



Published in final edited form as:

J Acquir Immune Defic Syndr. 2013 July ; 63(0 2): S161–S167. doi:10.1097/QAI.0b013e318298700e.

Overcoming Biological, Behavioral and Structural Vulnerabilities: New Directions in Research to Decrease HIV Transmission in Men who have Sex with Men

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Abstract

Men who have sex with men, including transgender women, comprise a heterogeneous group of individuals, whose sexual behaviors and gender identities may vary widely between cultures and among individuals. Their sources of increased vulnerability to HIV are diverse, including the increased efficiency of HIV transmission via unprotected anal intercourse, sexual role versatility, asymptomatic sexually transmitted infections, as well as behavioral factors that may be associated with condomless sex with multiple partners. Societal stigmatization of homosexual behavior and gender non-conformity may result in internalized negative feelings that lead to depression, other affective disorders, and substance use, which in turn are associated with increased risk taking behaviors. Social stigma and punitive civil environments may lead to delays in seeking HIV and STD screening, and later initiation of antiretroviral therapy. The iPrEX study demonstrated that chemoprophylaxis can decrease HIV acquisition in MSM, and the HPTN 052 study established the biological plausibility that earlier initiation of HAART can decrease HIV transmission to

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Sources of Support/Conflicts of Interest: None to declare

uninfected partners. Despite these advances, MSM remain among the most significantly HIV-affected population in resource rich and limited settings. New studies will integrate enhanced understanding of the biology of enhanced rectal transmission of HIV and the focused use of antiretrovirals for prevention with culturally-tailored approaches that address the potentiating social and behavioral factors associated with enhanced HIV spread among MSM.

Keywords

Men who have sex with men; Transgender Women; HIV Prevention; HIV Transmission

Introduction

The global HIV/AIDS epidemic was first recognized among men who have sex with men (MSM) in the early 1980s^(1,2), and people who are born male who have sex with other men have remained at high risk for HIV acquisition ever since⁽³⁾. Because of biological susceptibility⁽⁴⁾, a high concomitant STD burden, and ongoing risk taking behavior, in many parts of the world, MSM continue to be one of the populations with the greatest HIV incidence⁽³⁾. MSM represent a substantial proportion of those infected with HIV in many resource-constrained environments, including those with generalized epidemics⁽⁵⁾. MSM may be vulnerable to syndemics, the co-occurrence of health disparities which potentiate HIV risk⁽⁶⁾, and are exacerbated by societal stigma⁽⁷⁾. The demonstration that antiretroviral chemoprophylaxis decreased HIV incidence among MSM⁽⁸⁾ offers new opportunities for HIV prevention. HPTN 052 has suggested that early identification of HIV infection and HAART initiation could decrease HIV transmission in heterosexuals⁽⁹⁾, which should be relevant for MSM. Reducing HIV incidence in MSM will require multi-component and culturally-tailored interventions integrating scientific insights with community engagement that address their diversity.

Biological and Epidemiological Sources of MSM Susceptibility

Receptive anal intercourse is the most efficient sexual practice transmitting HIV⁽⁴⁾. MSM engaging in insertive anal sex can become HIV-infected, particularly if the partner has an STD, is untreated, or is uncircumcised. Because many MSM are sexually versatile, they can acquire HIV as the receptive partner, but after becoming infected, they may transmit to a new partner when they are insertive. Among some sexually active MSM, additional potentiators of transmission are frequent partner exchange, group sex or other traumatic practices. For other MSM, their individual risk practices may involve anal intercourse in the setting of long term or serial monogamy, but they may have selected a non-monogamous partner, and/or a partner from a subpopulation with high HIV prevalence (e.g. Black MSM in the US⁽¹⁰⁻¹²⁾).

Social and Behavioral sources of vulnerability of MSM to HIV

Sequelae of stigma

Internalized homophobia is associated with increased risk for HIV acquisition and transmission due in part to increased risk behaviors and decreased engagement in prevention and care⁽¹³⁻¹⁶⁾. Internalized homophobia has been linked to depression, low self-esteem and feelings of loneliness, as well as disregard for partners' and individual health, leading to unsafe sex^(18; 19). Accompanying distress may lead to substance abuse in order to mask the feelings of shame⁽²⁰⁾. The use of alcohol and other recreational drugs has been associated with having multiple partners and sex work, amplifying risks⁽²¹⁾.

