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Are Low- and Middle-Income Countries Repeating Mistakes Made by High-Income Countries in the Control of HIV for Men who have Sex with Men?

Han-Zhu Qian^{1,2*} and Sten H. Vermund¹⁻³

¹Vanderbilt Institute for Global Health, USA

Editorial

²Departments of Medicine, Vanderbilt University, Nashville, Tennessee, USA ³Departments of Pediatrics, Vanderbilt University, Nashville, Tennessee, USA

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Men who have sex with men (MSM) have been represented disproportionately in the HIV epidemic in high income countries since the first HIV/AIDS cases were reported in MSM in 1981.Among all vulnerable HIV populations, MSM account for the preponderance of prevalent AIDS cases in Western Europe [1,2]. Similarly, the largest numbers of persons with newly diagnosed HIV infections (range 45%-65%) are MSM in the United States, Canada, Australia, and New Zealand [3-7]. In contrast, in many low- and middle-income country (LMICs) HIV epidemics were driven by injection drug use (IDU), heterosexual sex, and/or contaminated blood collection and transfusion [8,9]. In recent years, rapid increases in the HIV epidemic among MSM have been observed LMICs in Asia [10], Africa [11], South America [12] and Eastern Europe and Central Asia [13]. For example, MSM account for nearly one third of prevalent AIDS cases in Thailand [14] and Brazil [15], and 30% -75% of estimated new HIV infections in various parts of Laos and China [16,17]. A small number of epidemiologic studies have also shown high incidence (6.8/100 person-years) among MSM in Kenya and South Africa [18] and high HIV prevalence (4-23%) in Ukraine [19], though MSM comprise a small proportion of the total HIV cases in Africa, Eastern Europe and Central Asia, perhaps due, in part, to stigmatization and underreporting.

As the HIV/AIDS epidemic enters its 4th decade post-recognition, many LMICs are repeating the mistakes made by high income countries in HIV control targeting MSM. A series of questions arise continually: Are MSM epidemics in LMICs driven by imported cases from high income countries? Have LMICs missed the window of opportunity to control the HIV epidemic among MSM? What experiences from the prevention and care for HIV among MSM populations have been learned from high income countries that could be applicable to the burgeoning MSM epidemic in LMICs?

Are MSM Epidemics in LMICs Driven by Imported Cases from High Income Countries?

Thailand is an informative case study to address the question of imported vs. autochthonous transmission of HIV among MSM. Western "sex tourists" likely contributed to the first wave of HIV epidemic among Thai MSM in the middle 1980s, judging from phylogenetic evidence (subtype/clade B virus predominated early) [20]. By the 1990s, however, subsequent waves of the epidemic of subtypes E and Thai subtype B (or B') were attributable to widely accessible commercial sex, IDU, heterosexual sexual transmission between couples, and from infected mothers to infants, in addition to MSM [21-23].

Was this the pattern elsewhere in Asia? Molecular epidemiology suggests imported cases to be influential among early MSM cases in Beijing, China, as the first HIV-1 recognized shared the genetic roots of viruses from the US and Western Europe [24]. Yet recent data showed the majority of infections in Chinese MSM to have a combination of HIV genotypes, with increasing genetic complexity likely a result of multiple local introductions of viruses to MSM from Chinese sub-populations infected with HIV-1 through drug injection or heterosexual transmission [25-27]. In Western Europe and North America, the early epidemic suggested an epidemic seeding different risk groups with similar viral clades and sequences, while more recent epidemic expansions of HIV to injection drug users (IDUs) in Eastern Europe have been associated with specific strains introduced and then rapidly transmitted locally [28].

Hence, HIV infections from foreign sources are typical seeding events, suggested by genetic similarities of the viruses, followed by local expansion of the epidemic from domestic sexual or drug user behaviors. For LMICs to see low MSM rates and assume that they have no problem they are missing an important lesson from the Western experience. The virus is easy to introduce, and once present, it spreads in predictable ways. This "blind spot" in policy is not unique to MSM. In Pakistan for instance, sero-prevalence in IDUs did not exceed 0.5% in most venues, and the government paid little mind; beginning in 2004, there has been an explosion of HIV transmission among IDUs in Pakistan such that current prevalence rates are typically over 15% and may reach 45% (Dr. Sharaf Ali Shah, unpublished data) [29,30].

Have LMICs Missed the Window of Opportunity to Control the HIV Epidemic among MSM?

HIV continues to spread among MSM in endemic high income countries [28,31]. LMICs are faced with the urgent challenge of tackling prevention challenges in this population before prevalence rates reach levels seen in the West. Given that the probability of transmission per receptive anal act of intercourse is comparatively high, LMICs can expect a rising proportion of all cases to occur among MSM in the absence of successful control [32], especially as control efforts in IDUs or heterosexual couples improve using known successful control strategies such as clean needle and syringe exchange, opiate agonist substitution therapy, and expanded combination antiretroviral therapy for prevention [33,34].

*Corresponding author: Dr. Han-Zhu Qian, 2525 West End Avenue, Nashville, Tennessee 37203, USA, Tel: +1-615-343-3159; E-mail: han-zhu.qian@vanderbilt.edu

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Human rights issues also play a role; nearly all LMICs ban or discourage marriage between homosexuals. Given poor acceptance of homosexuality societal norms, legislation, and attitudes of religious and other leaders, a failure to embrace human and civil rights for homosexuals may inhibit long-term faithful male-to-male sexual partnerships due to stigma and legal proscriptions.

MSM also face challenges related to the sexual culture prevalent particularly among many young MSM. High sexual mixing rates, concomitant non-injection drug and alcohol use, and low condom use all increase risks [35]. Sexual behavior is not easily modified by behavioral interventions; biomedical approaches such as pre-exposure prophylaxis (PrEP) are not widespread and likely not practical at a large scale over a sustained time period.

