

REVIEW

New features of the HIV epidemic among men who have sex with men in China

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Men who have sex with men (MSM) have accounted for an alarmingly increasing proportion of nationally reported human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) cases recently. While the latest HIV epidemic among this population was not well understood, the underlying reasons for the rapid increase of the HIV epidemic were even more rarely evaluated. This study reviewed all published articles and national surveillance data in recent years to analyze the new HIV epidemic among MSM in China, and this study finally concluded that a culture of risky sexual behaviors, low adoption of HIV testing and a high prevalence of syphilis infection were the major risk factors that predominantly facilitate homosexual HIV transmission. Both HIV infection and homosexuality remain highly stigmatized in China, which further exacerbates attempts at HIV prevention and control. A great deal of work still needs to be done for the national policy makers, programming, research and clinical sectors to help curb the HIV epidemic among Chinese MSM. *Emerging Microbes and Infections* (2013) 2, e45; doi:10.1038/emi.2013.45; published online 31 July 2013

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INTRODUCTION

With the extensive implementation of syringe exchange programs and methadone maintenance therapy among injection drug users and the universal screening of human immunodeficiency virus (HIV) at China's blood banks, the formerly dominant HIV transmission route from the use of shared needles and blood collection and supply channels has been curbed.¹ Currently, however, there are many new factors that can significantly increase the rate of HIV transmission among men who have sex with men (MSM), including low HIV testing rates, high HIV incidence, high prevalence of syphilis infection and migration. Compared with injection drug users and former illegal blood donors, MSM are not only a high-risk population for HIV infection, but also a potential bridge population for HIV transmission to low-risk MSM and the general population.

There are an estimated 5–10 million MSM in China,² and a high proportion of this population are at risk for HIV infection. According to reports from China's Ministry of Health, MSM comprised only 0.3% of all new reported HIV cases between 1985 and 2005, while in 2010, MSM represented 10.8% of newly reported cases.¹ More striking, between 2007 and 2009, the proportion of MSM among all new estimated HIV cases jumped from 12.2% to 32.5%.¹ MSM have become a major core population of the HIV/AIDS epidemic in China. The newly emerging HIV epidemic among MSM has been fueled by several factors, including low HIV testing rates, high prevalence of syphilis, persistent stigma against homosexuality and traditional concepts toward marriage and childbearing. Unique challenges exist regarding the prevention and control of HIV among Chinese MSM. Timely interventions that address these issues should be initiated to stem the rapid spread of HIV among MSM.

HIV EPIDEMIC AMONG MSM DURING 2008–2012

HIV/AIDS surveillance and epidemiological surveys, especially large-scale prospective cohort studies, demonstrate that the HIV epidemic in China is more severe than previously thought. In 2008, a large-scale cross-sectional survey of more than 18 000 MSM in 61 major cities of China found an HIV prevalence of 5.0% and a prevalence greater than 10% in several southwest cities.^{1,3} Our research team, supported by the China Program of the Bill & Melinda Gates Foundation, conducted a study in 2009–2010 in seven major cities and found an HIV prevalence of 6.8% (ranging from 2.8% to 10.8%) among 3321 high-risk MSM.

We also recently undertook a prospective study of 5271 MSM in 10 Chinese cities and found an incidence density of 5.9 per 100 person-years (PYs), which is notably higher than the average incidence previously found in female sex workers (1.4/100 PYs) and intravenous drug users (2.5/100 PYs).⁴ This incidence density is also high compared to that reported for populations of MSM in the Netherlands (1.13–3.75/100 PYs) and the United States (1.55–2.10/100 PYs).^{5–7}

Some subpopulations of MSM, including student MSM and ethnic minority MSM, who were previously believed to be at low risk for HIV infection, have also become high-risk groups for HIV infection. China has approximately 76.2 million high school and college students, of which the number of reported HIV/AIDS cases is increasing rapidly. Most of these cases are attributed to male-to-male sexual contact. We conducted a cross-sectional survey of 436 student MSM in Liaoning Province and found an HIV and syphilis prevalence of 3.0% and 5.0%, respectively.⁸ A recent literature review of 15 published articles from 2006 to 2012 pooled 3178 Chinese student MSM and found an HIV and syphilis prevalence of 4.0% (95% confidence interval (CI): 2.8%–5.7%) and 5.2% (95% CI: 4.4%–6.2%), respectively. Additionally, the