Structural factors, such as low education, unemployment, and poverty may also be related to HIV risk and infection^(10, 22, 23). Societal rejection and criminalization of homosexuality is a crucial structural factor associated with HIV risk in MSM. In the US, Black MSM who experienced homophobic events were more likely to be HIV-infected and to engage in unprotected sex⁽²³⁾. Experienced discrimination may potentiate the adverse health outcomes⁽²⁴⁾. Structural factors may impede MSM access to condoms and HIV/STD testing⁽²⁵⁻²⁸⁾ and to HIV care⁽²⁴⁾.

Physical and virtual venues

MSM socialize and find sexual partners in a variety of places, including bars/clubs, bathhouses, parks, and online⁽²⁹⁾. Some studies found sexual risk behaviors more prevalent in specific venues, while others did not⁽³⁰⁻³⁶⁾. Social norms may differ by venue. For instance, HIV status disclosure was high among men who met their most recent partner online and lower among men who met their most recent partner in a public place⁽³²⁾. Some venues, e.g. bathhouses, can enhance HIV prevention initiatives⁽³⁷⁾, including onsite HIV and STD screening⁽³⁸⁾.

Advances in electronic communication may affect HIV prevention in negative and positive ways⁽³⁹⁻⁴¹⁾. Social media enhance the ease to meet potential sexual partners, including those who prefer unprotected sex⁽⁴²⁻⁴⁴⁾, though studies differ in correlating Internet use with unprotected intercourse⁽⁴⁵⁻⁴⁸⁾. E-dating seems more prevalent among MSM who live in non-urban areas⁽⁴⁹⁾. Internet sexual behavior seems highly correlated with MSM's behavior offline⁽⁵⁰⁻⁵⁵⁾. E-technologies also facilitate engagement of hard-to-reach populations in accessing sexual health information⁽⁵⁵⁻⁵⁷⁾ and can facilitate HIV prevention⁽⁵⁸⁻⁶¹⁾.

Recent findings that inform MSM prevention research

Treatment as Prevention

HPTN 052 demonstrated that earlier initiation of HAART in asymptomatic HIV-infected individuals decreased their likelihood of HIV transmission to their uninfected primary partner by 96%⁽⁹⁾. However, only 3% of enrollees were MSM. HIV may be detected in rectal secretions of MSM with undetectable plasma viremia, although the clinical significance of low copy numbers requires further study⁽⁶¹⁾. Ecological data from areas where treatment access is high and where MSM have constituted the largest numbers of new infections have been mixed, with decreases in HIV incidence seen among MSM in San Francisco⁽⁶²⁾, but not in London⁽⁶³⁾. Observational studies of MSM couples are underway in Europe and Australia. However, other data suggest that that "test and treat" approaches could decrease HIV incidence in MSM. Individuals who are aware of their HIV status are less likely to engaging in potential transmitting behaviors⁽⁶⁴⁾ and successful suppression of plasma viremia with HAART has been associated with marked reductions in the detection of seminal HIV^(65,66). Additionally, those who initiated treatment sooner in HPTN 052 had better clinical outcomes⁽⁶⁷⁾, and large observational studies also indicate that earlier treatment results in decreased morbidity⁽⁶⁸⁾. Operational questions remain, given that social stigma may result in delays in accessing testing and treatment services. Earlier HIV identification through self and partner-testing^(69,70) may enhance prevention efforts.

Chemoprophylaxis

At present, substantial numbers of MSM are unaware of their HIV status. The most optimistic test, link and treat programs will take years to have an appreciable impact in lowering community viral load for MSM. To have maximal impact, wider expansion of testing and earlier treatment for HIV-infected MSM, accompanied by focused programs of

chemoprophylaxis for the riskiest MSM, may be most efficient in arresting HIV spread among MSM.

MSM diversity

Although MSM engage in similar practices, the term defines a transmission category, without recognizing the diverse identities, behaviors, and social realities that it includes. To address the global AIDS epidemic, an understanding that different MSM subcultures require tailored interventions to achieve “an AIDS-free generation.”

