HIV in men who have sex with men 1

Global epidemiology of HIV infection in men who have sex with men

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Epidemics of HIV in men who have sex with men (MSM) continue to expand in most countries. We sought to understand the epidemiological drivers of the global epidemic in MSM and why it continues unabated. We did a comprehensive review of available data for HIV prevalence, incidence, risk factors, and the molecular epidemiology of HIV in MSM from 2007 to 2011, and modelled the dynamics of HIV transmission with an agent-based simulation. Our findings show that the high probability of transmission per act through receptive anal intercourse has a central role in explaining the disproportionate disease burden in MSM. HIV can be transmitted through large MSM networks at great speed. Molecular epidemiological data show substantial clustering of HIV infections in MSM networks, and higher rates of dual-variant and multiple-variant HIV infection in MSM than in heterosexual people in the same populations. Prevention strategies that lower biological transmission and acquisition risks, such as approaches based on antiretrovirals, offer promise for controlling the expanding epidemic in MSM, but their potential effectiveness is limited by structural factors that contribute to low health-seeking behaviours in populations of MSM in many parts of the world.

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This is the first in a **Series** of seven papers about HIV in men who have sex with men

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See **Online** for appendix

Introduction

In 2012, men who have sex with men (MSM) are at substantial risk for HIV infection in virtually every context studied (panel 1).[1,3,4] This risk has been present since the syndrome now known as AIDS was first described in previously healthy homosexual men in Los Angeles (CA, USA) in 1981.[5–7] Despite decades of research and community, medical, and public health efforts, high HIV prevalence and incidence burdens have been reported in MSM throughout the world.[8] In many high-income settings—including Australia, France, the UK, and the USA—overall HIV epidemic trends are in decline except in MSM, where they have been expanding in the era of highly active antiretroviral therapy (HAART) in what have been described as re-emergent epidemics in MSM.[9,10] In the USA, HIV infections in MSM are estimated to be increasing at roughly 8% per year since 2001.[9] And in much of Africa, Asia, and Latin America, the highest rates of HIV infection in any risk group are in these men.[8]

However, our understanding of worldwide epidemiology is far from complete. By the end of 2011, 93 of 196 countries had not reported on HIV prevalence in MSM in the previous 5 years.[11] In several regions, notably the Middle East, north Africa, and sub-Saharan Africa, data for HIV infections in MSM are only emerging.[12,13] Data gaps and challenges to HIV research, surveillance, and epidemiological characterisation in MSM are largely the result of the hidden and stigmatised nature of MSM populations in much of the world, and of ongoing criminalisation of homosexuality and other forms of same-sex behaviour.[11] These structural realities have limited our understanding, and might also have crucial roles in the vulnerability of MSM to HIV.[14,15] We review the global epidemiology and disease burden of HIV infection in MSM; individual-level, couple, and network-level risks for HIV acquisition and transmission; biological aspects of anorectal HIV transmission; and molecular epidemiology advances, with the aim of understanding why MSM continue to bear such disproportionate burdens of HIV. We also developed and report on stochastic agent-based simulation models of HIV transmission to further clarify the drivers of HIV spread in MSM.[16] Finally, we discuss the public health importance of our emerging understanding of the epidemiology of HIV in MSM.

Disease burden of HIV in MSM

We did a comprehensive search for HIV burden and risks in MSM from Jan 1, 2007, to June 30, 2011 (search criteria in the appendix). We retrieved 2105 unique citations, and we identified and reviewed 68 additional surveillance studies in the public domain. We included country progress reports submitted to the UN General Assembly Special Session on HIV/AIDS (UNGASS). We obtained data from 82 peer-reviewed publications on disease burden of HIV in MSM, from 12 of the 68 surveillance reports, and from 38 of 186 country progress reports submitted to UNGASS in 2010.

Figure 1 shows aggregate HIV prevalence estimates in MSM by region derived from the comprehensive search (references in the appendix). Pooled HIV prevalence ranged from a low of 3·0% (95% CI 2·4–3·6) in the Middle East and north Africa region to a high of 25·4% (21·4–29·5) in the Caribbean. The CIs for these pooled estimates must be interpreted with caution, since they only account for sampling variation and not the inherent biases of non-representative samples, and so undoubtedly underestimate actual variances. Nevertheless, HIV prevalences were relatively consistent across North, South, and Central America, south and southeast Asia, and sub-Saharan Africa (all within the 14–18%

Key messages

- HIV epidemics in men who have sex with men (MSM) are expanding in countries of all incomes in 2012, and these epidemics are characterised by high HIV burdens, substantial clustering of infections within networks, and high forces of infection.
- The disproportionate HIV disease burden in MSM is explained largely by the high per-act and per-partner transmission probability of HIV transmission in receptive anal sex.
- The molecular epidemiology of HIV in MSM shows substantial clustering of HIV infection, a high frequency of multiple transmitted variants, and more rapid spread through networks, challenging vaccine and other biomedical approaches to prevention.
- If the transmission probability of receptive anal sex was similar to that associated with unprotected vaginal sex, 5 year cumulative HIV incidence in MSM would be reduced by 80–98%.
- Role reversal in MSMs, whereby individuals practise both insertive and receptive roles, helps HIV spread by overcoming the low transmission rates from receptive to insertive partners. Our modelling shows that limiting MSM to either insertive or receptive roles (50% for each, as in heterosexual networks) reduced 5 year cumulative HIV incidence by 19–55% in high-prevalence scenarios.
- Casual partnerships are also a substantial driver of the epidemic in MSM. If unprotected anal intercourse in casual partnerships instead happened within long-term main partnerships, HIV prevalence would be reduced by 29–51%.

Panel 1: Taxonomies of men who have sex with men, sexual orientation, and gender identity

Men who have sex with men (MSM) is a term introduced in 1992 to attempt to capture a range of male–male sexual behaviours and avoid characterisation of the men engaging in these behaviours by sexual orientation (homosexual, bisexual, heterosexual, or gay) or gender identity (male, female, transgender, queer).[1] MSM includes gay-identified men, heterosexually identified men who have sex with men, bisexual men, male sex workers who can have any orientation, men engaging in these behaviours in all male settings, such as prisons, and the rich and wide array of traditional identities and terms for these men across cultures and subcultures. Biological men who choose female identities are generally referred to in work on HIV as transgender or transgender women if they have undergone gender-reassignment surgery. Transgender people born male might share some biological risks with MSM, most importantly receptive anal intercourse, but their female gender identity places them in quite different categories from MSM; hence they are not included as a subgroup of MSM in this Series.

Scientific work suggests that sexual orientation in men represents a lifelong preference for sexual and romantic partners of the opposite, same, or both sexes.[2] MSM is a broader category and includes non-gay-identified MSM, those married to women, and other subgroups who might be more hidden, difficult to reach for surveillance, and less willing to disclose sexual practices than gay-identified men, challenging epidemiological characterisation and HIV responses. This is particularly true in contexts where same-sex behaviour is stigmatised or criminalised. Nevertheless, MSM has become the standard term in the work on HIV. We use the term recognising its shortcomings.

range). Comparing HIV infection levels in MSM with UNAIDS 2009 estimates of general population adult male HIV prevalence shows that levels in MSM are substantially higher in every context (figure 2).[18] Most countries worldwide had not reported HIV rates in the previous 5 years in MSM, so these are aggregate regional values of available and present data. Figure 2 depicts HIV prevalence in MSM in countries where prevalence data could be obtained through peer-reviewed publications, behavioural surveillance reports, or UNGASS reports.

Figure 3 shows HIV incidence in MSM, which was available from 27 peer-reviewed publications. Data were reported from 15 countries overall; reports included nine from the USA, three from Europe, six from Asia, six from Latin America, two from Australia, and one from Africa (Kenya; references in the appendix). Overall incidences show sustained epidemic patterns, with no evidence of declines. The two Asian states for which incidence was available, China and Thailand, both show rising rates of HIV infection. Kenya, the only African country with an incidence report, had the very high rate of greater than 20% annual incidence in a selected sample of men who have sex with men only, in Mombasa.[19]

These findings suggest several important patterns for epidemiology in MSM. First, incidence continues to be sustained at levels sufficient for epidemics in the MSM population to continue, and, in some settings, expand. The available incidence data from Thai, Chinese, and Kenyan samples of MSM suggest these epidemics are in rapid expansion phases. With only one African incidence report, it is clear that more work needs to be done to understand the emerging HIV epidemics in African MSM.