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analysis found a significant increasing trend in HIV prevalence over time (from 3.0% (95% CI: 2.1%–4.2%) during 2003–2006 to 4.5% (95% CI: 3.5%–5.6%) during 2007–2008, then to 6.8% (95% CI: 4.7%–9.4%) during 2009–2012) (in press by *PLoS ONE*). These results highlight that student MSM, despite their high level of education and the previous perception that they are a low-risk group by researchers, have actually become a high-risk population for HIV infection in China.

There are 56 ethnicities in China, the majority of which is the Han ethnicity (91.5%), and Chinese ethnic minority MSM are considered to be a high-risk subpopulation of MSM. Our prospective cohort study of MSM in Kunming, Yunnan Province found that the incidence of HIV among minority MSM was 10.1/100 PYs, which was significantly higher than Han-ethnic MSM (2.3/100 PYs).⁹ Additionally, minority MSM are also at risk of spreading HIV to the general population. Zhu *et al.*'s¹⁰ study showed that ethnic minority MSM were more likely to have sex with women compared to MSM who are of Han ethnicity. HIV prevention and behavioral intervention programs should focus their efforts on targeting these subpopulations of student and minority MSM.

LOW HIV TESTING RATES AND HIGH PROPORTION OF UNPROTECTED ANAL INTERCOURSE

Low HIV testing rates and high rates of high-risk sexual behaviors are major factors that correlate with the HIV epidemic among MSM. The knowledge of one's HIV status is fundamental for HIV-positive MSM to take steps to prevent secondary transmission. HIV testing rates among Chinese MSM are very low, and only a small proportion knows their HIV status, which may provide an environment for the rapid transmission of HIV among this population. A meta-analysis found that the rates of lifetime HIV testing among Chinese MSM were 24% and 47% during the periods of 2000–2006 and 2007–2012, respectively.¹¹ A study of high-risk MSM in Jinan City, Shandong Province found that only 19.3% of participants had been tested for HIV in the past 12 months,¹² while the proportion of past 12 month HIV testing among high-risk MSM was 18% in Beijing¹³ and 6.9% in Guangzhou.¹⁴ Low HIV testing rates are accompanied with poor HIV knowledge and high proportions of unprotected anal intercourse. Previous studies have reported that MSM can correctly answer approximately only 60% of questions about HIV/AIDS transmission and prevention.^{15,16} Rates of high-risk behaviors among MSM are also concerning. A recent meta-analysis conducted using 66 published studies reported the condom use rate with male sexual partners among a national sample of MSM was only 32.5% (95% CI: 28.6%–36.7%) in 2003–2005 and 36.3% (95% CI: 33.7%–38.9%) in 2006–2008.¹⁷

HIGH PREVALENCE OF SYPHILIS INFECTION

There is epidemiological synergy between HIV and other sexually transmitted diseases. Syphilis infection, in particular, is significantly correlated with sexual HIV transmission.¹⁸ A meta-analysis found a prevalence of 9.1% among Chinese MSM, which is almost four times that of HIV prevalence in the same population (2.5%). High syphilis prevalence indicates a potential for a more severe HIV epidemic.¹⁹

We conducted cross-sectional and prospective cohort studies of high-risk MSM in Liaoning and Yunnan Provinces and found high syphilis prevalence (5.0%–25.4%) and incidence (5.3–38.5/100 PYs).^{8,9,20} Additionally, syphilis infection increased the risk of new HIV infections in this population by 5.6–11.4 times.^{9,20} Ruan *et al.*'s²¹ survey of Beijing MSM also found a significant positive correlation between syphilis and HIV infections. Syphilis infection is

often asymptomatic at the early stages of infection, and a lack of treatment could increase the risk of HIV infection. To prevent the rapid spread of HIV among MSM, prevention, treatment and control of syphilis is urgently needed.

