As through a glass, darkly: the future of sexually transmissible infections among gay, bisexual and other men who have sex with men

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Abstract. The trajectory of sexually transmissible infection (STI) incidence among gay and other men who have sex with men (MSM) suggests that incidence will likely remain high in the near future. STIs were hyperendemic globally among MSM in the decades preceding the HIV epidemic. Significant changes among MSM as a response to the HIV epidemic, caused STI incidence to decline, reaching historical nadirs in the mid-1990s. With the advent of antiretroviral treatment (ART), HIV-related mortality and morbidity declined significantly in that decade. Concurrently, STI incidence resurfaced among MSM and increased in scope and geographic magnitude. By 2000, bacterial STIs were universally resurgent among MSM, reaching or exceeding pre-HIV levels. While the evidence base necessary for assessing the burden STIs among MSM, both across time and across regions, continues to be lacking, recent progress has been made in this respect. Current epidemiology indicates a continuing and increasing trajectory of STI incidence among MSM. Yet increased reported case incidence of gonorrhoea is likely confounded by additional screening and identification of an existing burden of infection. Conversely, more MSM may be diagnosed and treated in the context of HIV care or as part of routine management of pre-exposure prophylaxis (PrEP), potentially reducing transmission. Optimistically, uptake of human papillomavirus (HPV) vaccination may lead to a near-elimination of genital warts and reductions in HPV-related cancers. Moreover, structural changes are occurring with respect to sexual minorities in social and civic life that may offer new opportunities, as well as exacerbate existing challenges, for STI prevention among MSM.

Introduction

In the context of the HIV pandemic, behavioural risk information is generally available in most regions of the world. Even countries with only modest surveillance capacity are able to assess the proportion of HIV cases among men who have sex with men (MSM) by modelling modes of transmission with the assistance of international partners. This is perhaps owing to the relatively recent emergence of HIV and an appropriately robust international public health surveillance effort. In stark contrast, there continues to be a paucity of MSM-specific risk information available globally for persons diagnosed with other bacterial and viral sexually transmissible infections (STIs). In many regions of the world, STI surveillance is further challenged by largely syndromic case identification and treatment. The relative scarcity of even minimal case-based evidence for STIs among MSM is often aggravated by severely constrained resources for all disease surveillance in general. In light of these challenges, the broader landscape of STIs among MSM globally remains largely unmapped. The few clearly marked paths available for traversing this ground generally exist in high-income settings, limiting the breadth of global coverage with respect to STIs among MSM.

Even in countries and regions with advanced public health systems and relatively well-resourced disease surveillance
STIs among MSM before HIV

As early as the mid-1960s, there was widespread speculation in higher-income countries that syphilis and gonorrhoea were highly prevalent among ‘homosexuals’.1–17 In one clinic in London, 62% of syphilis cases and 14.8% of gonorrhoea cases among men in 1965 were attributable to same-sex sexual behaviour. Similarly, among patients diagnosed with STIs in a metropolitan Toronto clinic, 62% of males with syphilis and 22.4% of males with gonorrhoea acknowledged same-sex sexual behaviour. In the US, there was also evidence that homosexual patients named two- to five-fold more partners than heterosexuals during case investigations, leading to the conclusion that transmission was likely ongoing and suggesting a largely undiagnosed and potentially increasing burden of disease in this group.7,14,15 Similarly, overall increases in gonorrhoea were noted in Europe and New Zealand in the 1960s, and difficulties controlling syphilis and gonorrhoea in the UK in that decade were, in part, attributed to ecological factors that included an observed increase in ‘prostitution and homosexuality’.5,16,17 This type of characterisation is typical of the literature of the period, with MSM often aggregated into atypical and sometimes derogatory groupings not explicitly separable from heterosexuals.

Though the proportion of all cases in the broader population attributable to MSM was not explicitly measured during the 1960s, the overall incidence of syphilis and gonorrhoea increased across the decade. For example, rates of primary and secondary syphilis increased from near zero in 1960 to between 150 and 300 cases per 100,000 in Oslo, Copenhagen and Stockholm.16 Evidence for increasing or decreasing trends among MSM was largely anecdotal, or based on small clinical cohorts and specific patient populations, yet these studies do suggest STIs were endemic in MSM in many urban centres. Moreover, these men were increasingly being recognised as a behavioural group specifically in need of additional STI services.

