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Epidemiology of Gonorrhea: A Global Perspective

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Abstract

Although understanding the local epidemiology of gonorrhea 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, we review current epidemiology of gonorrhea 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 15–49 year olds in 2016. Gonorrhea rates are rising in many countries. Gay, bisexual, and other men who have sex with men, racial/ethnic minorities, indigenous populations, and sex workers appear to bear disproportionate burdens of gonorrhea. International travel can facilitate spread of gonorrhea, including resistant strains, across international borders. We highlight critical gaps in epidemiological knowledge, including data on gonorrhea among transgender persons and the burden of extragenital gonorrhea. Even as we continue to gather data, action — informed by currently available data — is needed now to confront this growing international threat.

Summary text for the online Table of Contents:

Better understanding of the international epidemiology of gonorrhoea may inform national and international prevention and control strategies and among whom to focus resources. We review the current epidemiology of gonorrhoea through an international lens. Sexual, gender, racial and ethnic minorities are disproportionately affected by gonorrhoea, but gaps in knowledge, such as the epidemiology of gonorrhoea among transgender people, should be addressed.

BACKGROUND

Gonorrhea is a sexually transmitted infection (STI) caused by the bacterium *Neisseria gonorrhoeae*. Following transmission, *N. gonorrhoeae* infects mucosa of exposed anatomic

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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 approximately 50% per sex act, and of vaginal-to-penile transmission is approximately 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 healthcare 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 influence 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 gonorrhea 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 birth weight, and spontaneous abortions.⁵⁻⁸ Infants born to mothers with untreated cervical gonorrhea can develop hyperacute conjunctivitis (neonatal ophthalmia), which can rapidly lead to corneal perforation and blindness if not rapidly treated. Infrequently, gonorrhea can progress to bacteremia and systemic involvement (disseminated gonococcal infection), leading to septic arthritis, endocarditis, and rarely, meningitis. Gonorrhea is also associated with heightened risk of HIV acquisition and transmission.⁹⁻¹¹

Particularly in countries where diagnostic testing and screening for gonorrhea 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 gonorrhea control and worsen ongoing management challenges.

To address the threat of gonorrhea globally, prevention and control programs need to be strengthened and novel prevention approaches are needed. A robust and current understanding of the epidemiology of gonorrhea can inform these efforts. Although understanding the local epidemiology of gonorrhea 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 gonorrhea through an international lens and with a focus on selected populations.

We searched for 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 behavior* 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 6,496 articles for relevance and hand-searched bibliographies.

INTERNATIONAL OVERVIEW

The World Health Organization (WHO) estimated the pooled 2016 global prevalence of urogenital gonorrhea (the proportion of the world’s population with gonorrhea in a given year) to be 0.9% in women and 0.7% in men, corresponding to a total of 30.6 million gonorrhea 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 categorized as low-income by World Bank criteria had the higher prevalences than those categorized as high-income.¹³ Prevalence estimates from specific countries further highlight heterogeneity across geographic areas. From 1999–2008, the overall prevalence of urogenital gonorrhea in the United States (USA) was 0.3%; during 2010–2012, the gonorrhea 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 15–24 years old in South Africa was 4.6%, and across studies of higher risk 15–24 year olds in East Africa 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, gonorrhea 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, gonorrhea 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 gonorrhea notification rate in the European Union(EU)/European Economic Area (EEA) increased during 2012–2016 with a few fluctuations.²¹ The largest relative increases in rates within the EU/EEA during 2015–2016 were observed in Iceland (108.7% increase: 13.7 to 28.6), Ireland (49.1% increase: 27.7 to 41.3), Finland (49.0% increase: 5.1 to 7.6), and Spain (36.1% increase: 10.8 to 14.7).²¹ The rate of gonorrhea 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 gonorrhea, marginalized and at greater risk for poor sexual health outcomes, and/or might play important roles in transmission. In this section, we summarize epidemiological data published during the past decade on gonorrhea 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 gonorrhea 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 sex partner is not routinely collected in case reports in this country. Yet the gonorrhea 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

Gonorrhea 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 STD clinics in the United States during 2010–2012, 11.1% tested positive for urethral gonorrhea, 10.2% tested positive for rectal gonorrhea, and 7.9% tested positive for pharyngeal gonorrhea.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 gonorrhea, 1.8–9% had rectal gonorrhea, and 0.5% pharyngeal gonorrhea at baseline.^{28–31} In one of the most robust estimates of community prevalence to date, a recently-conducted multisite assessment of 2,077 MSM attending community venues, such as bars and clubs, in the USA demonstrated a 4.5% prevalence of rectal gonorrhea and 4.6% prevalence of pharyngeal gonorrhea.³²