The available epidemiological data must be interpreted with some caution. Probability and population-based sampling methods have been important in measuring HIV epidemics. Demographic and related household-based survey approaches have helped define HIV spread at community levels and provide important denominators for assessment of HIV prevalence and incidence densities.[20,21] These approaches are problematic for hidden and stigmatised populations, and for measures of socially constrained behaviours. Many of the key epidemiological and population-based studies of HIV in developing countries collect no measures of male same-sex behaviour, restricting our understanding of this component of global HIV.[11] When MSM risk assessment has been included, strong social response biases have often made such assessments unreliable. Size estimation of the numbers of MSM in any particular population have also been limited by the hidden nature of these men, heterogeneity in the populations, and low rates of participation (panel 2).[31,32]

These realities have led to many innovations in sampling, surveillance, and size estimation research in MSM. Past innovations have included the use of respondent-driven sampling, with its well described limitations, venue-day-time sampling, internet-based sampling, and the use of molecular methods for biological sampling. Size estimation approaches have included capture–recapture, multiplier methods, and the wisdom-of-the-crowd approach.[14] Although no single method or approach is ideal or sufficient, the body of evidence on HIV in MSM is nevertheless substantial and growing.

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Risks for HIV infection

Individual-level risks for HIV acquisition in MSM have been well documented, and include unprotected receptive anal intercourse, high frequency of male partners, high number of lifetime male partners, injection drug use, high viral load in the index partner, African-American ethnic origin (in the USA), and non-injection-drug use, including use of amphetamine-type stimulants (ATS).[33–35] Recent data suggest individual-level risks might be insufficient to explain the high transmission dynamics evident in MSM outbreaks, and that biological, couple, network-level, and community-level drivers might be crucial to understand why HIV transmission rates remain so high in MSM populations.[36] These factors might be crucial to understand why HIV prevalence rates in these men seem to have increased in the HAART era, both in settings where HIV epidemics are newly described or emerging and in settings where MSM have access to a broad range of HIV services, civil liberties, and organised and visible community structures.[10,37–39] Present understanding of the role of HAART is that new infections should decline in populations where more people have reduced likelihood of transmission because of the effect of HAART on viral load.[40]

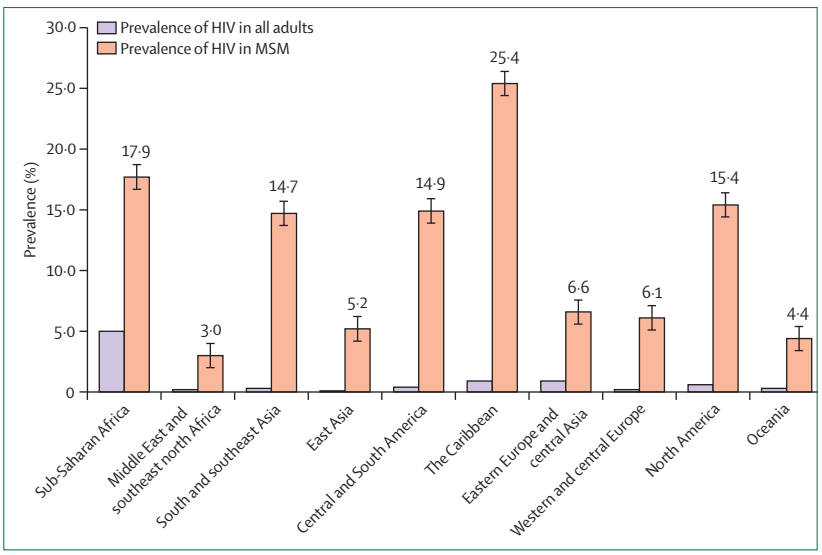

Figure 1: **Global prevalence of HIV in MSM compared with regional adult prevalence reported by UNAIDS, 2010**
We obtained prevalence estimates of HIV reported in MSM by country from reports published after 2007 from studies done during or after 2000. Prevalence in all adults was from UNAIDS 2010.[17] We include prevalence reported from biobehavioural surveillance without methods, sample size, or number positive in the prevalence map but not regional prevalence estimates. Error bars are 95% CIs. MSM=men who have sex with men.

A framework for characterising HIV epidemics in MSM in wider epidemiological contexts has been proposed.[8] This approach described four epidemiological scenarios for epidemics in MSM in low-income and middle-income countries. The first, primarily in South America, was characterised by MSM predominance—these men were the largest contributors to HIV prevalence in general populations with very low rates of infection. In the second scenario, which was found in eastern Europe and central Asia, epidemics in MSM were within HIV epidemics primarily driven by injection drug use. Epidemics in MSM during widespread epidemics in heterosexual people were generally evident in southern and eastern Africa, and here men had substantial HIV acquisition risks both from female and male partners. And finally epidemic contexts where heterosexual spread, sex work, MSM risks, and injection drug use were all contributors to HIV spread were evident in the complex epidemics of south and southeast Asia.

The role that sex with female partners might have in HIV risks for MSM has been studied in several populations. By contrast with widely held views, the data suggest that men who have sex with men and women have somewhat lower rates of HIV infection than men who only report sex with men.[41] These men might be more likely to use condoms with male partners than other MSM, or they might be less likely to engage in receptive anal intercourse than men who are willing to report exclusively male sex partners.[41–44]

ATS have been widely reported as risk factors mediating higher risk sexual practices in MSM, including recent reports from San Francisco (CA, USA)[45] and Bangkok (Thailand).[46] San Francisco MSM who self-reported stimulant use during sex were much more likely to report serodiscordant unprotected anal intercourse (UAI) compared with when no drug use.[45] In Bangkok, MSM reporting ATS use increased significantly from 3·6% in the previous three months in 2003 to 17·5% in 2005, and 20·8% in 2007 (p for trend <0·001). HIV prevalence in this cohort increased from 17·3% in 2003, to 28·3% in 2005, and 30·8% in 2007 (p for trend <0·001).[46] Of 595 young MSM in the USA aged 12–24 years, greater than 10% (64 of 595) reported recent ATS use.[47] Young MSM reporting drug use also reported higher risk sexual practices including serodiscordant sex, sex with an injecting drug user, and more sexual partners.[47]

Seroadaptive behaviours and risks

Seroadaptation, including serosorting and strategic or seropositioning, are strategies MSM have used as prevention approaches based on self and partner HIV status.[48] Serosorting refers to choosing HIV-concordant sex partners, whereas seropositioning refers to a choice of sex acts based on serostatus. These behaviours have not been rigorously assessed as HIV prevention approaches, and some might pose unintended risks for MSM when partner or sex-act choices reduce condom use.[49] It is well established that people with acute and early HIV infection are highly infectious, so men with a recent HIV negative test, yet newly infected, might be risky partners. Deliberate avoidance of condoms, or barebacking, is also a concern.

Barebacking was defined in 2004 as "intentional condomless anal sex in HIV-risk contexts".[50] Reports from US and UK studies, primarily through analysis of internet barebacking sites, suggested that some MSM, including men living with HIV, were deliberately seeking anal sex

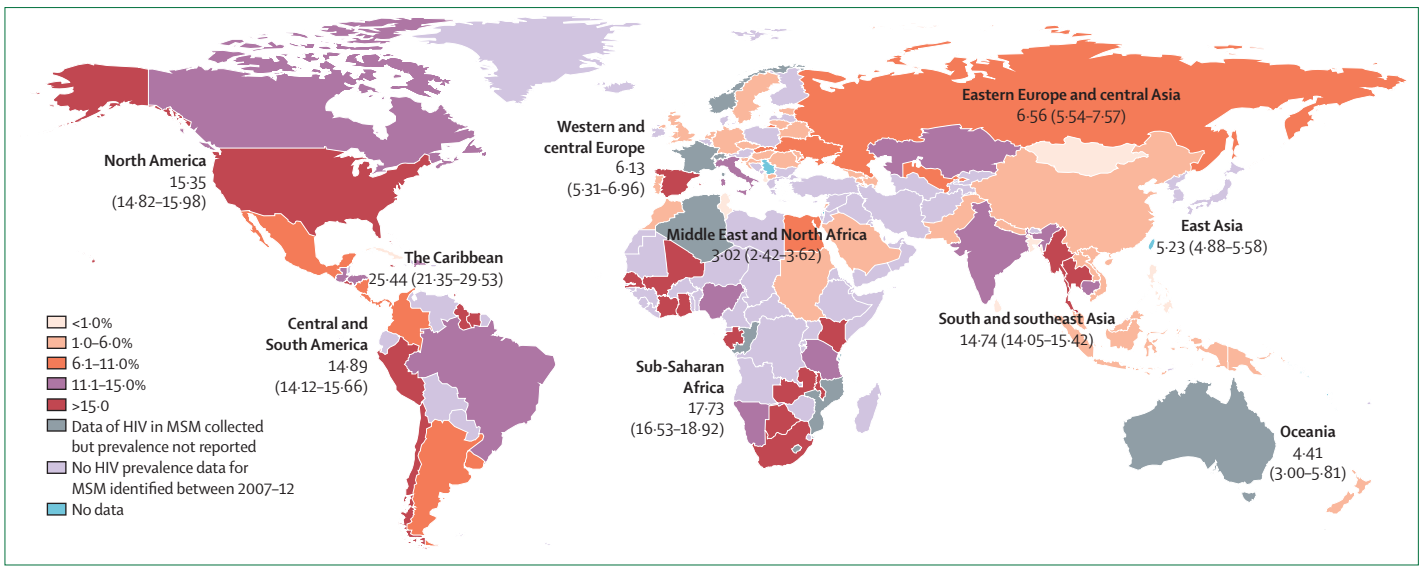

Figure 2: **Global HIV prevalence in MSM, from studies published 2007–11**
Data are prevalence (95% CIs). Sources listed in the appendix. MSM=men who have sex with men.