Cultural influences from high income countries, so-called "Westernization", may lead to increased social liberties and personal freedoms, including migration from home towns and villages to larger cities where they are more likely to find social and sexual groups with fewer lifestyle inhibitions [36-38]. The increased use of modern technologies such as mobile phones and the Internet allows easier access to a large social network; these modalities are used for privacy in finding friends and/or sexual partners [39,40]. Mainstreaming homosexual social norms without concomitant human and civil rights changes may paradoxically increase sexual mixing, without reinforcing longer-term partnerships.HIV transmission is fueled by complex social and structural issues, alongside psychological and economic ones; among these diverse themes are unrecognized HIV infection due to social stigma and structural barriers to widespread testing, larger social/sexual networks, fear of accessing stigmatized HIV clinical care or prevention services, male sex work, and a history of childhood sexual abuse [41].

Countries experiencing rapid development of globalized market economies tend to lose prior strict religious or other social taboos that kept homosexuality underground and suppressed, e.g., China, Brazil, Mexico, South Africa, Vietnam, Peru, many Caribbean nations [42-45]. Even lower income nations such as Malawi and Uganda are facing the clash of vicious homophobia from political and religious circles, met with human rights activities often driven by MSM themselves [46,47]. It may be a matter of time before issues of sexual orientation are viewed with more tolerance worldwide (note recent actions by the new Malawian President Joyce Banda to make clear her opposition to criminalization of homosexual activity); in a more open and engaged environment, public health, political, religious, and community activist leaders can work with more synergy with afflicted communities. Given that testing and linkage to care seem to be among the most promising prevention strategies [48], openness and engagement are essential prerequisites for successful programs [47,49-52].

What Experiences from the Prevention and Care for HIV among MSM Populations Have Been Learned from High Income Countries That Could Be Applicable to LMICs?

Some intervention approaches have been applied in public health programs for effectively preventing HIV in IDUs, commercial sex workers, and other vulnerable groups. For example, "100% condom programs" successfully reversed the rapid rising HIV epidemic in FSWs in Thailand [53]. Implementation of large-scale needle exchange and methadone substitution programs has led substantial decline of HIV new infections among drug injectors worldwide, including recent successes in China [54,55]. Closing illicit plasma collection stations also helped eliminating HIV spread among plasma donors in China [56]. However, public health programs have been underwhelming in their successes in controlling the HIV epidemic among MSM. Perhaps the most promising is the mixture of structural and behavioral approaches to implement expanded testing and linkage to care in San Francisco and Vancouver where early data suggest a possible decline in HIV incidence as antiretroviral treatment reaches more persons [57-59]. LMICs with increasing HIV transmission and sero-conversions among MSM are similarly constrained as to the tools available that are likely to tackle this challenge.

In high income nations, significant ethnic disparities in HIV risk among MSM have been documented; Black and Hispanic MSM have higher risks of infection than their white counterparts, though their risk behavior profiles are not very different [41,60,61]. The higher HIV risk in Black MSM is almost certainly not contributable to more risky sexual behaviors, but is more likely due to higher prevalence rates in sexual networks, structural barriers to safer sex and access to services; high prevalence backgrounds would increase HIV risk, and social factors could also exacerbate risk, including lower socio-economic status, less health insurance, lower access to HIV antiretroviral therapy and other HIV care [60]. As long as MSM communities continue to endure stigma, discrimination, and unavailability of HIV services, LMICs can expect HIV to rise among MSM.

Although PrEP intervention has shown promise for preventing HIV among MSM, including iPrEx study [62], this was in an optimized clinical trial setting. More operational research is needed for effective and safe deployment of innovative interventions into public health programs in LMICs. Given gaps in treatment coverage, it is improbable that policymakers will use AIDS monies for PrEP when ART is lacking for HIV sero-positive persons. The importance and value of engaging MSM communities in such operational research is one lesson to take from high income country experiences. MSM community activists have contributed substantially to HIV/AIDS research by suggesting concepts, engaging communities, and educating policymakers, among many other roles in both prevention and therapeutic arenas [63].

No behavioral study of MSM has demonstrated a significant and sustained impact on HIV sero-incidence among MSM. Nonetheless, the US CDC have identified prevention interventions targeting HIVinfected or non-infected MSM that have had a significant impact on self-reported behavioral risks, including HIV testing and linkage to care, antiretroviral therapy (ART), access to condoms and sterile syringes, screening and treatment for other sexually transmitted infections, and others [64-75]. For successful control of HIV in MSM, experts believe that integrated combination prevention approaches are needed. For example, expanding HIV testing and linkage to care based on antiretroviral therapy and additional therapeutic attention to such comorbidities as tuberculosis, mental health and substance use issues, and nutritional deficiencies are worthy of testing among MSM as is being done for general populations in such studies as the HIV Prevention Trials Network (HPTN) 065 and 071 protocols, the ANRS/Africa Centre study, and Iringa and Botswana studies. The implementation science work to improve the continuum of HIV care is essential. Even in the high income US, among an estimated 1.2 million HIV-infected Americans, only about one third are on ART and a quarter are virally suppressed [76]. The theory behind test-link-care is that the amount of virus circulating in a community will decline with the increase in HIVinfected persons who know their status, are effectively linked to and retained in antiretroviral therapy (ART)-based care, and who adhere to

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their medicines and change behaviors to reduce risk of transmitting the virus [58,77-80]. This approach is challenging [81], but may represent the best public health opportunity for LMICs to control the epidemic in MSM.

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