The early 1970s was a time of phenomenal social change with marginally increasing cultural acceptance for MSM in many urban settings across the world. Less prescriptive attitudes towards same-sex sexual partnerships were becoming more widespread and represented the vanguard of popular urban culture, with at least somewhat broader social acceptance. By 1973, the American Psychiatric Association had removed homosexuality as a psychiatric disorder from its diagnostic literature.18 Openly gay-identified communities emerged and flourished in many metropolitan areas in the US and in Europe. The South Australia and Australian Capital Territory legislatures repealed outdated sodomy laws in the middle of that same decade,19 reflecting similar social trends in the southern hemisphere. Concurrently, in many urban centres around the world, a consensus on the part of clinicians and the public health community was gradually emerging that recognised STIs among MSM as an increasingly important public health issue.20–22

STI incidence among MSM was also becoming more commonly measured, as an increasing number and variety of clinical settings sought to adopt non-judgmental attitudes in deliberate efforts to better serve MSM communities. This encouraged disclosure on the part of patients and facilitated better capture of this information in clinical records. In places as diverse as Cincinnati, Denver, Toronto, San Diego, San Francisco, New York, London, Copenhagen, Melbourne, Oslo and elsewhere, it was clear that a substantial majority of the early syphilis cases diagnosed among men in many primary genitourinary medicine (GUM) and STD clinics were attributable to same-sex practices.2,7,9,11–13,16,21 For example, at a large GUM clinic in London, 84.5% of early syphilis cases diagnosed in 1971 were among MSM.21 Throughout the decade, there was a growing body of evidence suggesting that gonorrhoea and syphilis were common among MSM in multiple countries.
Yet the burden of STIs among MSM in comparison to heterosexuals at the population level was only measured by crude indicators like male-to-female case ratios, supplemented in limited clinical settings by eliciting MSM exposure from male patients. Due to the mostly anecdotal nature of the evidence, rate ratios and other measures of unequal incidence remained unavailable to the public health community because of a lack of denominator data for MSM and complete information on gender of sex partners. Nevertheless, it seems clear that STIs were increasing and prevalent at high levels wherever there were sizable communities of MSM. In settings where comparative studies with heterosexuals were undertaken, the likelihood of MSM presenting with gonorrhoea, syphilis and other STIs was found to be significantly higher than among age- and race-matched heterosexual men. In one large STD clinic in the US (Denver, Colorado), an analysis of over 17,500 initial clinic visits among men presenting for care found that 30.3% of MSM had gonorrhoea compared with 19.8% of heterosexuals, and that MSM were statistically more likely to be diagnosed with early syphilis as well (1.08% of MSM vs. 0.38% in heterosexual men).

By the close of the 1970s, all signposts pointed towards markedly high incidence and prevalence of STIs among MSM, especially in urban centres. Absolute numbers of MSM cases appeared to be increasing, but there are few data available to conclusively demonstrate population-level trends given the lack of denominators or standardisation in capturing gender of sex partners for surveillance purposes. With increasing ascertainment of same-sex behaviour, these reports are limited and potentially biased. But perhaps equally telling, the literature from this time documents sporadic incidence of Lymphogranuloma venereum (LGV), high prevalence of herpes simplex virus (HSV), high prevalence of the viral hepatitides and numerous outbreaks of enteric pathogens not ordinarily associated with sexual transmission among clinical cohorts of MSM. Despite limitations, it seems reasonable to consider that STIs were hyperendemic among MSM by the close of the 1970s. This is especially true for syphilis and gonorrhoea, which provide a reasonable baseline for comparative purposes in subsequent decades.

