadaptive behaviours, the introduction of HIV PrEP and proliferation of circuit parties and group sex events, particularly those involving chemsex, might contribute to changes in behaviour and development of large and dense sexual networks that may facilitate gonorrhoea transmission.^{46–57}

Emerging gonococcal antimicrobial resistance — particularly resistance to the only remaining currently recommended antimicrobials — among MSM is of grave concern. While the pattern is not universal, gonococcal isolates from MSM often demonstrate greater prevalence of antimicrobial resistance than isolates from heterosexuals.^{58–61} Although new resistant strains are often initially detected in heterosexuals, such strains can disseminate rapidly in sexual networks of MSM.^{62–64} The spread of resistant strains among MSM may be facilitated by the partnership and network phenomena outlined above. Furthermore, infection of the oropharynx (which is often asymptomatic, undiagnosed and prevalent among MSM) might also contribute to emergence of antimicrobial resistance among MSM. Pharyngeal gonorrhoea can be difficult to treat with recommended therapy (perhaps enhancing selection for resistant strains) and may have enabled, through horizontal gene transfer from commensal microorganisms, acquisition of mosaic *penA* genes responsible for most resistance to extended-spectrum cephalosporins.⁶⁵

Transgender persons

Transgender is an umbrella term used to describe a group of individuals whose gender identity or presentation differs from the sex that they were assigned at birth.⁶⁶ This umbrella classification, though important for advancing epidemiological research and clinical care, belies substantial heterogeneity of identity, behaviour, use of body modifications or gender-affirming therapy, sexual orientation and STI risk.^{66,67} In this section, we also include third-gender, non-binary and other gender-variant populations, such as the hijra community in South Asia.

Although data on gonorrhoea among transgender people are limited, transgender people bear a strikingly disproportionate burden of HIV.^{66,68,69} Available data have highlighted several factors thought to contribute to heightened STI risk: societal transphobia, discrimination and experiences of abuse; lack of legal authorisation for gender-congruent identification; barriers to gender-affirming health care; poverty; mood disorders; internalised transphobia contributing to depression and substance abuse; and particularly germane to STI risk, difficulty finding employment with resulting engagement in sex work and transactional sex; and condomless receptive anal

intercourse.^{67,69–71} A disproportionate incidence or prevalence of gonorrhoea is probable and worthy of exploration.

Available data do suggest a substantial prevalence of gonorrhoea among transgender women, particularly at extragenital anatomic sites. Whereas the gonorrhoea positivity of urogenital specimens ranged from 0.1% (among 764 women from drop-in centres in Thailand) to 2.8% (among 406 STI clinic attendees at multiple sites in the USA), positivity of pharyngeal specimens ranged from 3.5 to 37.3% across studies (with positivity of 8.1–9.8% in the two largest studies from Thailand and the USA).^{72–75} Positivity among rectal specimens ranged from 6.3 to 43% (9.6–11.8% in the Thailand and USA studies).^{72–76} Two studies that did not mention the anatomic site of specimen collection found a prevalence among transgender women of 2.1% (among 63 young adults in the USA) and 4% (among 77 STI clinic attendees in Australia).^{77,78}

Although data on transgender men are even more scarce, available data hint at high gonorrhoea prevalence. Among 105 transgender men attending STI clinics, urogenital positivity was 7.1%, pharyngeal positivity was 5.9% and rectal positivity was 14.7%.⁷⁴ Comparable positivity was found among other samples from San Francisco, California, USA and Melbourne, Australia.^{73,78} In contrast, none of the 82 transgender male youth attending a community health clinic in Boston, Massachusetts, USA, had gonorrhoea.⁷⁷

A single study of gonorrhoea among persons identified as hijras, a long-recognised third gender in South Asia, found a 4% prevalence of urethral gonorrhoea and a 0% prevalence of rectal gonorrhoea among 203 persons from Lahore, Pakistan, and 4% and 29% prevalence, respectively, among 206 persons from Karachi, Pakistan.⁷⁹