Not only is gonorrhea 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, gonorrhea incidence among MSM was calculated as having increased from 14.1 per 100 person-years (PY) in 2010 to 24.6/100 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 gonorrhea 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} Gonorrhea incidence among MSM appears to be increasing. These gonorrhea increases parallel those of other STIs among MSM, including infectious syphilis, lymphogranuloma venereum, and even sexually transmitted enteric infections.^{18,39,40} Gonorrhea among MSM is likely associated with increased numbers of sexual partnerships, concurrency, heightened density of same-sex sexual networks, and high underlying prevalence of gonorrhea 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 behaviors, the introduction of HIV PrEP, and proliferation of circuit parties and group sex events, particularly those involving chemsex, might contribute to changes in behavior and development of large and dense sexual networks that may facilitate gonorrhea 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 gonorrhea 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 and/or presentation differs from the sex which they were assigned at birth.⁶⁶ This umbrella classification, though important for advancing epidemiological research and clinical care, belies substantial heterogeneity of identity, behavior, 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 gonorrhea 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 authorization for gender-congruent identification; barriers to gender-affirming healthcare; poverty; mood disorders; internalized transphobia contributing to depression and substance abuse; and particularly germane to STI risk, difficulty finding employment with resulting engagement with sex work and transactional sex, and condomless receptive anal intercourse.^{67,69–71} A disproportionate incidence or prevalence of gonorrhea is probable and worthy of exploration.

Available data do suggest a substantial prevalence of gonorrhea among transgender women, particularly at extragenital anatomic sites. Whereas the gonorrhea positivity of urogenital specimens ranged from 0.1% (among 764 women from drop-in centers in Thailand) to 2.8% (among 406 STI clinic attendees at multiple sites in the USA), positivity of pharyngeal specimens ranged from 3.5%–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%–43% (9.6%–11.8% in the Thailand and USA studies).^{72–76} Two studies that did not mention 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 gonorrhea 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 Comparably, positivity was found among other samples in 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 gonorrhea.⁷⁷

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

Racial/ethnic minorities and indigenous populations

Because racial/ethnic categories are not routinely collected as part of STI surveillance in most high-income countries and few cross-sectional data stratified by race/ethnicity are available, data on gonorrhea among racial/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 gonorrhea case reports), people of black race/ethnicity have the highest population rates of reported gonorrhea.^{18,22} In the USA, the overall rate of reported gonorrhea cases among Blacks in 2017 was 8.3 times 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 (nearly 300 per 100,000 in 2017).²² Within this group, black Caribbean and black non-Caribbean/non-African people had the highest diagnosis rate of all ethnic groups (4–6 times the rates of White British), whereas black Africans had relatively low rates (over twice the rate of White British, but comparable to rates among White Irish).⁸⁰ Among the Garifuna, an ethnic minority of African-Caribbean origin, in Honduras, the prevalence of urogenital gonorrhea 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 gonorrhea. In 2017, the rate of reported gonorrhea cases among Hispanic/Latinx people, at 113.7 per 100,000, was 1.7 times the rate among Whites.¹⁸

In the USA, Canada, and Australia, indigenous populations bear disproportionate rates of STIs, including gonorrhea. In the USA, the rate of reported gonorrhea cases among American Indians/Alaska Natives (AIAN) (301.9 cases per 100,000) was nearly 5 times the rate among Whites in 2017.¹⁸ AIAN women 20–24 years had rates as high as 1,037.7 per 100,000 in 2017. Gonorrhea 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 Northwest Territories (815.9 per 100,000) and Nunavut (837.6) were approximately 15 times the national average.²⁰ In Australia, rates of gonorrhea in 2016 among Aboriginal and Torres Strait Islander people (581.8 per 100,000) were 7 times the rate of non-Indigenous people.⁸² Among Aboriginal and Torres Strait Islander people, women aged 15–19 years had the highest rate of 2,710.0 per 100,000.