MSM in Africa

Although sub-Saharan Africa was long believed to have an exclusively heterosexual epidemic, recent research indicates that the risk of being HIV-infected is higher among MSM than among heterosexual African men. HIV prevalence rates of up to 50% have been described⁽⁷²⁻⁸⁴⁾, with one study reporting an incidence of 8.6 per 100-person years in Kenyan MSM⁽⁸¹⁾. Several studies have reported high rates of bisexual behavior among African MSM, and one reported noted a high rate of bisexual concurrency (being sexually active with both a man and a woman in the same period) among MSM in Malawi, Namibia, Senegal and Botswana.⁽⁸²⁻⁸⁶⁾

MSM in Latin America

Across Latin America, the HIV epidemic is concentrated in MSM with HIV prevalence estimates between 7.9% and 21.2%, 33.3 times higher than the general population⁽⁷³⁾. Transgender women are at an even greater risk of HIV acquisition, with HIV prevalence estimates between 18.8% and 33.5% in Uruguay and Argentina, respectively. Compared to Latin American adults aged 15-49 years, transgender women 50-fold more likely to be HIV-infected⁽⁸⁷⁾. Although HIV prevention and treatment efforts have improved, efforts to control the spread of the disease among MSM have been hampered by poverty, inadequate health services, stigma, discrimination, violence, homophobia and transphobia^(88,89). Modeling data from Peru suggest that earlier treatment initiation and improved treatment adherence must be integrated into comprehensive HIV prevention⁽⁹⁰⁾

MSM in Asia

HIV in Asia is a concentrated epidemic, with disproportionate rates of HIV infection being found among MSM in virtually all the countries where it has been studied⁽⁹¹⁾. Social stigmatization of homosexuality and negative affect because of pressure to have a wife and children has been associated with HIV risk behaviors in several Asian settings⁽⁹²⁻⁹⁴⁾. Successful social mobilization campaigns like the Avahan initiative in India suggest that community engagement can help to attenuate HIV spread⁽⁹⁵⁾, but recent data from Thailand, suggest that high rates of new infections are being noted in younger MSM, often in conjunction with non-parenteral recreational drug use⁽⁹³⁾. Asia has perhaps the greatest cultural diversity of same sex identities and social expressions of same sex behavior.^(96, 97) Many of traditional categories, including the Hinjra of South Asia, and the Koetey of Southeast Asia, include feminized categories of males who are seen as quite different from gay identified or homosexual men, and for whom outreach requires targeted and culturally appropriate programs.

Intersectionality

Racial and ethnic minority MSM may experience dual stigmas due to homophobia and racism. For example, Black MSM in the United States have the highest HIV concentration of any subpopulation, but have not been found to engage in higher levels of risk taking behavior than other MSM⁽²⁴⁾. Recent data have found HIV-incidence rates of close 3%

annually in a 6 city study of Black MSM, with incidence being higher in younger, gay-identified Black MSM (¹²).

Adolescent and young adult MSM

Self-acceptance of sexual identity leads to healthful outcomes (^{99,100}), but MSM adolescents may experience rejection, placing them at increased risk for impaired physical, social and emotional health (¹⁰⁰). Although attitudes regarding homosexuality have become more supportive in many places, social stigma remains common for young MSM (¹⁰¹). Coming out can mean risking rejection and loss of support from family (¹⁰²). MSM adolescents are more likely than heterosexual peers to experience social isolation, truancy, prostitution, substance abuse, depression and STDs (¹⁰⁰). Sexual experimentation and perceptions of invincibility may make young MSM at increased risk for HIV acquisition (¹⁰³). Younger MSM had increased HIV incidence in iPrEX, consistent with decreased adherence (^{104,105}).

Transgender men and women

Transgender persons have been less studied than other sexual and gender minority populations, although transgender women (TGW, persons born biologically male and expressing female gender identities) have disproportionate HIV burdens. A recent global systematic review and meta-analysis about TGW in 15 countries found a pooled HIV prevalence of 19.1% (¹⁰⁶), indicating an urgent unmet need for HIV prevention and care. There is a paucity of data regarding Transgender Men (born biologically female and expressing male gender identities) and HIV risks, suggesting a need for further research.

New Directions in HIV Prevention Research for MSM

Expanding HIV testing

The engagement of men in HIV testing has been a challenge in many settings. HPTN 043, a randomized controlled trial comparing community-based HIV testing and counseling to clinic based voluntary counseling (VCT) showed considerable efficacy in engaging African and Thai men in HIV testing (¹⁰⁷). Men preferred community based and mobile VCT in times and places convenient for working adults, and in culturally appropriate settings. While HPTN 043 had relatively few MSM participants, the implications suggest that expanding testing for MSM will require innovations in how testing is provided, including home testing, and in entertainment settings that MSM frequent.