By 1980, the growing consensus in the public health community that MSM were at significantly increased risk of contracting STIs and related health issues also led to calls for an increasing focus on MSM in publicly funded STI clinical facilities. In large US, European and Australian cities, a significant and growing proportion of the patient populations in many speciality GUM or STI clinics comprised self-identified MSM, as these clinics purposely tailored both services and settings to better serve this community. HIV emerged and spread with frightening rapidity in just such concentrated MSM neighbourhoods with existing high incidence and prevalence of multiple STIs.

**Impact of HIV and AIDS anxiety on STIs**

By the time the World Health Organization began limited international surveillance for AIDS in October of 1983, the HIV pandemic was likely having a significant and increasingly dramatic impact on the sexual networks and practices of MSM. Population-based rates of gonorrhoea and syphilis fell throughout the latter half of the decade in many countries. Of particular note, the male-to-female case ratio – often a benchmark indicator for STI incidence among MSM – was falling incrementally towards parity in some locations.

These changes in STI incidence patterns were, at the time, attributed to multiple, sometimes related and inseparable factors. Yet chief among these, behavioural changes in response to the HIV pandemic and catastrophic mortality in MSM communities were thought to have had a significant impact on the transmission of bacterial STIs in some settings.

In the US alone, over 122,000 people had died of HIV-related causes by 1990, an overwhelming proportion of whom were MSM living in metropolitan areas. These men were integral to existing sexual networks in MSM communities, contributing to the size and density of sexual networks and likely occupying central positions in these same networks. Loss of network cohesion, and a generalised decrease in the number of network participants as a result of HIV mortality, likely contributed to decreasing STI transmission in many MSM communities.

Individual-level behavioural changes were also observed in response to anxiety generated by HIV-related morbidity and mortality, including reporting fewer overall sex partners, slower partner exchange rates, increased use of condoms and intensified public health behavioural interventions.

The loss of such a large number of sexually active MSM due to the impact of continuing HIV morbidity on the sexual behaviour of those living with HIV disease and widespread behaviour change among those not infected, likely created conditions conducive to rapid and substantial decreases in the incidence of other STIs. Reported gonorrhoea incidence among all populations fell dramatically across the decade of the 1980s. In the US, overall gonorrhoea rates decreased from 445 per 100,000 in 1980 to 278 per 100,000 in 1990. Much of this decline was among men, as demonstrated by the male-to-female case ratio, which declined steadily throughout the decade in both the US and Europe, reaching a low of 1.04 male to females cases in the US by 1996. Primary and secondary (P&S) syphilis, considered in retrospect to have been a good proxy for HIV incidence, saw similar declines, falling from 14.1/100,000 in 1983 to reach a historic low of 2.1 per 100,000 in the US in 2001. This decline, in both men and women, was sufficiently precipitous by 1998 to encourage the public health community in the US to consider the possibility of completely eliminating indigenous syphilis transmission. However, evidence also existed at the time to indicate that the remaining burden of P&S syphilis was likely concentrated among MSM, as the overall male-to-female case ratio of 1.5 to 1 in 1998 and male-to-female ratios of 38:1 and 25:1 in Seattle and San Francisco, respectively, that same year suggests.

**Resurgence of STIs in 1995–2010**

There were decreasing trends in STIs diagnosed among MSM emerging globally through the early 1990s. Yet by the middle of that decade, there were indications that these promising trends might be short-lived. Increased sexual risk-taking and increased STIs were being observed among MSM in urban centres in the US, Europe, the UK and Australia. This apparent
resurgence of STIs gained traction and became more widespread into the first decade of the new millennium. Potentially even more troubling, increases in the incidence of bacterial STIs among HIV-positive MSM were being observed in many regions.\textsuperscript{56–59} With the synergistic relationship between HIV and other STIs well established, additional focus was directed towards determining the HIV status of MSM being diagnosed with syphilis and gonorrhoea.\textsuperscript{57,58} The burden of STIs, especially syphilis, among HIV-positive MSM was found to be quite high in major urban centres globally, most likely attributable to dramatic reductions in HIV-related morbidity as prophylaxis for opportunistic infections and antiretroviral therapy (ART) gradually became more widely used in the late 1990s and early 2000s.\textsuperscript{28}