THE EFFECT OF TRADITIONAL CHINESE CULTURAL ON THE HIV EPIDEMIC

The effect of traditional Chinese culture is another major factor that is correlated with the HIV epidemic among MSM in China. HIV advocacy groups understand that relying solely on biomedical approaches and technical breakthroughs are not sufficient for controlling the HIV epidemic. More attention should be paid to social and cultural factors, which influence the epidemic because they can significantly affect vulnerability to HIV.²² HIV/AIDS-related discrimination and traditional ideals regarding marriage and childbearing are two types of Chinese cultural factors that can significantly impact the spread of HIV²³ and weaken China's effect of HIV/AIDS prevention and control efforts.

Community discrimination toward HIV and homosexuality

Both HIV and homosexuality remain highly stigmatized in China. Community discrimination is inversely associated with HIV testing and may also lead to high-risk sexual behaviors. It is difficult to eliminate community discrimination of HIV and homosexuality. Chinese society emphasizes the importance of social status, and therefore, many MSM do not disclose their sexual orientation to their friends, family members, and physicians. Some MSM decline to test for HIV to prevent disclosing their sexual orientation to public health providers.²³ Li *et al.*'s²⁴ study of Beijing MSM revealed that HIV/AIDS-related stigma and discrimination were also very common among MSM, and discrimination was inversely associated with recent HIV testing behavior; their study highlights the urgent need to reduce HIV/AIDS-related stigma and discrimination of MSM.

Other research indicates that social discrimination is correlated with negative psychological health among MSM, which may promote high-risk sexual behaviors.^{25–27} Zhang *et al.*'s study showed that experiencing discrimination was significantly associated with suicide attempts among MSM.²⁸ An unpublished study by our research team of MSM in Liaoning Province found that the prevalences of depression and suicide attempts among Liaoning MSM were 36.8% and 10.9%, respectively. Multivariate analysis indicated that moderately depressed MSM and those MSM who had ever attempted suicide were 2.0 and 3.0 times more likely to have unprotected anal intercourse, respectively. Zheng *et al.*'s²⁹ study of MSM in Anhui Province also found a similar phenomenon, in which anxiety and depression were both positively associated with risky sexual behaviors. In addition to widespread discrimination against homosexuality, the Chinese general population knows little about the HIV epidemic and the populations at greatest risk; many even incorrectly believe that HIV/AIDS cases are still mainly concentrated among former illegal blood donors, as was the case at the beginning of China's HIV epidemic.³⁰

Bisexual behaviors and marriage to females

Chinese traditional culture, which is, in part, a result of China's agrarian tradition, promotes the concept of continuing the family line, the belief that more children bring greater happiness, and that children are a means of insurance in old age.³¹ These ideals are still very prevalent in China and provide great challenges to HIV/AIDS prevention and control efforts. MSM are often pressured to get married, and this phenomenon is more common in rural areas where the proportion of

MSM married to females is estimated to be as high as 90%.³² Our cross-sectional study in Shenyang found that 45% (161/358) of unmarried MSM planned to marry females, of which 96.9% (156/161) planned to bear children with their future female partners.

The primary pressure for MSM to conceal their sexual identity from their wives comes from pressure to marry and have children and to uphold the family reputation and lineage. Our meta-analysis of 28 739 Chinese MSM found that 31.2% (95% CI: 28.1%–34.5%) of Chinese MSM have had recent female sexual partners (in the past 6 months).³³ To bear children with their wives, married MSM will have unprotected vaginal sex with their wives, thus putting their wives and unborn children at risk of HIV and other sexually transmitted diseases. Our meta-analysis also showed that having sex with both men and women seems to be a significant risk factor that increases the odds of HIV infection by 30% compared with MSM who only had male sex partners (5.4% vs. 3.8%). Thus, it is critical to address cultural norms to prevent HIV transmission.³³