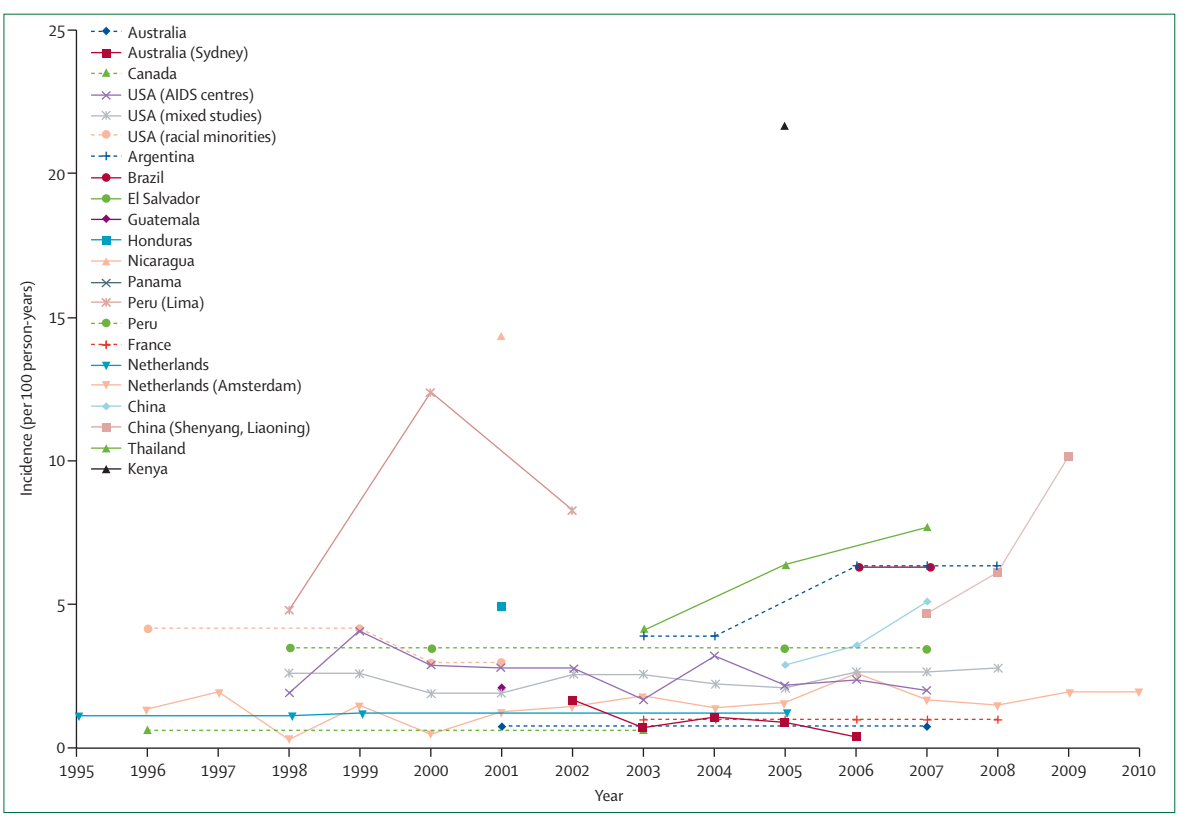

Figure 3: **HIV incidence in MSM populations, 1995–2010**
Dashed lines represent cohort studies that report only total incidence over the study period. Authors were contacted for yearly incidence but these data were not provided. MSM=men who have sex with men.

without condoms.[51,52] Barebacking in HIV concordant sex partners was associated with transmission of other sexually transmitted infections (STIs) and with superinfection of HIV-positive MSM—transmissions that might include drug-resistant HIV variants.[53,54] A 2009 meta-analysis of US studies[55] identified that most

MSM who were aware of their HIV status protected partners from HIV infection, but that condomless sex was more common between HIV-positive partners, at some 30% (95% CI 25–36). A consistent finding across US studies has been that ethnic minority MSM are less likely to engage in these risk behaviours than are other MSM.[55]

Network-level risks

In MSM, sexual-network-level risks can be both important drivers of HIV spread and key entry points for the delivery of interventions.[56–58] Larger networks can provide more opportunity for exposure to varied sexual practices and HIV-positive potential partners. In a study of Australian MSM,[59] the number of reported anal sex partners was higher with increased size and decreased network density (odds ratio [OR] 0·014, 95% CI 0·002–0·008). Larger sexual networks have also been associated with increased reporting of UAI in MSM in Shanghai, China.[60,61] These findings are consistent with studies of US MSM where social networks have been associated with a greater number of male partners (p=0·03) and transactional sex (p=0·0009).[62] These network-level risks might have particularly important roles for ethnic and racial minority MSM communities, including black MSM in Canada, the UK, and the USA.[47]

Structural risks

Structural factors can also mediate risks for HIV acquisition and transmission in MSM. Although structural risk factors are the least studied of risk factors for HIV in epidemiological assessments, they are relevant targets for prevention in many contexts.[37] In many high-income settings, ethnic and racial minority MSM carry a disproportionate burden of HIV.[63] These issues are explored in the fifth report in *The Lancet* HIV in MSM Series,[64] which shows that the increased burden of disease is not explained by higher risk sexual practices in these men.[65,66] Rather, black MSM seem to have higher rates of untreated STIs (OR 1·64, 95% CI 1·07–2·53), and HIV-positive black MSM are less likely to be aware of their serostatus and less likely to be taking antiretrovirals (0·43, 0·30–0·61) compared with white MSM.[63,67,68] Since antiretroviral use and access is low in black MSM, we would expect mean community viral load to be higher in sexual networks in black MSM compared with those in white MSM. Also, higher rates of untreated STIs within these sexual networks would facilitate transmission in cases of similar levels of condom use. Higher prevalence of STIs and undiagnosed HIV infection are markers of suboptimum access to health care.[69] The lack of access to clinically competent and appropriate health care has also been noted to reduce HIV-related health-seeking behaviour in African MSM. In a study of MSM in Botswana, Malawi, and Namibia,[70] any interaction with health care was associated with MSM reporting fear of seeking health care (2·6, 1·6–3·9), having been denied health-care services (6·4, 2·5–16·1), and having been blackmailed (2·1, 1·4–3·2).[70] Decreases in health-seeking behaviour because of human rights abrogation have also been reported from Lesotho, Senegal, and South Africa.[71–73]

***Panel 2:* Sampling, biases, and innovations for MSM HIV surveillance and research**

In earlier years of the HIV epidemic, non-probability methods such as convenience and snowball sampling were commonly used for research and surveillance in men who have sex with men (MSM), injecting drug users, and sex workers.[22] In convenience sampling, study participants are drawn from segments of the population accessible to researchers. During snowball sampling, individuals are asked to refer their peers with similar risk characteristics. Both methods are subject to selection bias and study results cannot be generalised. However, over the past two decades substantial progress has been made in creating alternative sampling frames that allow random sampling and can yield probability estimates of hard-to-reach population variables. Venue-day-time (VDT) sampling uses a sampling framework based on counts of venue visits of populations of interest (from MSM venues such as bars, clubs, saunas, and others) in specified timeframes.[23] First, VDT units are randomly or otherwise selected, with subsequent random or other sampling of venue attendees for study purposes. Data obtained need adjustment for clustering effects and must be weighted for the frequency of venue attendance of enrollees.[23]

Respondent-driven (RD) sampling elaborates on traditional snowball sampling with several mathematical procedures.[24] Although the sampling of participants is non-random, investigators have suggested that study results become generalisable when a sample reaches a specific equilibrium state, such that distributions on key variables of interest remain stable despite accrual of additional participants.[25,26] At this equilibrium point, additional waves of recruitment will no longer change or add to the demographic composition of samples. Since RD sampling will generally oversample people with large network sizes, data should be weighted for individual network sizes of participants.[25,26]

More recently, the internet has provided ample opportunities to access and research previously hard-to-reach and hidden populations in relative privacy and anonymity. Both VDT and RD sampling and several other methods and approaches are being adapted at present for use via the internet.[27–30] Nevertheless, the fundamental problems of research in hard-to-reach populations at risk for HIV infection remain, such as the absence of proper sampling frames, the lack of probabilistic sampling methods, and the resultant restricted generalisability of study findings.