The emerging belief in the early 2000s that ART might reduce the risk of HIV transmission, shared among both public health officials and MSM communities, was soon reinforced by treatment-as-prevention messages leveraging the demonstrable population-level impact of viral suppression on HIV transmission.\textsuperscript{60–62} A highly visible decrease in HIV/AIDS-associated morbidity among those infected, emerging optimism with respect to HIV transmission, and an overall prevention fatigue among MSM, appeared to be leading to increased sexual risk-taking as evidenced by greater numbers of MSM being diagnosed with STIs.\textsuperscript{63–69} With syphilis and gonorrhoea, incidence among MSM increasing, it is not surprising that beginning in 2000 modest increases in newly reported HIV infections among MSM were also observed in the US, Western Europe and Australia.\textsuperscript{30}

The inescapable conclusion from the available evidence was that, along with ecological and social changes, individual protective behaviours adopted in response to the HIV pandemic appeared to be on the wane. STI incidence, especially syphilis, was rebounding towards pre-HIV levels in many regions simultaneously. In 2010, the P&S syphilis rate among men in the US had reached 7.9 per 100 000, with at least 68% of cases attributed to MSM. Similarly, reported rates of P&S syphilis among males in Australia reached 8.9 per 100 000.\textsuperscript{71} While some of the increase across the 2000s was likely the result of greater awareness on the part of MSM and their healthcare providers of the importance of screening for and treating STIs that resulted in the identification of previously undiagnosed or asymptomatic infections, there were also social and demographic changes in the broader society and within MSM communities that mitigated against sustaining decreases in STI incidence noted in the 1980s and 1990s.\textsuperscript{30}

Tremendous reductions in AIDS mortality also meant that the size of sexually active MSM populations was rebounding. Additionally, as HIV prevention efforts reached a level of maturity and professionalism in many higher-income countries, the level of community activism and direct involvement with prevention efforts may have begun to wane.\textsuperscript{69} In the early 2000s, a new cohort of sexually active MSM was coming of age into a very different social as well as HIV prevention milieu than their immediate predecessors. With a high baseline prevalence of STIs newly re-established among MSM, age-bridging and consistently high rates of partner exchange between older and younger cohorts set the stage for more generalised STI epidemics among MSM. STIs, including HIV, were clearly spreading across generation cohorts of MSM towards the end of the first decade of the 2000s.\textsuperscript{70,73,74}

Moreover, emergence of a host of non-venue-based channels and modes for locating potential sex partners through Internet and smart-phone applications was clearly having an impact on sexual networks. Most of these technologies facilitate real-time, on-demand identification of potential partners in convenient geographic proximity.\textsuperscript{75–82} These likely increased the density of anonymous sexual contacts beyond the reach of traditional disease management activities, such as partner and provider referral, where those were available. Moreover, increases of syphilis, a primary focus of traditional public health activities, among MSM were occurring in an era of declining resources for STI control in general. In many areas of the US and Europe, investments in public health disease control activities were either beginning to decrease, were increasingly insufficient for the rising burden of disease, or perceived to be under threat as a result of the downturn in economic activity.\textsuperscript{83,84} By 2010, conditions were seemingly ripe for rapid and sustained increases in STIs among MSM in the US, Europe and elsewhere.

**Current epidemiology of STIs in MSM for 2011–2016**

There appears to be universally resurgent epidemics of syphilis, gonorrhoea and, where data exists, chlamydial infection among MSM across higher-income settings.\textsuperscript{85–102} Incidence of syphilis among MSM is surging dramatically in many regions globally and likely represents only the most visible burden of STI among MSM. Rate of reported P&S syphilis cases among men recently exceeded 10 cases per 100 000 in Australia, Canada and the US, and significant increases in the number of MSM cases were reported in multiple European Union (EU) countries.\textsuperscript{100–102} A recent estimate of the incidence of P&S syphilis specifically among MSM in the US indicated the overall rate to be 154 per 100 000 and 353 per 100 000 among African American/Black MSM.\textsuperscript{103} Gonorrhoea and chlamydial infections are also increasing significantly in numerous settings.\textsuperscript{85,87,90,98} Though the data are less universally available to fully characterise gonorrhoea and chlamydia incidence among MSM, it is informative to note that guidelines for screening MSM for gonorrhoea and chlamydial infection at non-genital anatomic sites have been recently issued in numerous countries.\textsuperscript{104–107}