Racial and ethnic minorities and Indigenous populations

Because racial and ethnic categories are not routinely collected as part of STI surveillance in most high-income countries and few cross-sectional data stratified by race or ethnicity are available, data on gonorrhoea among racial or ethnic minorities across the globe are limited. Available data include recent case report data from the USA and England and test positivity data from Honduras. In the USA and England (two countries in which race/ethnicity is routinely collected as part of gonorrhoea case reports), people of black race or ethnicity have the highest population rates of reported gonorrhoea.^{18,22} In the USA, the overall rate of reported gonorrhoea cases among Blacks in 2017 was 8.3-fold the rate among Whites (548.1 per 100 000 among Blacks and 66.4 per 100 000 among Whites). Among Blacks, particularly high rates were observed in women aged 20–24 years (2066.8 per 100 000) and men in the same age category (2154.8 per 100 000).¹⁸ In England, the highest population diagnosis rate by ethnicity was also among people of black ethnicity (369.1 per 100 000 in 2018).²² Within this group, black Caribbean and black non-Caribbean/non-African people had the highest diagnosis rate of all ethnic groups (4- to 6-fold the rates of white British people), whereas black Africans had relatively low rates (over twice the rate of white British people, but comparable to rates among white Irish people).⁸⁰ Among the

Garifuna, an ethnic minority of African-Caribbean origin, in Honduras, the prevalence of urogenital gonorrhoea was high among women (1.8%), but relatively low (0.3%) in men.⁸¹ In the USA, Hispanic/Latinx people also bear disproportionate rates of gonorrhoea. In 2017, the rate of reported gonorrhoea cases among Hispanic/Latinx people, at 113.7 per 100 000, was 1.7-fold the rate among Whites.¹⁸

In the USA, Canada and Australia, Indigenous populations bear disproportionate rates of STIs, including gonorrhoea. In the USA, the rate of reported gonorrhoea cases among American Indians/Alaska Natives (AIAN) (301.9 cases per 100 000) was nearly five-fold the rate among Whites in 2017.¹⁸ AIAN women aged 20–24 years had rates as high as 1037.7 per 100 000 in 2017. Gonorrhoea rates in Canada have been highest in the two provinces where Indigenous peoples comprise the majority of the population; the 2015 rate in the Canadian North-west Territories (815.9 per 100 000) and Nunavut (837.6) were ~15-fold the national average.²⁰ In Australia, rates of gonorrhoea in 2016 among Aboriginal and Torres Strait Islander people (581.8 per 100 000) were seven-fold the rate of non-Indigenous people.⁸² Among Aboriginal and Torres Strait Islander people, women aged 15–19 years had the highest rate, which was 2710.0 per 100 000.

The marked inequities by race and ethnicity and among Indigenous peoples are not explained by differences in individual behaviour. Legacies and enduring effects of mistreatment, institutional racism (including residential segregation and persistent inequalities in income, wealth, education, housing and living conditions, access to health care, and incarceration rates) contribute to poor health outcomes and support observed inequities.^{80,83–89} Assortative mixing within networks of persons with high gonorrhoea prevalence further reinforces disease transmission.^{84,89} In the USA, undocumented Latinx immigrants also face substantial barriers to healthcare access.^{85,90,91} Among Indigenous populations, legacies of mistreatment and forced dislocation from traditional lands, communities and culture likely played critical roles in giving rise to current structural determinants, including poverty, educational disadvantage, poor living conditions and barriers to accessing high-quality healthcare.^{91–97} These factors in turn contribute to substance abuse and poor sexual health outcomes (young age of sexual debut, inconsistent condom use and multiple partners) among Indigenous youth.⁹⁷

Sex workers

The category of sex workers (SWs) encompasses a diverse population who exchange sexual activity for income, employment, survival (e.g. food or shelter) or drugs. SWs include persons of all genders, span the socioeconomic range from the economically disadvantaged engaging in survival sex to escorts of higher socioeconomic status (SES), and likely vary in STI risk. The Joint United Nations Programme on HIV/AIDS (UNAIDS) has estimated that ~8 million persons are classified as SWs globally.⁹⁸

Recently published estimates of urogenital gonorrhoea positivity among STI clinic attending-female SWs (FSWs) range from 2.7% among women in England in 2011 ($n =$

2534) to 21.2% among those in Guatemala in 2012 ($n = 3213$).^{25,99–103} Data on prevalence of rectal and pharyngeal gonorrhoea among FSWs are sparse, but a large retrospective cohort study of 18 475 FSWs attending 42 sexual health clinics in Australia during 2009–15 reported an overall incidence of urogenital gonorrhoea of 1.4 per 100 PY, pharyngeal gonorrhoea was 3.6 per 100 PY, and rectal gonorrhoea was 0.3 per 100 PY.¹⁰⁴ The annual incidence of each increased during the analytic period, including from 1.6 per 100 PY in 2009 to 4.9 per 100 PY in 2015 for pharyngeal gonorrhoea.