POPULATION MIGRATION

China's rapid economic development resulted in the creation of as many as 145 million migrants from rural areas to large cities. Migrants are usually young and sexually active, although they often come from low education backgrounds and know little about HIV/sexually transmitted disease prevention methods or how to access local HIV prevention services, such as free condoms. A study of MSM in nine cities in China found that migrant MSM had significantly more sexual partners, higher frequencies of anal and oral intercourse, but lower rates of condom use with male and female sexual partners compared with resident MSM.³⁴ Furthermore, migrants seldom seek out public health services, such as HIV voluntary and counseling testing, mainly for fear of disclosing their behavior.²³ It is reported that migrants account for 70.2%–89.5% of the annually reported HIV/AIDS cases in several large cities in China.^{35,36} A study in Shanghai found that migrant MSM had more sexual partners, more casual sexual partners, and a higher prevalence of HIV infection compared to non-MSM male migrants.³⁷ MSM migrants are another special subpopulation of MSM; their frequent movement and engagement in sex with strangers may increase their risk for HIV infection, and may also promote the rapid transmission of HIV.

OTHER FACTORS THAT CAN AFFECT THE SPREAD OF THE HIV EPIDEMIC AMONG MSM IN CHINA

Although studies in developed countries have found that illegal drug use can significantly increase HIV infection risk,³⁸ surveys of Chinese MSM have failed to find statistically significant correlations between illegal drug use and HIV infection.^{9,15,20,21,39} Only one research study in Liaoning Province found that drug-using student MSM had significantly higher HIV prevalence compared with the student MSM who did not report using illegal drugs.⁸ With the increasing reports of illegal drug use among Chinese MSM, the relationship between illegal drug use and HIV infection should continue to be monitored in this population.

Blood donation from MSM may also lead to HIV transmission because the traditional HIV antibody testing techniques of China's blood bank are not able to detect acute HIV infection. Previous surveys found that 24.0% of high-risk MSM had a history of blood donation,⁴⁰ and 36.8% of screened HIV positive samples at blood stations were donated by MSM.⁴¹ Our recent cross-sectional study of 98 acutely infected MSM in Beijing, Liaoning, and Yunnan Provinces also found that 20.4% (20/98) of MSM had recently donated blood. The rapidly

increasing HIV epidemic combined with the high proportion of MSM donating blood may pose a high risk to the clinical blood security in China. We reported this potential risk to the Ministry of Health in 2010, which consequently implemented a nucleic acid amplification test pilot screening program in 2011 for HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) in China's blood donation stations. The RNA pilot screening program identified several acute HIV infections, acute HBV infection and acute HCV infection in donated blood samples. Nucleic acid amplification test screening for HIV, HBV and HCV is now a routine procedure for most blood donation stations in China.

Information technology is becoming more widespread worldwide. China currently has the largest number of internet users in the world, of which most are mobile phone users. The number of smart phone users in China is also ranked first in the world (222 million users). Geosocial networking (GSN) phone applications such as Grindr and Wechat, which run on smart phones, now play a huge part in helping Chinese MSM meet sex partners. Several surveys in developed countries have shown that MSM who seek sexual partners via the Internet had significantly more sexual partners and an increased risk of HIV and other sexually transmitted infections.^{42,43} GSN users had a significantly higher proportion of positive gonorrhoea and Chlamydia test results compared with non-Internet/non-GSN users and a slightly higher proportion than Internet/non-GSN users.⁴⁴ However, little research has been conducted to explore HIV infection risks and associated risky sexual behavior among Internet- and/or GSN-using Chinese MSM. It is urgent to learn more about these technologies and their use in China to develop appropriate interventions to target these high-risk MSM.