Anecdotal evidence and facility-based research indicates that screening in non-genital anatomic sites is becoming, appropriately, more wide-spread in clinical settings serving significant populations of MSM. This increase in screening is likely identifying a previously undiagnosed burden of anorectal and pharyngeal infections.\textsuperscript{56,108–114} In light of this fact, it is not clear whether the increases of these two STIs noted in clinical cohorts and in various sentinel surveillance projects reflect a true increase in incidence, an artefact of enhanced screening or, more plausibly, some combination of both. The incontrovertible evidence documenting accelerating incidence of syphilis among MSM would suggest that at least some proportion of the observed volume of new gonorrhoea and chlamydial infections may represent a trend towards increasing incidence as well.

With respect to gonorrhoea incidence in particular, there is evidence from the US that MSM are particularly vulnerable.
to the emergence of antimicrobial resistant strains of *N. gonorrhoeae*.115,116 This is potentially quite troubling when considering evidence for increasing incidence of gonorrhoea in MSM globally. Current recommendations for first-line therapy include parenteral treatment with Ceftriaxone and Azithromycin, effectively limiting the settings in which all persons with gonorrhoea must present for appropriate treatment.104–106

There have been documented treatment failures observed using widely available oral cephalosporins,116 and it is becoming clear that expedited options for partner treatment, a key disease control measure available in some countries, are quickly narrowing. The implications for persistent and/or difficult-to-treat gonorrhoea infections, often across multiple anatomic sites, among MSM are not fully understood but may well represent an unacceptable future burden in terms of quality of life, as well as diagnostic and treatment costs.

Against this rather pessimistic backdrop there are, however, promising trends with respect to at least one viral STI. The incidence of genital warts caused by human papillomavirus (HPV), appears to be changing in response to HPV vaccination efforts. While the data are most striking for young women, given the initial targeting of vaccination efforts to girls, in countries where vaccine uptake is robust in both girls and boys, the burden of genital warts in the general population appears to have fallen to levels that could reasonably be characterised as presaging eradication of the associated HPV types.117–120 While more work is clearly needed to understand the burden and distribution of HPV types associated with genital warts, anorectal, penile and other cancers of the head, neck and throat in MSM, current evidence suggests that vaccination efforts can be highly successful at the population level, and would plausibly have a similar impact in reducing incidence of disease among MSM.

Recently emergent trends in primary HIV prevention, including post/pre-exposure prophylaxis (PEP/PrEP), are also changing the social and ecological landscape of STIs among MSM.121–126 Clearly, a conceptual decoupling of HIV and STI prevention is underway among MSM, as well as in the public health community.127 Though the impact of this decoupling is not yet fully understood, there will inevitably be implications for STI incidence among MSM across the full spectrum of pathogens. As PrEP becomes more widespread and accepted among MSM, there will likely be marked and significant increases in reports of syphilis, gonorrhoea and chlamydial infection cases. It is tempting to make a snap judgment and assume that individual risk behaviours and community-level prevalence and incidence will naturally increase, thus leading to a higher volume of cases reported to public health and more frequent infections diagnosed and treated in MSM patients. But the reasons for increasing reports will be considerably more complex than the simplistic, reductionist explanation of increased risk behaviour would suggest. The standard of care for monitoring PrEP use will likely bring increasing numbers of MSM into an ongoing relationship with providers. As a result, the opportunities for detecting and treating STIs will no doubt increase as well. The population-level benefit of normalising STIs screening, diagnosis and treatment into routine care will take time to be fully realised. Yet it will likely identify and treat a significant number of asymptomatic gonorrhoea and chlamydia infections resulting in initial increases in reported cases. This may also lead to reductions in the duration of infectiousness that may have a mitigating effect on incidence in the long run.