Biological factors

The biology of anal sex, the gut tropism of HIV-1,[74] and the practices and behaviours associated with anal sex, might at least partly explain the high transmission efficiency of HIV infection for this practice. A recent systematic review and meta-analysis of HIV transmission risks in anal sex[24] reported a 1·4% per-act probability (95% CI 0·2–2·5) of transmission for anal sex and a 40·4% per-partner probability (6·0–74·9).[24] Per-act probabilities did not differ for MSM or heterosexual anal sex. The 1·4% per-act probability is roughly 18-times greater than that which has been estimated for vaginal intercourse.[75] This review also noted that per-partner risks for infection were similar for people reporting exclusive unprotected receptive anal intercourse and both unprotected receptive and insertive anal intercourse—common behavioural patterns for most MSM worldwide. Only self-reporting of exclusive unprotected

insertive anal intercourse had lower, but still substantial, per-partner risks: 21·7% (0·2–43·3).[24]

In addition to the high per-act and per-partner probability of infection noted in receptive anal sex, the likelihood that significant proportions of MSM engage in both receptive and insertive anal sex might have a crucial role in enhancing the efficiency of HIV spread within MSM networks, as opposed to heterosexual ones.[75,76] In networks of heterosexual spread, insertive and receptive roles are biologically determined and transmission probabilities from women to men might be lower, and can be reduced further with male circumcision. For MSM, uniquely, the relatively low HIV acquisition probability for insertive anal sex can be overcome in MSM populations since individual MSM can become infected through receptive sex and then transmit through insertive sex. It might also be relevant that substantial proportions of MSM—including high-risk subsets such as young MSM, men who use stimulants or alcohol with sex, and MSM who trade or sell sex—might have more partners than is common in other sexually active groups.[4] High rates of acute HIV infection in MSM might further drive incidence, since acute and recently infected people can be more infectious.[77] And male dyads might have substantial rates of extra-dyadic sex partners.[34]

STIs have also been associated with biological risk for HIV infection in MSM, notably syphilis and infection with herpes simplex virus type 2, and more recently, anal infection with human papillomavirus.[78] For MSM, oropharyngeal and anal STIs can also be associated with HIV infection. Infection with hepatitis C virus is also sexually transmitted between men, and might be facilitated by HIV co-infection in MSM.[79] The hidden and stigmatised nature of male same-sex behaviour in many settings might limit access to STI treatment and care for MSM and exacerbate the biological role of undiagnosed and untreated STIs.[70] Higher rates of undiagnosed and untreated syphilis have been reported,[63] and associated with the substantially higher rates of HIV infection noted in US black MSM.[63] Fear of discrimination and blackmail has been associated with reducing willingness to seek care for STIs in MSM in a three-country study in southern Africa.[70]

Adult-male circumcision has been shown to reduce men's risk of acquiring HIV infection from women by roughly 60% in three African trials.[80–82] The epidemiological evidence for circumcision and HIV risk in MSM has been inconsistent.[83,84] This is presumably because receptive anal intercourse, where a man's own circumcision status is irrelevant, has such a higher per-act transmission probability than anal or vaginal insertive sex.[24] MSM who engage only in insertive sex with other men are a minority, but such practice might plausibly lower their risk of HIV acquisition if circumcised. No trial of circumcision in MSM has been done. One large prospective study in MSM in the USA[85] recorded lack of circumcision associated with incident HIV infection after adjustment for sexual practices and substance use (adjusted OR 2·0, 95% CI 1·1–3·7), but a large study of black and hispanic MSM in the USA did not identify any protection in circumcised MSM.[86] The Sydney Health in Men cohort study[87] also did not identify differences in HIV acquisition by circumcision status in homosexual men.[87] In a subsequent analysis of these data assessing men with higher insertivity ratios (a higher proportion of reported insertive sex) a slight protective effect was noted for circumcision.[88] In the only African study of circumcision status and HIV risk in MSM,[89] the investigators reported lower HIV prevalence in circumcised MSM (adjusted OR 0·2, 95% CI 0·1–0·2); however, most also reported female sex partners.

Molecular epidemiology of HIV-1 in MSM

Recent reports from molecular epidemiology, phylodynamic studies, and HIV virology are providing insights into transmission and acquisition risks for MSM, transmission dynamics in MSM networks, and challenges to HIV prevention for these men. In a 2008 report on HIV transmission dynamics across the city of London,[38] episodic bursts of transmission in large linked clusters were identified as characteristics of transmission within MSM populations.[38] About 25% of all HIV infections in MSM were linked to one of several clusters. Later work noted that only 5% of infections in UK heterosexuals were similarly linked, and that infections were spreading much more slowly within heterosexual networks than homosexual ones.[90] Investigators who used single-genome amplification and a model of viral evolution in a cohort of acutely infected US MSM[91] noted that MSM were more than twice as likely as heterosexually exposed people to be infected with multiple HIV viruses (p=0·042). They also reported on the other available studies (n=5), which showed that this substantially higher rate of multiple-variant transmission held for MSM compared with heterosexual samples (p=0·008), and that 38% of acutely infected MSM had multiple variants. The investigators attributed this higher rate to the epidemiological risks these men reported: receptive anal intercourse with many partners and the differing anatomical and immunohistological characteristics of the male and female genital tracks and the lower gastrointestinal tract.[91] Greater genetic variation in infection, faster spread in networks, and clustering of HIV infections in high-transmission bursts are clearly features of real relevance for understanding the epidemiology of HIV in MSM.

Figure 4 shows the results of a HIV-1 molecular epidemiology search in MSM (search strategy in appendix). HIV-1 subtype data were available for MSM samples in 14 countries, including at least three in Africa, the Americas, Asia, and western Europe. For North and South America, and for western Europe, subtype B continues to predominate in MSM (figure 4). This seems to be the case despite many reports of increasing non-B subtype variants in heterosexual transmission cases in

Europe, largely attributable to HIV cases in African migrant populations to Europe.[90,92] Several reports from Europe, the UK, and the USA noted high levels of clustering of MSM sequences, suggesting dense networks of spread.[38,90,91] Clustering of infections has been significantly associated with visiting bath houses,[93] group sexual exposures,[91] homosexual versus heterosexual network membership,[94,95] and younger age.[95]

For Africa, where data were restricted to Kenya, Senegal, and South Africa, the mix of HIV variants in MSM seemed similar to those variants circulating in the wider population of those at risk in each country, which suggested local spread.[96,97] In the multiethnic MSM population of Cape Town (South Africa) and surrounding township communities, an early segregation of HIV subtypes by race and risk group was reported in the 1980s, with B-clade infection recorded in white gay men, and C-clade infections in African heterosexual populations. This segregation seems to have changed. Reports on subtypes in Cape Town MSM identified clade-C variants in 92% of black MSM, 69% of so-called Cape Coloured MSM, and 36% of white MSM, suggesting substantial bridging across these populations.[97]

For Asia the situation is somewhat more complex. Subtype B predominated in Mongolia, in Beijing in 2007, and in Taiwan,[93,98,99] but more recent reports from China suggested an increase in non-B-clade infections in MSM with an increase in the CRF01_AE subtype predominant in southeast Asia.[100] In Thailand and in Singapore, the CRF01_AE virus predominates in all populations, and also accounted for most infections in MSM.[95,96] Although subtype C predominates in India, there have been no recent reports that disaggregated HIV variants by risk group for that large population.

Taken together, these notably incomplete findings suggest several patterns for MSM. First, in the northern hemisphere, and in the Americas overall, subtype B continues to predominate in MSM and to circulate with substantial clustering in large MSM networks. In Africa and Asia, outbreaks in MSM seem more embedded within wider epidemic contexts, with the subtypes in MSM generally related to the diversity of epidemic contexts, with some variation in proportions of infections by risk category.

