

Global Prevention of HIV Infection for Neglected Populations: Men Who Have Sex with Men

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The global epidemiology of human immunodeficiency virus (HIV) infection among men who have sex with men (MSM) suggests both reemergent spread among men in resource-sufficient countries since 2000 and emerging epidemics among MSM in resource-limited countries. Both epidemic contexts are evidence of the current limits of prevention of HIV infection in MSM. A range of evidence-based preventive interventions exist, but few new interventions have shown efficacy among MSM. Circumcision has not been investigated for MSM. New interventions are needed. Trials of preexposure prophylaxis are pending and may markedly alter the prevention landscape. For MSM in developing countries, basic services for prevention of HIV infection have yet to reach the large majority of men. Homophobia and discrimination limit access of MSM to prevention services and markedly increase vulnerability, as does criminalization of same-sex behavior. Decriminalization of same-sex behavior is a structural intervention for prevention of HIV infection and has recently been embraced by a nonbinding statement from the United Nations.

In the third decade of the human immunodeficiency virus (HIV) and AIDS pandemic, we face a painful reality—although men who have sex with men (MSM) were among the first affected populations and, in well-resourced countries, communities of MSM were pioneers in prevention of HIV infection and behavior change, there is now evidence of multiple reemerging epidemics of HIV infection among these men [1, 2]. A recent analysis of data from 8 industrialized countries, including the United States, United Kingdom, the Netherlands, France, Germany, Spain, Australia, and Canada, found that, although the prevalence of diagnosis of HIV infection generally decreased from 1996 through 2000, diagnoses of HIV infection among MSM have increased by ~3% per year from 2000 through 2005 [2]. Marked increases in the rate of diagnosis of syphilis among MSM in 5 of these 8 countries over the same period suggest that at least some of the increase

in the prevalence of HIV infection was attributable to increases in sexual risk-taking behavior [2]. Among US MSM, a particular concern is the disproportionate burden of HIV infection among MSM of color, especially among African American MSM, who are at strikingly higher risk of HIV infection, even after controlling for individual-level sexual risk behaviors [3, 4]. Rates of undiagnosed HIV infection among black MSM are also strikingly higher than those among MSM of other race and ethnicity groups, suggesting that HIV testing, counseling services, and messages are failing to reach these men, even as rates of HIV infection increase [4].

In resource-limited countries, such as Dakar, Senegal, Bangkok, Thailand, and Peru, there is mounting evidence of emerging HIV epidemics among MSM, often in settings marked by discrimination, homophobia, and criminalization [5]. A recent systematic review by myself and colleagues identified high rates of HIV infection among MSM virtually in all areas where data were available (sub-Saharan Africa, Latin America and the Caribbean, southern and Southeast Asia, China, and the Russian Federation) [6]. It is perhaps most disturbing that these subepidemics among MSM are occurring in multiple settings where rates of HIV infection in the general population of reproductive-age adults are decreasing, where HIV infection has come under reason-

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able control (eg, Thailand and Senegal), or where HIV infection has never spread widely among heterosexual populations (eg, China and Mexico), but where, nevertheless, rates of infection among MSM are markedly high [6].

Whether these subepidemics in resource-limited countries represent recrudescence of HIV infection among MSM, ongoing epidemics that are only now being uncovered, or new subepidemics is unclear in many settings, particularly in the understudied MSM populations in sub-Saharan Africa, Asia, and the Middle East and North Africa. Indeed, surveillance data on MSM and, particularly, the data on incidence that would allow for study of epidemic trajectories, remain strikingly limited globally. Nevertheless, enough is known to prove that prevention of HIV infection in MSM is not achieving what is most urgently needed—stable and decreasing rates of new HIV infection among MSM and, particularly, among young MSM. Many arguments have been proposed for these prevention failures; they include treatment optimism in the era of highly active antiretroviral therapy, the emergence of the internet as a new risk environment for MSM, increasing understanding of the transmission risks associated with anal intercourse, and the structural failure to provide MSM with friendly services in the many developing countries.

We now understand that prevention of HIV infection throughout life for persons at risk is not simple and that explanations of prevention failures or the lack of uptake and use of existing prevention methods is likely to be no less complex and multifaceted. No single existing intervention appears to be effective on its own, and although combination prevention strategies are the norm in practice, they have only recently been rigorously evaluated [7]. It is also clear that, in multiple settings and communities of MSM, a range of community-generated prevention approaches are being used by men, including serosorting (ie, selecting partners on the basis of known or assumed HIV status), strategic positioning (ie, limiting receptive or insertive roles in anal intercourse on the basis of self or partner known or assumed HIV status), penile withdrawal before ejaculation, and “negotiated safety,” by which men in stable couples may agree to not use condoms and maintain either mutual fidelity or practice only protected extra-relationship sex. Most of these approaches to reduce risk of HIV infection have not been subjected for formal study, some may be ineffective, and some may increase health risks [8].