Recent case reports hint that FSWs might be at elevated risk of acquisition and transmission of antimicrobial-resistant *N. gonorrhoeae*. In 2009, Ohnishi *et al.* reported the first case of ceftriaxone-resistant *N. gonorrhoeae* (minimum inhibitory concentration [MIC] = 2 $\mu\text{g mL}^{-1}$), which was identified in a 31-year-old FSW with pharyngeal gonorrhoea who had visited a clinic in Kyoto, Japan.¹⁰⁵ More recently, Katz *et al.* reported a cluster in Hawaii, USA, of *N. gonorrhoeae* isolates with high-level azithromycin resistance (MICs $\geq 256 \mu\text{g mL}^{-1}$) and decreased ceftriaxone susceptibility (MICs 0.06–0.125 $\mu\text{g mL}^{-1}$).¹⁰⁶ Four of the six male cases reported recent sexual contact with FSWs in Honolulu.

Although data are sparse for male SWs, recently published data have provided estimates of prevalence by anatomic site. Among 53 male SWs in Tel Aviv, Israel, 1.8% had urethral gonorrhoea and 7.5% had pharyngeal gonorrhoea.¹⁰⁷ Rectal gonorrhoea positivity was 9.9% among 334 male SWs in India and 8.5% among 96 men attending a sex worker clinic in Abidjan, Côte d'Ivoire.^{108,109} In estimates that aggregated infections by anatomic site, 17.4% of 488 male clinic-attending SWs in England had gonorrhoea (a markedly higher positivity than the 2.8% positivity among other male clinic attendees).¹¹⁰

SWs experience multiple and layered risks that heighten their risk of STIs including gonorrhoea. At the most proximate, inconsistent condom use with clients and other partners increases gonorrhoea acquisition risk. Yet, misogyny, sexual violence and physical abuse, substance abuse, financial coercion and inaccessibility of condoms may limit the ability of SWs to negotiate condom use.^{101,111–115} The percentage of SWs reporting condomless sex with clients or difficulty using condoms with clients ranged from 2.1% among female SWs in South Africa to 70% among male SWs in India.^{101,111,112,114–117} Drug use has been commonly described, and has been associated with greater numbers of clients, forced sex and unstable housing.^{118,119} Some cities have clinics dedicated to SW care; however, SWs who lack access to such clinics may face barriers to sexual health services due to lack of health insurance, mistrust of the healthcare system, local reliance on syndromic management and concern that positive tests may adversely affect their ability to work. Transgender and male SWs may also face intersectional compounded vulnerabilities based on transphobia and homophobia.¹²⁰

International travellers

Air travel and increased globalisation fuel rapid human mobility across international borders, which in turn can facilitate international spread of infectious diseases. During

1980–2016, the number of international travellers increased from 278 million to 1.2 billion.¹²¹ Sexual mixing with partners from other countries while travelling can facilitate international spread of STIs, including gonorrhoea. A large meta-analysis of sexual risk-taking during international travel reported a pooled prevalence of sex with a new partner abroad of 34% (range by studied population: 4–86% of young British seasonal workers in Ibiza).¹²² Across studies, 16.8% (pooled estimate) reported having engaged in condomless sex while travelling.

Available data from Nordic countries (Denmark, Finland, Norway and Sweden) indicate a substantial proportion of diagnosed gonorrhoea cases were travel-associated. During 2008–13, 25.5% of 12 645 gonorrhoea cases were deemed travel-associated, of which 86% ($n = 2432$) were in men; 652 (26.8%) were identified as MSM.¹²³ Nearly half of travel-associated cases were thought to have been acquired in Asia — particularly Thailand (31.2% of travel-associated cases) and the Philippines (8.0%) — and 32% acquired in Europe. The highest proportions were from Spain (7.1%) and Germany (6.2%).