Modelling HIV risk in MSM

We developed a stochastic agent-based network simulation model of HIV transmission to show the size of some key drivers of HIV epidemics for MSM discussed above (details given in the appendix). These drivers include the high per-act transmission rate for anal sex relative to vaginal sex; the unique ability for MSM to be role versatile within high-transmission acts; and the existence of high numbers of partners within a subset of the population. The model thus shares some goals of previous work (Goodreau SM, unpublished), but extends it into a much more detailed modelling framework for both the underlying biology and behaviour. This framework was originally developed and parameterised for the Prevention Umbrella for MSM in the Americas (PUMA) project (Goodreau SM, unpublished). Since some of these are inherent to MSM, the model is not meant to be an explicit representation of any specific intervention. Rather, it is structured as a counterfactual experiment—eg, if anal sex were as infectious as vaginal sex, with all other things being equal, how much smaller would the HIV epidemic be in specific populations of MSM? Country-specific model inputs include demographics: sexual behaviours within main and casual partnerships, circumcision

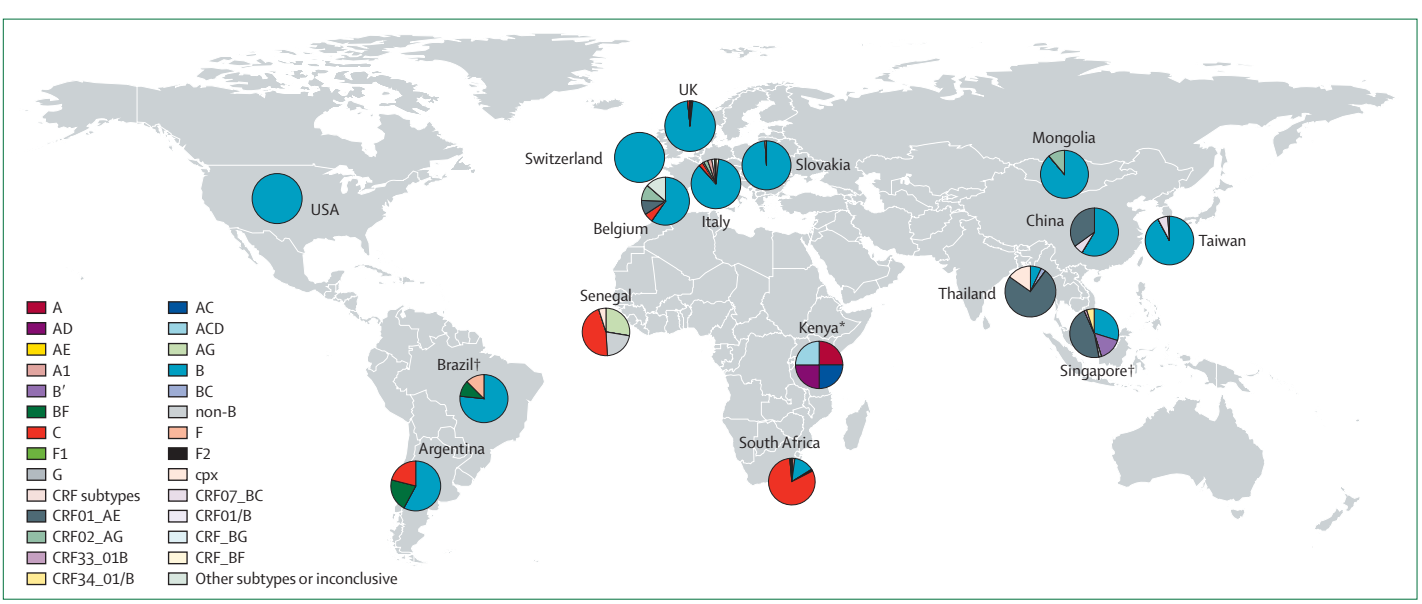

Figure 4: **Molecular epidemiology of HIV subtypes in MSM, 2007–11**
Study details and references in the appendix. MSM=men who have sex with men. *Proportions by subtype not reported. †Proportions for all samples, MSM proportions not reported.

prevalence, testing frequencies, and existing treatment levels. The model was first parameterised with multiple datasets from urban USA (a high-income country) and urban Peru (a middle-income country). We then considered additional scenarios in which testing and treatment were both much less common (both at a third of present levels), as an attempt to roughly represent the situation in low-income countries with low access or use of health services by MSM. We ran all models with an initial prevalence of 15%, similar to worldwide HIV prevalence for MSM. We repeated the exercise for other initial prevalence values, with qualitatively similar results (not shown). Initial population size for all runs was 5000 men in each country.

We computed the cumulative number of infections over a 5 year period for our baseline model, and for each counterfactual scenario. We then calculated the fraction of infections attributable to each factor by comparing the proportion reduction in cumulative incidence from baseline to counterfactual. Specific scenarios we considered were those in which transmission rates for unprotected anal sex were lowered to match those for unprotected vaginal sex; scenarios where all men were restricted to a specific role (50% insertive and 50% receptive); the combination of these first two scenarios; and a scenario where all casual UAI was replaced by an equal amount of UAI within the setting of new main partnerships, the duration and UAI frequency for these new main partnerships matched values noted in the main partners data, and the number of partnerships added was that needed to maintain the overall amount of UAI from baseline. We summarise our findings in figure 5.

The greatest reductions were associated with the scenarios that entailed reducing transmission probabilities to those of vaginal intercourse; in all settings, this quickly reduced incidence by greater than 80%, and in some by as much as 98%. This emphasises that the biological factors specific to anal sex have a fundamental effect in driving HIV epidemics in MSM worldwide. The ability of MSM to be role versatile also predisposes them to large epidemics—removing this practice so as to mimic a heterosexual population in this regard reduced incidence by 19–55%, although we recognise that changing sexual practices on the scale needed to see these effects is an unrealistic prevention goal. This metric revealed major differences by setting, since role versatility is much more prevalent in US MSM than Peruvian MSM. The existence of high casual numbers of UAI partners for some men also facilitates HIV transmission, but to a lower extent than the specific biological factors of anal sex, and about as much as the existence of role versatility. Converting all casual UAI into the same amount of UAI within long-term main partnerships reduced HIV prevalence by 29–51%. Here too there were regional differences, with HIV prevalence dropping more in the high prevalence Peru scenario than the US one, since a higher proportion of UAI happens within the context of casual contacts in Peru than in the USA.

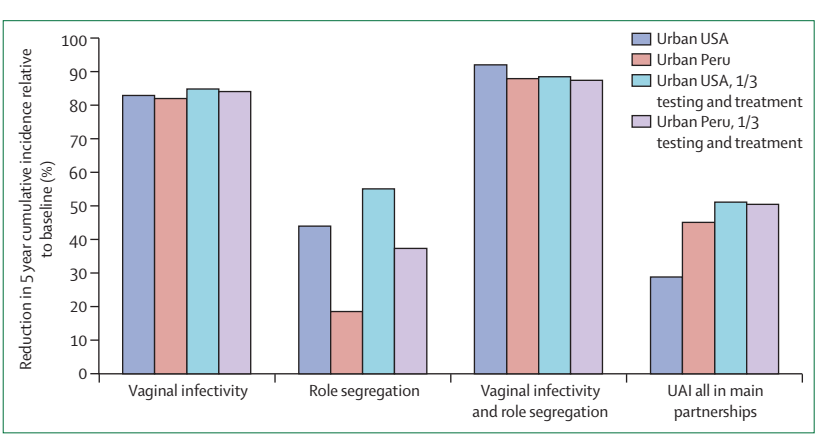

Figure 5: **Agent-based stochastic modelling results for HIV infection in MSM in urban Peruvian and urban US scenarios**

Percent reduction in cumulative incidence for each scenario and location, for runs with 15% initial prevalence. In the role segregation scenario, all men are assigned fixed and mutually exclusive roles in anal sex, 50% insertive and 50% receptive, mimicking heterosexual networks. MSM=men who have sex with men. UAI=unprotected anal intercourse.