The landscape for prevention of HIV infection among MSM in resource-limited countries is even more problematic. The great majority of MSM in developing countries have yet to be reached by HIV prevention services; a recent Joint United Nations Programme on HIV/AIDS estimate shows that <1 in 5 MSM globally have access to the most basic interventions, such as information on risk of HIV infection in MSM and use of condoms [5]. It may make little sense to compare the high

transmission rates among urban US MSM with those associated with the explosive epidemic that has emerged among populations of MSM in resource-limited regions. However, it is hard not to see consistency in some of these situations. Furthermore, similar questions relating to services for prevention of HIV infection among MSM prevail. Do we have an effective toolkit of combination prevention strategies that is being underused, and if so, why? If we need additional tools, what is the status of development and roll-out of these new interventions?

EVIDENCE-BASED INTERVENTIONS: WHAT WE KNOW

Valdiserri et al [9] reviewed the evidence base for prevention of HIV infection in 2003 and identified 5 approaches with compelling evidence for success in prevention of sexual transmission. These included small group behavioral interventions, HIV counseling and testing, community-level interventions, structural interventions, and diagnosis and treatment of sexually transmitted infections (STIs). Male circumcision should now be added to this list, at least for heterosexual men in African epidemic settings [10, 11, 12]. Each of these interventions (besides circumcision) has been used with some success for MSM, and of note, each has been a part of prevention services for many years. Indeed, the existing toolkit for prevention of HIV infection in MSM has changed surprisingly little over the past decades. The primary risk for acquisition remains unprotected receptive anal intercourse, and the primary risk for transmission is unprotected insertive anal intercourse; therefore, these continue to be the focus of interventions. Condom promotion and distribution are primary prevention measures, as is use of water-based lubricants, which are particularly important for the naturally unlubricated anal skin (and which remain expensive and difficult to access in much of the world). Behavioral interventions are by far the most studied, and the goal of most of these interventions has been a reduction in the risk-taking behavior involved in anal intercourse; thus, condom and lubricant use are also part of the final common pathway for these interventions. Strategies based on HIV testing and counseling have been extensively evaluated for MSM and remain a focus of new operational research efforts. Other evidence-based approaches include treatment of other STIs, including diagnosis and treatment of rectal and oropharyngeal STI in MSM, and the development of MSM-friendly STI and voluntary counseling and testing services, which combine elements of both STI and voluntary counseling and testing and structural interventions [13].

A recent review by Johnson et al [8] assessed behavioral interventions for reduction of sexual risks among MSM, with a primary focus on studies aimed at reducing self-reported unprotected anal sex [9]. The review identified 44 studies evaluating ~58 interventions, with a total of 18,585 participants.

The interventions included those aimed at individual-level behavior change (21 studies), small group-level approaches (26 studies), and community-level interventions [11]. Of the 58 interventions, 16 (27.6%) were targeted at HIV-infected men. Overall, Johnson et al [8] reported modest but optimistic findings: there was a statistically significant decrease of 27% in reporting of unprotected anal intercourse in the 40 interventions in which control conditions provided little or no intervention and an overall 23% reduction in reporting of any unprotected anal intercourse among the participants [9]. It was encouraging that somewhat larger effect sizes were found in the 40 studies in the subset of non-gay-identified MSM, a challenging population to reach in many contexts. The review also highlighted a major challenge for prevention among MSM globally, because two-thirds of all interventions were conducted in the United States, and nearly all the others were from the United Kingdom, Australia, New Zealand, and Canada. Only 2 studies were not from these resource-rich areas: one study from Brazil and one that included MSM in Russia and Bulgaria. That the most HIV-affected regions globally, including Africa and Asia, contributed not a single behavioral intervention trial for MSM is indeed evidence of the limited resources focused on MSM in most of the world.

NOVEL BIOMEDICAL PREVENTION APPROACHES

Several biomedically based interventions for prevention of HIV infection have targeted MSM or included enough MSM in sample sizes such that subgroup analyses are feasible. Recent results of trials of several modalities have failed to demonstrate efficacy. Although MSM have been active participants in many of the first-generation HIV-preventive vaccine trials, the results to date have been disappointing [14].