Reprise

To sum up what has admittedly been a facile, high-octane journey through 50 years of evidence for evolving trends in STIs among MSM, a couple of observations seem particularly pertinent. First, the evidence base for global comparative and population-level assessment of STIs in MSM remains woefully inadequate. This limits the ability of the public health community to generalise surveillance findings to encompass the full richness and diversity of MSM communities. Assessments of the burden of disease among MSM in the past, out of necessity, are constrained to non-representative clinical populations or to estimates based on sentinel and enhanced investigations. This scarcity of information has perhaps led to an epidemiological tunnel-vision of sorts, reifying the problem of STIs among MSM and leading to generalising beyond the evidence. Despite limitations in the available evidence, trends in incidence of STIs in MSM over the past generation have indeed risen from the available data, and the narrative is not particularly encouraging. Incidence among MSM was likely quite high in the 1960s and 70s, fell considerably in the beginning of the HIV pandemic through the 1990s, and has rebounded steadily to the present day.

Towards 2020

The future can only be glimpsed through a glass, darkly. Yet given the somewhat grim assessment of current trends in STIs among MSM at present, there is perhaps little reason to be sanguine looking towards 2020. The current ecology of high prevalence, emerging evidence of sustained incidence coupled with well-founded optimism regarding advances in reducing HIV transmission, suggests that ongoing syphilis transmission in MSM will continue globally and will likely increase in magnitude and geographic distribution. Reports of gonorrhoea and chlamydial infections will also inevitably continue to increase for some time to come, though the interpretation of these increases will need to be tempered by findings from expanded research into the type and frequency of sexual health services being accessed by MSM, including those using PrEP and those accessing HIV primary care.

Increases in STIs among MSM will be especially pronounced in urban areas where dense sexual networks, population churn and high prevalence of anonymous partnerships sustain ongoing transmission. These network factors, as well as community intervention preferences, are critical for the public health community to address in the development of a fuller understanding STI incidence. Far more attention needs to be paid to such factors in designing interventions to supplement the currently inadequate inventory of interventions targeted to reducing STIs among MSM.128,129 More reliable estimates of the proportion of MSM not routinely accessing sexual health services are also needed, along with well-designed and intensive efforts to link these men with appropriate primary care that includes comprehensive STI services.
STIs among MSM will manifest in disconcerting trends for some time to come. There is cause for heightened vigilance for the emergence and spread of novel sexually transmitted pathogens into MSM networks such as hepatitis C, Zika and Ebola viruses, as conditions clearly exist for rapid spread. Yet there is also cause for cautious optimism in the longer term. The trajectory of gonorrhoea and chlamydial infection may flatten over time if comprehensive sexual health services become broadly integrated into MSM health care, especially if the paradigm is shifted to focus on STIs with potentially more significant health impacts, such as HPV and syphilis. Better understanding and articulating the risks in MSM-specific health communications may help reduce barriers to more comprehensive STI care. But the greatest impact on the sexual health of MSM may lie in recognising that STI risk is not simply an issue of individual behaviour but is more fully explained in the context of broader social and epidemic factors; considerations of community and global context are critical elements needed in responding to STIs among MSM.

The good news, however, is that the public health evidence base for STIs among MSM has been improving significantly over the past decade. Efforts are underway in many countries to improve ascertainment of gender of sex partners both in routine and enhanced surveillance, to collect sexual orientation and gender identity as structured data in health records for analytic purposes and to develop reliable estimates of the size of sexual minority populations. These efforts will inevitably lead to more valid, broadly representative estimates of the burden of STIs in MSM. Moreover, sweeping social and cultural changes occurring in many countries towards integrating MSM and other sexual and gender minorities into civic and cultural institutions may presage significant changes in STIs as well. The structural impact these changes may have on sexual behaviours and the dynamics of STI transmission is yet to be fully revealed, but these are welcome steps towards reducing widely acknowledged inequities in health outcomes experienced by sexual minorities globally. Pragmatism with respect to the near term, tempered by determination to pursue what must still be achieved, and a steadfast, unwavering zeal to address both the human and informational needs of MSM sexual health should be the signposts guiding the public health community on the road ahead.

Conflicts of interest
No conflicts of interest identified or declared.

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