Public health significance

Our findings on the epidemiology of HIV in MSM have many implications for HIV prevention, treatment, and care. The second[101] and third[102] reports in this Series will address these implications in detail and propose a targeted set of interventions for prevention for these men. First, the high transmission probability, high force of infection, and the potent effect of prevalent HIV infections in networks clearly suggest that interventions to reduce infectiousness, such as HAART for HIV-positive MSM, will probably be essential to achieve control of these epidemics. Our modelling outputs suggest that even substantial behaviour change, such as reductions in extra-primary partnerships, would not reduce transmission frequency enough to control HIV incidence in MSM networks. Interventions that reduced the probability of acquisition for men engaging in unprotected receptive anal intercourse, such as oral pre-exposure prophylaxis, rectal microbicide, or successful treatment for prevalent HIV infections, will probably be key. The high burden of infections in MSM demands more vigorous and scientifically informed responses, and the development and implementation of strategies to address the high biological risks associated with anal sex.

The molecular epidemiology of HIV in MSM also has several important implications for public health. An HIV vaccine based on subtype B (assuming subtypes, as currently understood, have roles in vaccine design) would have wide applicability in Europe, North and South America, and parts of Asia. This reality has already been of proven use to HIV vaccine trials.[85] The CRF01_AE component, proposed for trials in MSM in Thailand, would protect against an additional and substantial proportion of infections in MSM in Asia. The apparent clustering of transmission events in MSM, the speed with which HIV can move through MSM networks, and the reported high heterogeneity of HIV in acute infections in MSM might be

a challenge to HIV vaccines for this route of exposure. That daily oral pre-exposure prophylaxis with a combination of emtricitabine and tenofovir disoproxil fumarate is so far the only biomedical intervention with evidence for efficacy in MSM[102] suggests that this intervention might address these dynamics and might eventually be combined with vaccine strategies. Viral suppression within high-density networks of MSM might also be an approach fit to the molecular epidemiology of MSM transmission.

However, the public health importance of our new understanding might be affected by several important factors. First, the available data for HIV prevalence and incidence in MSM remain incomplete, with only one incidence estimate from Africa, two from Asia, and very few prospective cohorts of MSM in any setting. More than 30 years after the discovery of a viral infection in this population, 93 countries have no available reports on MSM in the past 5 years. What data we do have are hampered by the lack of population-based measures of the prevalence of same-sex behaviours in men, the size of the populations at risk, and the great diversity of these populations in differing social, cultural, and political contexts. Social response biases against reporting some behaviours, including receptive anal sex, are likely to affect risk factor assessment.

Improved size estimation approaches are urgently needed. Encouragingly, these limitations have led to a range of innovations in epidemiology and are proving of use to the description of other hidden, stigmatised, or otherwise hard-to-reach populations.[103,104]

Other biases in the global evidence base include the disproportionate urban sampling of MSM populations, the relative lack of data from the Middle East and north African region, and the lack of data for adolescents in sexual and gender minorities, who are systematically undersampled in most contexts. What data are available on younger MSM suggest that they are high-incidence groups in need of targeted interventions, and that waiting until they are aged 18 years, or older, is, as with girls in many high-risk transmission contexts, inadequate to protect them against early acquisition of HIV.[105]

If HIV infection in MSM is heavily biologically determined, do present approaches to HIV programming for MSM, which rely heavily on information, education, and behaviour change strategies, make sense? The epidemiology suggests that urgent reform is needed. Programmes and research efforts need to be informed by the realities of HIV transmission risks for MSM. The reduction of those risks will probably need combination approaches, the use of antiretrovirals for both treatment and prevention, and much greater understanding of why these men, their networks, and their communities, continue to bear such heavy burdens of HIV. HIV remains uncontrolled in MSM in 2012. This reality demands reinvigorated effort, new approaches grounded in biology and epidemiology, and concerted effort to reduce the structural risks that aid and abet HIV spread in these men.

Contributors

CB, RB, and FvG designed the study. SDB, ALW, and CB searched for and reviewed published work. ALW and SDB produced the figures. SDB and ALW assessed the systematic review. SMG did the mathematical modelling. CB, RB, and FvG were involved in the interpretation and writing of the report.

Conflicts of interest

We declare that we have no conflicts of interest.

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References

1 Doll LS, Petersen LR, White CR, Ward JW, The Blood Donor Study Group. Homosexuality and non-sexually identified men who have sex with men: a behavioral comparison. *J Sex Res* 1992; **29:** 1–14.

2 Gonsiorek JC, Sell RL, Weinrich JD. Definition and measurement of sexual orientation. *Suicide Life Threat Behav* 1995; **25:** 40–51.

3 Baral S, Sifakis F, Cleghorn F, Beyrer C. Elevated risk for HIV infection among men who have sex with men in low and middle income countries 2000–2006. *PLoS Med* 2007; **4:** e339.

4 van Griensven F, de Lind van Wijngaarden JW, Baral S, Grulich A. The global epidemic of HIV infection among men who have sex with men. *Curr Opin HIV AIDS* 2009; **4:** 300–07.

5 CDC. Follow-up on Kaposi's sarcoma and *Pneumocystis* pneumonia. *MMWR Morb Mortal Wkly Rep* 1981; **30:** 409–10.

6 CDC. Kaposi's sarcoma and *Pneumocystis* pneumonia among homosexual men—New York City and California. *MMWR Morb Mortal Wkly Rep* 1981; **30:** 305–08.

7 CDC. *Pneumocystis* pneumonia—Los Angeles. *MMWR Morb Mortal Wkly Rep* 1981; **30:** 250–52.

8 Beyrer C, Baral S, Walker D, Wirtz A, Johns B, Sifakis F. The expanding epidemics of HIV-1 among men who have sex with men in low and middle income countries: diversity and consistency. *Epidemiol Rev* 2010; **32:** 137–51.

9 CDC. Prevalence and awareness of HIV infection among men who have sex with men—21 cities, United States, 2008. *MMWR Morb Mortal Wkly Rep* 2010; **59:** 1201–07.

10 Sullivan P, Hamouda O, Delpech V, et al. Reemergence of the HIV epidemic among men who have sex with men in North America, western Europe, and Australia, 1996–2005. *Ann Epidemiol* 2009; **19:** 423–31.

11 Beyrer C, Wirtz A, Walker D, Johns B, Sifakis F, Baral S. The global HIV epidemics among men who have sex with men. Washington, DC: The World Bank, 2011.

12 Mumtaz G, Hilmi N, Akala FA, et al. HIV-1 molecular epidemiology evidence and transmission patterns in the Middle East and north Africa. *Sex Transm Infect* 2011; **87:** 101–06.

13 Mumtaz G, Hilmi N, McFarland W, et al. Are HIV epidemics among men who have sex with men emerging in the Middle East and north Africa?: a systematic review and data synthesis. *PLoS Med* 2010; **8:** e1000444.

14 Luan R, Zeng G, Zhang D, et al. A study on methods of estimating the population size of MSM in southwest China. *Eur J Epi* 2005; **20:** 581–85.

15 Marcus U, Schmidt AJ, Kollan C, Hamouda O. The denominator problem: estimating MSM-specific incidence of STI and prevalence of HIV using population sizes of MSM derived from Internet surveys. *BMC Public Health* 2009; **11:** 181.

16 Cassels S, Clark S, Morris M. Mathematical models for HIV transmission dynamics: tools for social and behavioral science research. *J Acquir Immune Defic Syndr* 2008; **47** (suppl 1)**:** S34–39.

17 UNAIDS. Report on the global AIDS epidemic—2010. Geneva: UNAIDS, 2010. http://www.unaids.org/globalreport/global_report.htm (accessed April 24, 2012).

18 McAllister SM, Dickson NP, Sharples K, et al. Unlinked anonymous HIV prevalence among New Zealand sexual health clinic attenders: 2005–2006. *Int J STD AIDS* 2008; **19:** 752–57.

19 Sanders EJ, Okuku HS, Mwangome M, et al. Risk factors for HIV-1 infection among MSM in coastal Kenya. 18th Conference on Retroviruses and Opportunistic Infections; Boston, MA, USA; Feb 27–March 2, 2011. Abstract 1042.

20 WHO. HIV/AIDS: data and statistics. http://www.who.int/hiv/data/en/ (accessed April 24, 2012).

21 UNAIDS. Data and analysis. http://www.unaids.org/en/dataanalysis/ (accessed April 24, 2012).

22 Faugier J, Sargeant M. Sampling hard to reach populations. *J Adv Nurs* 1997; **26:** 790–97.

23 Semaan S. Time-space sampling and respondent driven sampling with hard-to-reach populations. *Methodological Innov Online* 2010; **5:** 60–75.

24 Baggaley R, White R, Boily M. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *Int J Epidemiol* 2010; **39:** 1048–63.

25 Heckathorn D. Respondent-driven sampling: a new approach to the study of hidden populations. *Soc Probl* 1997; **44:** 174–99.

