

China, HIV, and Syphilis Among Men Who Have Sex With Men: An Urgent Call to Action

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(See the Major Article by Wu et al on pages 298–309.)

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The story of sexually transmitted diseases (STDs) in China is complicated and compelling [1]. Before the formation of the People's Republic of China (PRC) in 1949, sexually transmitted infections were a major source of disease [2]. For example, in 1949, 84% of sex workers in Beijing were estimated to have syphilis [3]. In this same year 10% of all infants born at Beijing Medical College suffered from congenital syphilis, and among some of China's national minority groups syphilis prevalence exceeded 50% [4]. In the face of this staggering burden of disease, the early leaders of the PRC prioritized public health. By 1964, extraordinary national initiatives had virtually eliminated syphilis [1].

But syphilis and other STDs have returned to China with a vengeance [5, 6]. China now faces a substantial burden of STDs in the general population [7–9], and alarmingly high prevalence of STDs among at-risk populations including sex

workers and men who have sex with men (MSM) [10–12]. Recognizing the gravity of the problem, in 1987, the government developed a mandatory case reporting system [8]. Between 2004 and 2011, this national sentinel surveillance system recorded a >4-fold increase in syphilis cases [5]. In 2011, China's syphilis incidence of 32.0 new cases per 100 000 residents [5] stood in sharp contrast to syphilis incidence in the United States (4.5 new cases per 100 000) [13] and England (5.6 new cases per 100 000) [14].

How can we explain this rapid resurgence of STDs? China's unprecedented social, political, and economic changes beginning in the 1980s favor the transmission of STDs [15, 16]. Earlier sexual debut, later marriage, more lifetime partners, and more commercial sex [17–19] have vastly accelerated the spread of STDs. Population-level biological forces may also play a role. Following syphilis infection, the immune system registers a memory response that could result in heightened immunity or alter the course of disease [20]. Grassly et al demonstrated the plausible impact of this response leading to herd immunity through a modeling study of syphilis trends in the United States [21]. If their argument is correct, the great success of China's earlier eradication campaigns may have de facto led to heightened susceptibility

across a general population with virtually no immune experience with syphilis for several generations.

Globally, it has become clear that the spread of STDs and human immunodeficiency virus (HIV) among MSM deserves intense attention [22]. In this issue of *Clinical Infectious Diseases*, Wu and colleagues describe a remarkable national study of HIV and syphilis prevalence among MSM in China. The investigators conducted a 61-city, cross-sectional study of >47 000 MSM. The results are sobering. The prevalence of HIV infection in the population surveyed was 4.9% and the prevalence of syphilis infection was 11.8%. This disease prevalence is consistent with reports of the spread of syphilis and the disproportionate burden of HIV among MSM worldwide [23].

At the patient level, Wu et al's data reflect the fierce synergy between HIV and syphilis. Among those with syphilis infection, HIV prevalence was >3 times higher (3.9% vs 12.5%). Importantly, syphilis measurement assessed active or recent infection rather than lifetime exposure. This critical distinction supports the link between ulcerative STDs and heightened susceptibility to HIV infection [24].

Examination of the ecological and population-level results is more complicated. The investigators chose particular

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areas for their surveillance based on population size and the feasibility of recruiting a sufficient MSM sample. The country was divided broadly into 6 regions: East, North, Northeast, Northwest, South-central, and Southwest. Excluding undersampled Tibet, they found a wide city-level geographic range in HIV prevalence (0.0%–19.2%) and syphilis prevalence (0.9%–26.6%; see Supplementary Data). Such wide variation raises the question of sample accuracy or other important but other unexplained factors affecting the results. For example, the authors note significantly higher syphilis prevalence among participants who were sampled via respondent-driven sampling vs snowball sampling.

The investigators went forward to evaluate the city-level prevalence of syphilis and HIV by the 6 geographic regions. In 3 regions (East, Northwest, and South-central), they found a positive correlation between the prevalence of syphilis and the prevalence of HIV. However, the other 3 regions (North, Northeast, and Southwest) did not display a similar pattern. This interesting phenomenon reflects diverse transmission dynamics. In the Southwest the authors find high HIV and moderate syphilis. In this area, initial HIV transmissions primarily driven by injection drug use [25] likely played a more important role in transmission dynamics than the synergistic effect of sexually transmitted syphilis and HIV. This hypothesis is supported by the concomitant high prevalence of hepatitis C virus infection and HIV/hepatitis C coinfection associated with injection drug use in these regions [26, 27].

Conversely, in the North and Northeast regions, syphilis prevalence was high but HIV prevalence remained low. Wu and colleagues postulate that these patterns suggest areas with high sexual risk behaviors where mixing patterns have not allowed people with syphilis to interact with HIV. These regions must attract great attention because of the possibility—really the obligation—to stop the spread of these diseases.