Early treatment for HIV-infected MSM

There is strong biological plausibility for effective ART therapy to reduce sexual transmission of HIV between men. Ecological evidence from San Francisco suggests that early HAART initiation and high levels of treatment coverage may now be having an impact on HIV incidence among MSM at population levels (⁶⁵). However, recent epidemiologic and modeling data suggest that in many populations of MSM primary partnerships may account for substantially smaller proportions among heterosexuals.⁽⁹¹⁾ Networks may be the more relevant level in which to assess the impact of ART on HIV incidence densities among MSM. Such an approach may require community randomized designs, but could allow for definitive answers to the important question of the likely role of early ART for HIV prevention for MSM.

Optimizing chemoprophylaxis

iPrEX demonstrated that antiretroviral pre-exposure prophylaxis (PrEP) was effective in decreasing HIV incidence in MSM (⁸). However, MSM assigned to take TDF-FTC had drug detected only half the time that medication levels were measured (¹⁰⁸). For individuals with

episodic risks, peri-coital or intermittent fixed interval PrEP dosing is appealing, since it could save costs and potentially lower risks for toxicities. However, one early study of the feasibility of intermittent PrEP among MSM and female sex workers in Uganda and Kenya found that post-coital doses were often missed (¹⁰⁹). Studies are underway in the HPTN and research teams in the UK (MRC) and France (ANRS) to better understand how intermittent PrEP may be optimally deployed (www.hptn.org, www.avac.org). Because anal sex among MSM often entails the use of a lubricating gel, and because the CAPRISA 004 study showed that pericoital use of tenofovir gel decreased incidence in South African women (¹¹⁰), it is reasonable to postulate that a rectal gel might be acceptable and efficacious. Rectally administered tenofovir gel, that did not contain glycerin, which stimulated peristalsis in MTN 006(¹¹¹), was found to be acceptable in MTN 007(¹¹²). An expanded multi-national safety and acceptability study will evaluate the rectal gel and oral TDF-FTC (MTN 017), and may suggest how future chemoprophylaxis trials may be designed. Lastly, although tenofovir-based chemoprophylaxis has been found to be safe, questions about chronic use remain. Others have been interested in using antiretrovirals that are not mainstays of treatment in order to minimize the likelihood of the selection of drug-resistant mutants that could hamper future treatment scale up efforts. The first study of new oral regimens for chemoprophylaxis using maraviroc by itself or in combination with emtricitabine or tenofovir is currently enrolling 400 MSM at 12 US sites (HPTN 069/ACTG 5305). Further research evaluating formulations than can be given less often via injection (i.e. rilpivirine and newer integrase inhibitors) are underway, and could also be relevant for MSM.

Combination prevention strategies

Modeling has suggested that combined approaches to prevention may have the greatest impact in arresting the HIV epidemic among MSM (⁷¹). To begin the process of combining evidence approaches into culturally tailored prevention “packages” that may have the widest replicability, the NIH has recent funded consortia to develop prevention interventions for MSM in North and South America, China, and Africa. These projects entail a number of key components, including a comprehensive literature review of current HIV prevention interventions for MSM, a modeling exercise to estimate the impact that implementing a combination HIV prevention package will have on HIV transmission, pilot studies to explore the feasibility and acceptability of the prevention package. The package may will include condom promotion, risk reduction counseling, access to condom-compatible lubricants, linkage to care for HIV care and treatment, expanded HIV testing and counseling, STI testing and treatment, but each group will tailor additional components, such as engaging couples and/or networks, use of electronic media, and/or provision of PrEP based on preliminary studies and input from community advisory boards.

Structural interventions

New bio-behavioral HIV interventions for MSM could be enhanced by structural interventions that decrease stigma and promote social integration of MSM. Careful analyses of the impact of changes in laws regarding marriage and other civic enfranchisement in different countries are needed to evaluate whether they are a needed part of local “prevention packages.” Interventions that address economic disparities that may potentiate risk taking, e.g. conditional cash transfer for male sex workers and other economically disenfranchised MSM subpopulations, also deserve further evaluation.

Conclusions

Although MSM are disproportionately affected by HIV globally, reduction in incidence will require a diverse set of interventions, based on understanding of patterns of spread and local norms. Interventions that address stigma and associated sequelae must be culturally-tailored,

and can be augmented with new approaches to increase HIV testing and linkage to care, early initiation of treatment, identification of transmission networks, and chemoprophylaxis. In order to determine the optimal prevention package, ongoing dialogue with key community stakeholders remains essential, given the heterogeneity of MSM cultures, and the diverse drivers of risk globally.

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