26 Heckathorn D. Respondent-driven sampling II: deriving valid population estimates from chain-referral samples of hidden populations. *Soc Probl* 2002; **49:** 11–34.

27 Guo Y, Li X, Fang X, et al. A comparison of four sampling methods among men having sex with men in China: implications for HIV/STD surveillance and prevention. *AIDS Care* 2011; **23:** 1400–09.

28 Evans AR, Hart GJ, Mole R, et al. Central and east European migrant men who have sex with men in London: a comparison of recruitment methods. *BMC Med Res Methodol* 2011; **11:** 69.

29 Sullivan PS, Khosropour CM, Luisi N, et al. Bias in online recruitment and retention of racial and ethnic minority men who have sex with men. *J Med Internet Res* 2011; **13:** e38.

30 Johnston LG, Trummal A, Lohmus L, Ravalepik A. Efficacy of convenience sampling through the internet versus respondent driven sampling among males who have sex with males in Tallinn and Harju County, Estonia: challenges reaching a hidden population. *AIDS Care* 2009; **21:** 1195–202.

31 Lieb S, Trepka MJ, Thompson DR, et al. Men who have sex with men: estimated population sizes and mortality rates by race/ethnicity, Miami-Dade County, Florida. *J Acquir Immune Defic Syndr* 2007; **46:** 485–90.

32 McGarrigle CA, Cliffe S, Copas AJ, et al. Estimating adult HIV prevalence in the UK in 2003: the direct method of estimation. *Sex Transm Infect* 2006; **82** (suppl 3)**:** iii78–86.

33 German D, Sifakis F, Maulsby C, et al. Persistently high prevalence and unrecognized HIV infection among men who have sex with men in Baltimore: the BESURE Study. *J Acquir Immune Defic Syndr* 2011; **57:** 77–87.

34 Rosenberg ES, Sullivan PS, Dinenno EA, Salazar LF, Sanchez TH. Number of casual male sexual partners and associated factors among men who have sex with men: results from the National HIV Behavioral Surveillance system. *BMC Public Health* 2011; **11:** 189.

35 Koblin B, Husnik M, Colfax G, et al. Risk factors for HIV infection among men who have sex with men. *AIDS* 2006; **20:** 731–39.

36 Goodreau SM, Golden MR. Biological and demographic causes of high HIV and sexually transmitted disease prevalence in men who have sex with men. *Sex Transm Infect* 2007; **83:** 458–62.

37 Beyrer C. Global prevention of HIV infection for neglected populations: men who have sex with men. *Clin Infect Dis* 2010; **50** (suppl 3)**:** S108–13.

38 Lewis F, Hughes G, Rambaut A, Pozniak A, Leigh Brown A. Episodic sexual transmission of HIV revealed by molecular phylodynamics. *PLoS Med* 2008; **18:** e50.

39 Le Vu S, Le Strat Y, Barin F, et al. Population-based HIV-1 incidence in France, 2003–08: a modelling analysis. *Lancet Infect Dis* 2010; **10:** 682–87.

40 Charlebois ED, Das M, Porco TC, Havlir DV. The effect of expanded antiretroviral treatment strategies on the HIV epidemic among men who have sex with men in San Francisco. *Clin Infect Dis* 2011; **52:** 1046–49.

41 Beyrer C, Trapence G, Motimedi F, et al. Bisexual concurrency, bisexual partnerships, and HIV among southern African men who have sex with men. *Sex Transm Infect* 2010; **86:** 323–27.

42 Sanders EJ, Graham SM, Okuku HS, et al. HIV-1 infection in high risk men who have sex with men in Mombasa, Kenya. *AIDS* 2007; **21:** 2513–20.

43 Caceres CF, Konda KA, Salazar X, et al. New populations at high risk of HIV/STIs in low-income, urban coastal Peru. *AIDS Behav* 2008; **12:** 544–51.

44 Konda KA, Lescano AG, Leontsini E, et al. High rates of sex with men among high-risk, heterosexually-identified men in low-income, coastal Peru. *AIDS Behav* 2008; **12:** 483–91.

45 Colfax G, Santos GM, Chu P, et al. Amphetamine-group substances and HIV. *Lancet* 2010; **376:** 458–74.

46 van Griensven F, Varangrat A, Wimonsate W, et al. Trends in HIV prevalence, estimated HIV incidence, and risk behavior among men who have sex with men in Bangkok, Thailand, 2003–2007. *J Acquir Immune Defic Syndr* 2009; published online Nov 5. DOI:10.1097/QAI.0b013e3181c2fc86.

47 Freeman P, Walker BC, Harris DR, et al. Methamphetamine use and risk for HIV among young men who have sex with men in 8 US cities. *Arch Pediatr Adolesc Med* 2011; **165:** 736–40.

48 McFarland W, Chen YH, Raymond HF, et al. HIV seroadaptation among individuals, within sexual dyads, and by sexual episodes, men who have sex with men, San Francisco, 2008. *AIDS Care* 2011; **23:** 261–68.

49 Gorbach PM, Weiss RE, Jeffries R, et al. Behaviors of recently HIV-infected men who have sex with men in the year postdiagnosis: effects of drug use and partner types. *J Acquir Immune Defic Syndr* 2011; **56:** 176–82.

50 Carballo-Dieguez A, Bauermeister J. "Barebacking": intentional condomless anal sex in HIV-risk contexts. Reasons for and against it. *J Homosex* 2004; **47:** 1–16.

51 Halkitis PN, Wilton L, Wolitski RJ, Parsons JT, Hoff CC, Bimbi DS. Barebacking identity among HIV-positive gay and bisexual men: demographic, psychological, and behavioral correlates. *AIDS* 2005; **19** (suppl 1)**:** S27–35.

52 Elford J, Bolding G, Davis M, Sherr L, Hart G. Barebacking among HIV-positive gay men in London. *Sex Transm Dis* 2007; **34:** 93–98.

53 Paz-Bailey G, Meyers A, Blank S, et al. A case-control study of syphilis among men who have sex with men in New York City: association With HIV infection. *Sex Transm Dis* 2004; **31:** 581–87.

54 Smith DM, Richman DD, Little SJ. HIV superinfection. *J Infect Dis* 2005; **192:** 438–44.

55 Crepaz N, Marks G, Liau A, et al. Prevalence of unprotected anal intercourse among HIV-diagnosed MSM in the United States: a meta-analysis. *AIDS* 2009; **23:** 1617–29.

56 Kelly JA, Amirkhanian YA, McAuliffe TL, et al. HIV risk characteristics and prevention needs in a community sample of bisexual men in St Petersburg, Russia. *AIDS Care* 2002; **14:** 63–76.

57 Kelly JA, Amirkhanian YA, McAuliffe TL, et al. HIV risk behavior and risk-related characteristics of young Russian men who exchange sex for money or valuables from other men. *AIDS Educ Prev* 2001; **13:** 175–88.

58 Johnson W, Diaz R, Flanders W, et al. Behavioral interventions to reduce risk for sexual transmission of HIV among men who have sex with men. *Cochrane Database Syst Rev* 2008; **3:** CD001230.

59 Smith AMA, Grierson J, Wain D, Pitts M, Pattison P. Associations between the sexual behaviour of men who have sex with men and the structure and composition of their social networks. *Sex Transm Infect* 2004; **80:** 455–58.

60 Choi KH, Gibson DR, Han L, Guo Y. High levels of unprotected sex with men and women among men who have sex with men: a potential bridge of HIV transmission in Beijing, China. *AIDS Educ Prev* 2004; **16:** 19–30.

61 Choi KH, McFarland W, Neilands TB, et al. An opportunity for prevention: prevalence, incidence, and sexual risk for HIV among young Asian and Pacific Islander men who have sex with men, San Francisco. *Sex Transm Dis* 2004; **31:** 475–80.

62 Kelly JA, Amirkhanian YA, Seal DW, et al. Levels and predictors of sexual HIV risk in social networks of men who have sex with men in the midwest. *AIDS Educ Prev* 2010; **22:** 483–95.

63 Millett GA, Peterson JL, Wolitski RJ, Stall R. Greater risk for HIV infection of black men who have sex with men: a critical literature review. *Am J Public Health* 2006; **96:** 1007–19.

64 Millett GA, Jeffries WL IV, Peterson JL, et al. Common roots: a contextual review of HIV epidemics in black men who have sex with men across the African diaspora. *Lancet* 2012; published online July 20. http://dx.doi.org/10.1016/S0140-6736(12)60722-3.