Multiple case reports over several decades have underscored the contribution of international travel, especially travel from South-east Asia or the Western Pacific Region, to the spread of antimicrobial-resistant *N. gonorrhoeae*. In 1976, the first reported cases of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) were identified in an American service member recently returned from South-east Asia, and a woman in the United Kingdom with PID.^{124,125} The PPNG strains probably had their origins in independent genetic events in the regions of South-east Asia and West Africa.¹²⁶ Over subsequent decades, fluoroquinolone-resistant strains and then cephalosporin-resistant strains appeared to emerge first in East Asia before spreading globally via international travel (and at times through international linkages of sex work).^{127–137}

Recently identified cases of ceftriaxone-resistant strains, seemingly spread via international travel, highlight the importance of condom use and other safer sex approaches during travel. Two recent cases of ceftriaxone-resistant gonorrhoea were identified in the UK, both of which occurred in heterosexual men recently returned from East or South-east Asia.^{138,139} Two cases were identified in Australia, one of whom recently had sex in South-east Asia.¹⁴⁰ In late 2018, two additional cases (with high ceftriaxone and azithromycin MICs) were associated with travel of UK nationals to Ibiza, a popular holiday destination in Spain.¹⁴¹ Although recent ceftriaxone-resistant infections were identified in the UK and Australia, it seems probable that they were identified because of robust surveillance in these countries. The strains may be circulating elsewhere, but are yet to be detected.

Conclusions

As this review highlights, gonorrhoea disproportionately affects marginalised populations. The prevalence of gonorrhoea among sexually active young adults living in low-income countries, and — in many countries — among sexual, gender, racial and ethnic minorities, Indigenous communities and sex workers is markedly higher than among the general population in high-income countries. Increasing gonorrhoea incidence and

emerging antimicrobial resistance, which will undermine prevention and control efforts, will likely worsen and compound these health inequities.

Particularly in light of limited public health resources available to address this expanding public health threat, available prevention and control approaches — for gonorrhoea and antimicrobial-resistant strains — can be tailored to the populations most at risk. In high-income countries, sexually active persons within sexual, gender, racial and ethnic minority groups can be prioritised. Ensuring access to high-quality and culturally competent sexual health care, with ascertainment of sexual histories and adherence to screening recommendations, is crucial. Expanded testing and screening, such as through routine STI testing as part of PrEP, self-collection of specimens or use of point-of-care tests, might support prevention and control efforts. Tackling deeper structural determinants of health, which might be more effective on a population-level, will prove far more challenging and will require sustained multisectoral coordination and investment. In low-income countries, where diagnostic testing is rarely available and care is frequently rendered as syndromic management, prevention and control is far more challenging. Renewed support for condom promotion for primary prevention is worth considering. In many countries, regardless of the resources available for the public health and clinical infrastructure, gonorrhoea is increasing: clearly new prevention approaches, such as an affordable and effective vaccine, are urgently needed.

Continuing to advance our understanding of the epidemiology of gonorrhoea is critical. Strengthening surveillance across the globe, such as through greater adoption of standardised case definitions with reporting of a minimum dataset on cases, sentinel surveillance or — in resource-limited settings — syndromic surveillance with periodic laboratory testing, can advance this effort. Strengthening surveillance of *N. gonorrhoeae* antimicrobial resistance can also play an important role. Existing gaps in our knowledge about the risks of gonorrhoea among transgender people, including the risks of infection at different anatomic sites, need to be urgently addressed. Better data on the incidence of gonorrhoea, especially at different anatomic sites, can be used to optimise screening recommendations. Addressing existing gaps in knowledge about dynamic sexual networks and *N. gonorrhoeae* transmission within communities and networks further refine decision-making about the value of partner services and contact tracing. Although continued epidemiological investigations are important, *N. gonorrhoeae* is unlikely to wait for us to fill in all the gaps. So, even as we continue to gather data, action — informed by currently available data — is needed now to confront this growing international threat.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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