INCREASING HIV VIRAL COMPLEXITY AND RAPID DISEASE PROGRESSION

Molecular epidemiological studies show that persistent circulation of multiple HIV-1 subtypes and complex new recombinants are constantly occurring among Chinese MSM. The predominant HIV-1 epidemic strain changed from subtype B of US-European origin in 2005 to CRF01_AE in 2012.^{45–50} In 2005, subtype B accounted for 71.1% of cases among Beijing MSM, followed by CRF01_AE (24.4%) and CRF07_BC (4.4%).⁵¹ Follow-up surveys of Beijing MSM revealed that subtype B percentages decreased to 41.9% in 2007 and to 20% in 2009. In contrast, non-B subtypes increased rapidly: CRF01_AE increased from 3.7% in 2005 to more than 50% in 2009.^{45,52} Nearly during the same period (during 2006–2007), subtypes B, CRF01_AE, and CRF07_BC accounted for 35.7%, 35.7%, and 28.6%, respectively, of the MSM in Zhejiang Province, a coastal area of eastern China.⁴⁶ More recent studies have shown the dominance of CRF01_AE among MSM in several regions of China. In Shenyang, Liaoning Province, northeast China, CRF01_AE accounted for 81.3%–87.6% of HIV strains among MSM.^{47,48} Similar trends were observed in studies from Hebei Province⁴⁹ and Henan Province, north and central China.⁵⁰ In addition, new CRF01_AE/B recombinant strains have also been reported among MSM.⁵³ Two new CRFs: CRF55_01B^{39,54} and CRF59_01B (<http://www.hiv.lanl.gov>) were identified in Chinese MSM. According to the latest data from nine cities in China, three distinct lineages of HIV-1 strains (CRF01_AE clusters 1 and 2; CRF07_BC cluster 3) were identified,^{54,55} more than three-quarters of recent HIV-1 infections among Chinese MSM were demonstrated to be caused by these three strains.⁵⁴ Furthermore, many of these strains are resistant to one or more antiretroviral drugs, contributing to the high prevalence of HIV drug resistance among MSM. The epidemic of

drug-resistant HIV varies regionally, with an estimated prevalence of 15% in Beijing,⁵¹ 4.5% in Shenyang⁴⁸ and 4.6% in Chongqing.⁵⁶ With the expansion of the HIV epidemic throughout the MSM population, such genetic diversity and levels of resistance are expected to increase, creating further challenges to interventions, effective treatments and vaccine development.

Recent studies show that HIV subtypes can significantly impact the rate of disease progression. Studies from Thailand and Singapore have found that subtype CRF01_AE-infected patients had a rapid HIV progression.^{57,58} Our research team surveyed a large cohort of MSM in Beijing, Yunnan and Liaoning Provinces who were acutely infected with HIV and found that one year after infection, 35% had CD4⁺ counts decline to <350 cells/mL and the median time from HIV seroconversion to CD4⁺ T cells <350 cells/mL was only 27 months, which is significantly faster than European MSM and Chinese infected through other transmission routes. The prevalence of HIV-1 subtype CRF01_AE is high among Chinese MSM, which may partly explain the rapid rate of disease progression. The increasing trend of HIV prevalence and the rapid rate of HIV disease progression among MSM indicate the need for the Chinese government to provide additional funding for highly active antiretroviral therapy.

CHALLENGES AND OPPORTUNITIES FOR HIV/AIDS CONTROL AND PREVENTION

The proportion of nationally reported HIV/AIDS cases attributed to male-to-male homosexual route may be underestimated. The coexistence of low HIV testing rates and high HIV incidence indicate that numerous HIV-infected MSM may still fail to know their HIV infection status, which is the hidden danger for HIV transmission in China. Feelings of stigma and discrimination may compel some HIV-positive MSM to conceal their homosexual behavior, and therefore, these individuals may be categorized as 'unknown transmission route' or 'other HIV transmission route', which may be less stigmatizing in China.

To definitively learn about the HIV epidemic among MSM and prevent the rapid transmission of HIV, the Chinese government should further expand media, education, and HIV testing programs among MSM. Government sectors should increase the number of HIV testing sites, provide more choices for convenient HIV testing for MSM, and promote HIV/AIDS transmission and prevention knowledge education through mass media, MSM dating websites and sex partner-finding phone apps, to raise awareness and promote condom use. The China Centers for Diseases Control and Prevention (CDC) should cooperate with non-government organizations and encourage MSM peers to provide more outreach services to deliver health education, free condoms and encourage HIV testing among MSM. Medical workers in hospitals and clinics should be encouraged to offer provider-initiated HIV testing and counseling to outpatients who attend primary clinics and are unaware of their HIV status. China CDC staffs should provide more convenient means of HIV testing for MSM, such as on-site, rapid, oral fluid testing. China should protect the rights of people who live with HIV/AIDS and take substantial efforts, including legislative measures, to oppose social discrimination against HIV infection and homophobia.