In their analysis, Wu and coworkers retrospectively developed 3 loosely defined subgroups of MSM. The first group, “nonlocal MSM,” includes any men who were tested in an area other than their official household registration status (*hukou*). They are described as young, unmarried, self-identified gay, having moderate education status, and unlikely to have female partners. Additionally, they reported the highest number of male partners, highest prevalence of selling sex to men (14.4%), and a moderate level of buying sex from men (5.8%). These men, unsurprisingly, had the highest incidence and prevalence of HIV and syphilis among the 3 groups. Furthermore, given the high reported level of selling sex among these men, they are very likely to be mobile between numerous cities, not merely nonlocal to a single city [28].

The second group consisted of MSM who exclusively find male sex partners via the Internet. These men had moderate HIV prevalence, low syphilis, and low coinfection. Similar to nonlocal MSM, these men are characterized as young, unmarried, self-identified gay, and unlikely to have female partners. However, more of these men are students or are college educated, and few participated in male–male commercial sex. Of note, the Internet was the most common method for finding sex partners among *all* 3 subgroups, reflecting similar national trends of the importance of the Internet to gay life in China [29, 30]. Despite China’s militant oversight and censorship of the Internet, ironically the Internet has become a primary means for MSM to find sexual partners and buy and sell sex [30].

The third group consisted of bisexual MSM—primarily men who report sex with men but who are more likely to be married to women and may not self-identify as gay. More of these men were older and more reported buying and selling sex to other men. Female-partnering MSM attract terrific attention because of the (supposed) risk of bridging HIV/STD transmission from the gay population to

the general population [31]. The authors noted the lowest HIV burden in this group. While this may reflect lower male–male sexual exposure, these men reported a similarly high number of male sex partners to the overall sample.

Wu and coworkers’ subgroup analysis raises a number of compelling questions. First, to what extent is chronic vs incident infection fueling transmission among these 3 groups? Previously tested men and men who knew their HIV status were not explicitly excluded from this study. What proportion of the infections were acute/early infections, established infections, or perhaps men who had been infected but not yet seroconverted? A complex combination of biological, behavioral, and sexual network factors often facilitate HIV transmission in clusters among MSM. As measured through phylogenetic analyses of these clusters, acute and early infections seem to drive the spread of HIV among MSM in Canada [32, 33] and England [34]. Given the heightened prevalence of HIV and syphilis among “nonlocal” MSM, and the generally high mobility of MSM in China, genetic and sexual network–based research may greatly supplement venue and location-based analyses toward a more nuanced understanding of MSM transmission dynamics. Significant work in this vein is already under way in China [35–37]. Taken together with the rigorous epidemiologic work presented by Wu and coworkers, these methods could have considerable effect on prevention and treatment strategies deployed.

Second, the variation in average age among subgroups suggests differing lifetime exposure to HIV risk. Indeed, in the main analysis, older age was a significant predictor of both HIV and syphilis infection. Yet, the female-partnering MSM subgroup (who tended to be older) had the lowest HIV prevalence. Third, the 3 MSM subgroups are neither distinct nor exclusive. In their analysis men could be categorized in >1 group. Additionally, men almost certainly move among

groups over time. For example, younger men may exclusively have male partners, but eventually have at least 1 female partner if they follow societal pressures to marry [38]. Similarly, local MSM could easily become “nonlocal.” Furthermore, how should we categorize “nonlocal” MSM who return to their hometowns? Should men who frequently move locations (eg, male sex workers) bear the same “nonlocal” label as men who only migrate once? Finally, what proportion of the sample was not categorized in any of the 3 groups? Future work should explore more detailed variation and overlap among these proposed MSM subgroups.

Ten years ago, China anticipated a very large HIV epidemic that, thankfully, has not materialized [39]. Currently it is estimated that 780 000 people suffer from HIV infection, a general population prevalence of <0.1% [12]. China has introduced a terrific variety of HIV prevention and care programs including free anti-retroviral therapy (ART) for positive persons [40] and a 2012 commitment to scale up earlier initiation of ART [41]. However, there seems no doubt that the rapid spread of HIV and STDs among MSM jeopardizes the future of China’s HIV control.

Chinese society does not embrace same-sex lifestyles. MSM are highly stigmatized and virtually all men are expected to marry [42]. Stigma and discrimination act as barriers to HIV testing and education for Chinese MSM [43]. Despite national efforts that have increased HIV voluntary counseling and testing, 2011 surveillance estimates found that only 50% of MSM had received an HIV test in the past year and knew their results [44]. Interventions that address these barriers to testing and education at the individual, community, and structural levels are needed [45].

In the years following Wu and colleagues’ study, the national prevalence of HIV among MSM continued to rise to 6.3% in 2011 [12]. In that same year, 81.6% of new HIV infections in China were sexually transmitted, including 29.4%

attributed to MSM [12]. This underscores the need to think deeply and creatively about reducing STDs among MSM, especially in China.

Wu and coworkers have shined a bright light on a growing problem in China. Their results offer insight into the spread of syphilis and HIV, raise critical questions and—perhaps most important—point out the truly emergent need for intervention to stop the spread of these diseases. Further coalescence of these epidemics will amplify the spread of both diseases, and this synergy must be avoided. HIV prevention efforts must be redoubled in this population of special interest. This timely article provides critical fodder for action. The nature and success of that action will surely determine the future magnitude and spread of HIV in China.

Notes

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