The marked inequities by race/ethnicity and among indigenous peoples are not explained by differences in individual behavior. Legacies and enduring effects of mistreatment, institutional racism (including residential segregation and persistent inequalities in income, wealth, education, housing and living conditions, access to healthcare, and incarceration rates) contribute to poor health outcomes and support observed inequities.^{80,83–89} Assortative mixing within networks of persons with high gonorrhea 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), and/or drugs. They 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 National Programme on HIV/AIDS (UNAIDS) has estimated that approximately 8 million persons are classified as SWs globally.⁹⁸

Recently published estimates of urogenital gonorrhea positivity among female SWs range from 2.7% among women attending STI clinics in England in 2011 (n=2,534) to 21.2% among those attending STI clinics in Guatemala in 2012 (n=3,213).^{99–104} Data on prevalence of rectal and pharyngeal gonorrhea among female SWs are sparse, but a large retrospective cohort study of 18,475 FSWs attending 42 sexual health clinics in Australia during 2009–2015 reported an overall incidence of urogenital gonorrhea of 1.4/100 PY, of pharyngeal gonorrhea was 3.6/100 PY, and of rectal gonorrhea was 0.3/100 PY.¹⁰⁵ The annual incidence of each increased during the analytic period, including from 1.6/100 PY in 2009 to 4.9/100 PY in 2015 for pharyngeal gonorrhea.

Recent case reports hint that female SWs 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* (MIC=2 µg/ml), identified in a 31-year-old female SW with pharyngeal gonorrhea who had visited a clinic in Kyoto, Japan.¹⁰⁶ More recently, Katz et al reported a cluster in Hawaii, USA, of *N. gonorrhoeae* isolates with high-level azithromycin resistance (MICs ≥256 µg/ml) and decreased ceftriaxone susceptibility (MICs 0.06–0.125 µg/ml).¹⁰⁸ Four of the six male cases reported recent contact with female SWs 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 gonorrhea and 7.5% had pharyngeal gonorrhea.¹⁰⁸ Rectal gonorrhea 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.^{109,110} In estimates that aggregated infections by anatomic site, 17.4% of 488 male clinic-attending SWs in England had gonorrhea (a markedly higher positivity than the 2.8% positivity among other male clinic attendees).¹¹¹

SWs experience multiple and layered risks that heighten their risk of STIs including gonorrhea. At the most proximate, inconsistent condom use with clients and other partners increases gonorrhea 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.^{101,112–116} 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.^{101,112,113,115–118} Drug use has been commonly described, and has been associated with greater numbers of clients, forced sex, and unstable housing.^{119,120} 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.¹²¹

International travelers

Air travel and increased globalization fuel rapid human mobility across international borders, which in turn can facilitate international spread of infectious diseases. During 1980–2016, the number of international travelers increased from 278 million to 1.2 billion.¹²² Sexual mixing with partners from other countries while traveling can facilitate international spread of STIs, including gonorrhea. 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% to 86% of young British seasonal workers in Ibiza).¹²³ Across studies, 16.8% (pooled estimate) reported having engaged in condomless sex while traveling.

Available data from Nordic countries (Denmark, Finland, Norway, and Sweden) indicate a substantial proportion of diagnosed gonorrhea cases were travel-associated. During 2008–2013, 25.5% of 12,645 gonorrhea cases were deemed travel-associated, of which 86% (n=2,432) were in men; 652 (26.8%) were identified as MSM.¹²⁴ 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 Southeast 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 Southeast Asia, and a woman in the United Kingdom with PID.^{125,126} The PPNG strains probably had their origins in independent genetic events in southeast Asia and West Africa.¹²⁷ 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).^{128–138}

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 gonorrhea were identified in the UK, both of which occurred in heterosexual men recently returned from east or southeast Asia.^{139,140} Two cases were identified in Australia, one of whom had recently had sex in southeast Asia.¹⁴¹ In late 2018, two additional cases (with high ceftriaxone and azithromycin MICs) were associated with travel of UK nationals to a popular holiday destination in Spain.¹⁴² 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, though as of yet undetected.

Conclusions

As this review highlights, gonorrhea disproportionately affects marginalized populations. The prevalence of gonorrhea among sexually-active young adults living in low-income countries, and — in many countries — among sexual and gender minorities, racial/ethnic minorities and indigenous communities, and sex workers is markedly higher than among the general population in high-income countries. Increasing gonorrhea 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 gonorrhea and antimicrobial-resistant strains — can be tailored to the populations most at risk. In high-income countries, sexually-active persons within sexual, gender, and racial/ethnic minority groups can be prioritized. Ensuring access to high-quality and culturally competent sexual healthcare, 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 impactful 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, gonorrhea 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 gonorrhea is critical. Strengthening surveillance across the globe, such as through greater adoption of standardized 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 gonorrhea among transgender people, including the risks of infection at different anatomic sites, need to be urgently addressed. Better data on the incidence of gonorrhea, especially at different anatomic sites, can be used to optimize 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.

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