Rectal microbicides remain at early stages of clinical investigation. The preclinical and early human trial research effort regarding rectal microbicides has revealed how little—after 3 decades of research—is actually known about the physiology of anorectal infection with HIV, including site, initial target cells, mechanisms of transportation across the gut, and both viral and host characteristics that may facilitate this route (or routes) of transmission [15]. It is known that the risk of transmission per act of anal sex is significantly higher than that associated with vaginal sex, with some estimates as much as 80 times higher [16, 17].

Adult male circumcision for prevention of HIV acquisition among heterosexual men is among the few recent advancements in biomedical prevention science [11–13]. To date, there is no evidence base for circumcision as a tool for prevention of HIV infection in MSM, and, to our knowledge, no clinical trial has been conducted to investigate this potential modality. Circumcision might be expected to reduce the risk of acquisition of

HIV infection among insertive partners, as has been shown for penile-vaginal sex, but to have no direct impact and uncertain indirect impact on risk of acquisition among receptive partners. Observational data on circumcision in populations of MSM and risk of HIV infection are equivocal and have not provided the same consistency in epidemiologic findings that support circumcision trials for African heterosexual men [18].

Randomized controlled trials of antiviral therapy-based approaches to HIV infection, including daily preexposure prophylaxis (PrEP), are currently under way with populations including MSM, injection drug users, and African women at high risk of infection. If daily PrEP-based approaches prove to be efficacious, approaches for prevention of HIV infection in MSM are likely to be markedly altered. Many researchers in the prevention community expect that PrEP approaches with the potent and long-lasting antiretroviral drugs will show efficacy in controlled trials; however, it is clear that use outside the clinical trial context will likely differ, and the future effectiveness of these approaches will need careful study. Intermittent PrEP, rather than daily PrEP, is being investigated in at least 1 early-phase acceptability trial involving MSM in Bangkok, Thailand (F. van Griensven, personal communication). There is considerable optimism in the prevention field that intermittent PrEP may be a modality of prevention of HIV infection that has particular relevance to MSM.

Investigational methodologies aside, what would a minimum package of services for MSM include? The evidence suggests that health education, behavioral interventions, condom promotion and social marketing, access to water-based lubricants, voluntary HIV counseling and testing, diagnosis and treatment of STIs, antiretroviral treatment when indicated, access to care and support in nondiscriminatory settings, and other structural interventions are necessary [13]. Many of these elements now exist for MSM in industrialized countries. What about the great majority of MSM in resource-limited countries?

PREVENTION IN RESOURCE-LIMITED COUNTRIES

There have been several attempts to assess coverage of prevention services for MSM globally [19]. A recent review of the data by the Global Fund to Fight AIDS, TB and Malaria (GF) that was done for its funding strategy for sexual minorities estimated that basic prevention services were reaching <10% of MSM globally in 2007 [20]. Saavedra et al [5] recently published data from country reports to the United Nations on prevention expenditures for MSM. The authors found that, globally, “the disaggregated data indicate that a mere 0.6% of prevention expenditures were actually spent on targeted prevention for MSM” [5, p 3]. In this analysis, data were available for only the 38 developing countries that reported any programming for MSM; more countries reported that MSM pro-

grams were “not applicable” to their HIV/AIDS response [5]. Nevertheless, for the 38 states reporting MSM program indicators, the estimated funding needed to reach 80% coverage with a basic package of services was US \$29 million per year in 2007. Actual expenditures were ~US \$3 million in 2007. If the authors had included the states reporting no activity for MSM prevention, the gap between funding and need would have been even more stark. In short, for most United Nations member states, public sector prevention of HIV infection for MSM has either not started or is grossly underfunded by at least an order of magnitude. That this should be the case in 2009 is a signal failure of the global response to HIV infection and AIDS.

More encouragingly, the GF strategy for what it calls Sexual Orientation and Gender Identities (which includes MSM; lesbian, gay, bisexual, and transgender populations; and female, male, and transgender sex workers) from its Round Ten funding will support countries receiving GF funds in inclusion of MSM in prevention, in developing indicators and targets, and in monitoring national responses for these men [20]. The GF represents a substantial “carrot” for countries to receive funding for this essential work.

Substantial barriers exist to realizing basic prevention services for MSM globally. Not the least of these is the pervasive stigma, homophobia, discrimination, and in >80 countries, criminalization that MSM and other sexual minority populations face [21]. There is really no other explanation than homophobia to understand how the international community can have so significantly failed in its response to this component of the AIDS pandemic.