Previously published studies of Chinese MSM have provided important information for understanding the HIV epidemic among this vulnerable population, although many of these studies have had significant limitations. For example, the majority of studies were cross-sectional surveys, which are usually less expensive and more convenient to conduct, and can provide some information about HIV-related factors, but they cannot demonstrate causality.

Although prospective cohort studies are better, there were very limited numbers of short-term prospective cohort studies conducted on HIV incidence among Chinese MSM. Most studies asked about previous or recent sexual behaviors, but few asked about HIV testing behaviors and HIV infection status of the MSM participants' female and male sexual partners (HIV serosorting). Most studies directly collected the sensitive sexual behaviors of MSM participants through interviewer-administered questionnaires, which may have resulted in underreporting due to social desirability bias compared with self-administered questionnaires.

The HIV epidemic among Chinese MSM is rapidly increasing and MSM are likely to become the largest high-risk population for HIV infection in China. The Chinese government has realized the magnitude and severity of the HIV epidemic among MSM and has implemented some targeted policies, including issuing the China's Medium- and Long-Term Program (1998–2010), HIV/AIDS Reduction and Prevention Plan of Action (2006–2010) and the HIV/AIDS Reduction and Prevention Plan of Action (2011–2015), with the ultimate aim of further expanding the condom promotion and HIV screening programs and reducing new HIV infections. Additionally, China has established the State Council AIDS Working Committee, and invested more funds for HIV prevention and control. China invested more than four billion Yuan (approximately 0.65 billion US dollars) for HIV/AIDS control efforts during 2010–2011, which is more than eight times the amount invested in 2003. With increasing political support, more extensive and intensive HIV prevention and control measures should be made throughout China to curb the spread of HIV infection among MSM.

Research indicates that early antiretroviral therapy (ART) is able to reduce HIV transmission risk among HIV discordant couples,⁵⁹ which has promoted the concept of early HIV treatment as prevention among MSM. This prevention technique has been applied in some provinces in China, but the magnitude of ART transmission, viral suppression and its durability have not been evaluated among Chinese MSM. Early ART to HIV-positive MSM will inevitably increase the cost of HIV/AIDS prevention programming and cost-effectiveness analyses should be considered before this HIV prevention strategy is expanded across all of China. Compared with early HIV treatment strategies, condom promotion among HIV positive MSM is another effective strategy to prevent HIV transmission, especially because it is very inexpensive compared with administering early ART. Currently, China's CDCs are mainly responsible for HIV/AIDS disease progression surveillance and ART administration, but 100% condom promotion and risk reduction programs should be integrated with these activities to provide potential entry points for behavioral interventions. Non-government organizations that mainly address the provision of service and care for people who live with HIV/AIDS should also organize and cooperate with the CDC systems to provide intervention activities to prevent the spread of HIV, including the promotion of abstinence, being faithful to one's partner, and 100% condom use among sexually active people who live with HIV/AIDS.

Rapid changes in demographics, sexual behaviors and genetic features of HIV pose tremendous challenges in our efforts to develop interventions for Chinese MSM and to provide antiretroviral treatment and develop vaccines. China's HIV/AIDS prevention and treatment strategies have to be made more effective and sustainable at the beginning of the epidemic. Interventions should focus on decreasing sexual transmission of HIV and syphilis across subpopulations of MSM who are susceptible to HIV and are at high risk for HIV acquisition. The government should encourage large hospitals, especially

their sexually transmitted disease divisions, to join HIV/AIDS prevention efforts. MSM should be encouraged to obtain HIV testing at voluntary counseling and testing sites, instead of at blood banks. Additionally, the Chinese Ministry of Health should continually expand HIV RNA screening at blood banks to detect contaminated blood donated from those with acute infection to ensure the safety of the blood supply. Only through large-scale, coordinated, national efforts between policy, programming, research and clinical sectors will there be a significant reduction in new HIV infections among Chinese MSM.

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