65 Crosby R, Holtgrave DR, Stall R, Peterson JL, Shouse L. Differences in HIV risk behaviors among black and white men who have sex with men. *Sex Transm Dis* 2007; **34:** 744–48.

66 Magnus M, Kuo I, Phillips G 2nd, et al. Elevated HIV prevalence despite lower rates of sexual risk behaviors among black men in the District of Columbia who have sex with men. *AIDS Patient Care STDS* 2010; **24:** 615–22.

67 Oster AM, Wiegand RE, Sionean C, et al. Understanding disparities in HIV infection between black and white MSM in the United States. *AIDS* 2011; **25:** 1103–12.

68 Millett GA, Flores SA, Peterson JL, Bakeman R. Explaining disparities in HIV infection among black and white men who have sex with men: a meta-analysis of HIV risk behaviors. *AIDS* 2007; **21:** 2083–91.

69 White House Office of National AIDS Policy. National HIV/AIDS strategy for the United States. Washington, DC: US Government, 2011.

70 Fay H, Baral S, Trapence G, et al. Stigma, health care access, and HIV knowledge among men who have sex with men in Malawi, Namibia, and Botswana. *AIDS Behav* 2011; **15:** 1088–97.

71 Baral S, Burrell E, Scheibe A, Brown B, Beyrer C, Bekker LG. HIV risk and associations of HIV infection among men who have sex with men in peri-urban Cape Town, South Africa. *BMC Public Health* 2011; **11:** 766.

72 Poteat T, Diouf D, Drame FM, et al. HIV risk among MSM in Senegal: a qualitative rapid assessment of the impact of enforcing laws that criminalize same sex practices. *PLoS One* 2011; **6:** e28760.

73 Baral S, Adams D, Lebona J, et al. A cross-sectional assessment of population demographics, HIV risks and human rights contexts among men who have sex with men in Lesotho. *J Int AIDS Soc* 2011; **14:** 36.

74 Kaltsidis H, Cheeseman H, Kopycinski J, et al. Measuring human T cell responses in blood and gut samples using qualified methods suitable for evaluation of HIV vaccine candidates in clinical trials. *J Immunol Methods* 2011; **370:** 43–54.

75 Grulich A, Zablotska I. Commentary: probability of HIV transmission through anal intercourse. *Int J Epidemiol* 2010; **39:** 1064–65.

76 Goodreau SM, Peinado J, Goicochea P, et al. Role versatility among men who have sex with men in urban Peru. *J Sex Res* 2007; **44:** 233–39.

77 CDC. Acute HIV infection—New York City, 2008. *Morb Mortal Wkly Rep* 2009; **58:** 1296–99.

78 Chin-Hong PV, Husnik M, Cranston RD, et al. Anal human papillomavirus infection is associated with HIV acquisition in men who have sex with men. *AIDS* 2009; **23:** 1135–42.

79 Urbanus AT, van de Laar TJ, Stolte IG, et al. Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. *AIDS* 2009; **23:** F1–7.

80 Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet* 2007; **369:** 643–56.

81 Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* 2007; **369:** 657–66.

82 Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. *PLoS Med* 2005; **2:** e298.

83 Millett GA, Flores SA, Marks G, Reed JB, Herbst JH. Circumcision status and risk of HIV and sexually transmitted infections among men who have sex with men: a meta-analysis. *JAMA* 2008; **300:** 1674–84.

84 Vermund SH, Qian HZ. Circumcision and HIV prevention among men who have sex with men: no final word. *JAMA* 2008; **300:** 1698–700.

85 Buchbinder SP, Mehrotra DV, Duerr A, et al. Efficacy assessment of a cell-mediated immunity HIV-1 vaccine (the Step Study): a double-blind, randomised, placebo-controlled, test-of-concept trial. *Lancet* 2008; **372:** 1881–93.

86 Millett GA, Ding H, Lauby J, et al. Circumcision status and HIV infection among Black and Latino men who have sex with men in 3 US cities. *J Acquir Immune Defic Syndr* 2007; **46:** 643–50.

87 Templeton DJ, Jin F, Prestage GP, Donovan B, Imrie J, Kippax SC. Circumcision status and risk of HIV seroconversion in the HIM cohort of homosexual men in Sydney. 4th IAS Conference on HIV Pathogenesis, Treatment & Prevention; Sydney, NSW, Australia; July 22–25, 2007. Abstract WEAC103.

88 Templeton DJ, Jin F, Mao L, et al. Circumcision and risk of HIV infection in Australian homosexual men. *AIDS* 2009; **23:** 2347–51.

89 Lane T, Raymond HF, Dladla S, et al. High HIV prevalence among men who have sex with men in Soweto, South Africa: results from the Soweto Men's Study. *AIDS Behav* 2011; **15:** 626–34.

90 Hughes G, Fearnhill E, Dunn D, Lycett S, Rambaut A. Molecular phylodynamics of the heterosexual HIV epidemic in the United Kingdom. *PLoS Path* 2009; **5:** e1000590.

91 Li H, Bar K, Wang S, Decker J, Chen Y. High multiplicity infection by HIV-1 in men who have sex with men. *PLoS Path* 2010; **6:** e1000890.

92 Leoz M, Chaix ML, Delaugerre C, et al. Circulation of multiple patterns of unique recombinant forms B/CRF02_AG in France: precursor signs of the emergence of an upcoming CRF B/02. *AIDS* 2011; **25:** 1371–77.

93 Kao C, Chang S, Hsia K, et al. Surveillance of HIV type 1 recent infection and molecular epidemiology among different risk behaviors between 2007 and 2009 after the HIV type 1 CRF07_BC outbreak in Taiwan. *AIDS Res Hum Retroviruses* 2011; **27:** 745–49.

94 Kouyos RD, von Wyl V, Yerly S, et al. Molecular epidemiology reveals long-term changes in HIV type 1 subtype B transmission in Switzerland. *J Infect Dis* 2010; **201:** 1488–97.

95 Lee CC, Sun YJ, Barkham T, Leo YS. Primary drug resistance and transmission analysis of HIV-1 in acute and recent drug-naïve seroconverters in Singapore. *HIV Med* 2009; **10:** 370–77.

96 Arroyo MA, Phanuphak N, Krasaesub S, et al. HIV type 1 molecular epidemiology among high-risk clients attending the Thai Red Cross Anonymous Clinic in Bangkok, Thailand. *AIDS Res Hum Retroviruses* 2010; **26:** 5–12.

97 Middelkoop K, Williamson C, Rademeyer C, et al. HIV subtypes in MSM in Cape Town: evidence of bridging between epidemics. 6th IAS Conference on HIV Pathogenesis and Treatment; Rome, Italy; July 17–20, 2011. Abstract MOPE034.

98 Davaalkham J, Unenchimeg P, Baigalmaa C, et al. Identification of a current hot spot of HIV type 1 transmission in Mongolia by molecular epidemiological analysis. *AIDS Res Hum Retroviruses* 2011; **27:** 1073–80.

99 Zhang X, Wang C, Hengwei W, et al. Risk factors of HIV infection and prevalence of co-infections among men who have sex with men in Beijing, China. *AIDS* 2007; **21** (suppl 8)**:** S53–57.

100 Wang W, Jiang S, Li S, et al. Identification of subtype B, multiple circulating recombinant forms and unique recombinants of HIV type 1 in an MSM cohort in China. *AIDS Res Hum Retroviruses* 2008; **24:** 1245–54.

101 Mayer KH, Bekker L-G, Stall R, Grulich AE, Colfax G, Lama JR. Comprehensive clinical care for men who have sex with men: an integrated approach. *Lancet* 2012; published online July 20. http://dx.doi.org/10.1016/S0140-6736(12)60835-6.

102 Sullivan PS, Carballo-Diéguez A, Coates T, et al. Successes and challenges of HIV prevention in men who have sex with men. *Lancet* 2012; published online July 20. http://dx.doi.org/10.1016/S0140-6736(12)60955-6.

103 Malekinejad M, McFarland W, Vaudrey J, Raymond HF. Accessing a diverse sample of injection drug users in San Francisco through respondent-driven sampling. *Drug Alcohol Depend* 2011; **118:** 83–91.

104 Uuskula A, Johnston LG, Raag M, Trummal A, Talu A, Des Jarlais DC. Evaluating recruitment among female sex workers and injecting drug users at risk for HIV using respondent-driven sampling in Estonia. *J Urban Health* 2010; **87:** 304–17.

105 CDC. HIV prevalence among populations of men who have sex with men—Thailand, 2003 and 2005. *MMWR Morb Mortal Wkly Rep* 2006; **55:** 844–48.