STRUCTURAL INTERVENTIONS: ADDRESSING DISCRIMINATION AND DECRIMINALIZATION

As Piot et al [7] showed, structural interventions in which social and environmental factors increasing risk of HIV infection are addressed are part of the evidence base for prevention of HIV infection. Classic examples include expanding access to clean needles and syringes for injection drug users and the early closure of New York City’s gay bathhouses by health authorities when the baths were understood to be high-risk transmission settings for HIV. Discrimination against sexual minorities, such as MSM, and its legal forms, which include criminalization of same-sex behavior between consenting adults and outright criminalization of homosexuality, represent profound structural barriers to prevention of HIV infection [5]. Criminalization drives men away from services, reduces the likelihood of disclosure of risks to providers and partners, and makes men vulnerable to blackmail. In a recent 3-country study by our group that involved MSM in Malawi, Namibia, and Botswana, all states where homosexuality remains a crime, MSM who disclosed their sexual behaviors to family members and to

health care providers were substantially more likely to have experienced blackmail [22]. The most basic tools, such as water-based lubricants, were unavailable to many of these men and were as highly stigmatized as they were expensive [22]. MSM outreach workers have been physically abused by police in India and Nepal (before Nepal repealed its antisodomy laws in 2007) [23]. And in Senegal, health care staff at the first MSM-friendly clinic in the country were sentenced to 9 years in prison on sodomy charges (these men were released in April 2009 but remain highly vulnerable to attack) [24]. Men can hardly be expected to participate in prevention programs if they fear blackmail, arrest, social stigma, or police violence.

Both individual- and structural-level actions are needed to address these structural barriers to prevention. Addressing homophobia and providing MSM-friendly services would also be required, along with efforts to reduce the social-structural determinants of risk of HIV infection and vulnerability for these men. Primary among these is an effort at decriminalization of same-sex behavior for consenting adults and, more broadly, decriminalization of homosexuality as an intervention for prevention of HIV infection. Although even a few years ago, such a goal would have been seen as having little chance of success, the international lesbian, gay, bisexual, and transgender movement and the global HIV/AIDS advocacy community working for sexual minorities have made remarkable headway on this goal. Most recently, in December 2008, the United Nations General Assembly embraced an end to discrimination against sexual minorities in its landmark, though nonbinding, statement “Human Rights, Sexual Orientation, and Gender Identity” [25]. The United Nations High Commissioner for Human Rights, the Honorable Navanethem Pillay, in support of the UN statement, stated in December of 2008, “Those who are lesbian, gay or bisexual, those who are transgender, transsexual or intersex, are full and equal members of the human family, and are entitled to be treated as such” [26, p 1].

The United Nations General Assembly statement from 2008 explicitly calls for an end to discrimination in health care as one of its goals:

We reaffirm the principle of non-discrimination which requires that human rights apply equally to every human being regardless of sexual orientation or gender identity;

We are deeply concerned by violations of human rights and fundamental freedoms based on sexual orientation or gender identity;

We condemn the human rights violations based on sexual orientation or gender identity wherever they occur, in particular the use of the death penalty on this ground, extrajudicial, summary or arbitrary executions, the practice of torture and other cruel, inhuman and degrading treatment or punishment, arbitrary arrest or detention and deprivation of economic, social and cultural rights, including the right to health. [25, p 5]

This effort was opposed by several governments, including the US Administration of George W. Bush, but was endorsed by the Obama Administration in March 2009, bringing the United States in line with most European States, Canada, Australia, and other democracies [27].

DISCUSSION

Prevention of HIV infection in MSM arguably needs to proceed on 2 tracks. For many of the resource-limited countries, the effort to bring the basics of prevention to MSM is long delayed, must be galvanized, and must be supported with marked increases in funding commensurate with need. Data from the Joint United Nations Programme on HIV/AIDS suggest that a ≥ 10 -fold expansion in funding is necessary, and structural interventions are key to making this happen. As long as MSM are criminalized and stigmatized, prevention of HIV infection in these men will languish. In the third decade of AIDS, it is unconscionable that so many men at risk have yet to receive the basics of prevention. Access to prevention of HIV infection for MSM is an unmet public health need and an unrealized human right. Vigorous responses to these truths are long overdue.

For communities of MSM in industrialized countries, the basics appear to be insufficient, and new approaches are clearly needed. PrEP may be the game changer, and how antiretroviral therapy-based interventions will fit with existing prevention services (or not), if they prove to be effective, will likely be the major challenge for prevention in the near future. That said, other approaches, including circumcision in some settings and for some subsets of men, may warrant study, and rectal microbicides, particularly if they have dual function as sexual lubricants, may also prove to be potent tools.

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