Challenges and Future Directions

35

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Abstract

China has made remarkable achievements in advancing its HIV/AIDS prevention and treatment programs. Infrastructure for surveillance, laboratory testing, voluntary counseling and testing, outreach, intervention, and harm reduction for key populations, and antiretroviral therapy (ART) services for people diagnosed with HIV have been well developed. Meaningful reductions in HIV transmission have been observed among people who inject drugs, serodiscordant couples, and children of mothers living with HIV. The "Four Frees and One Care" policy has facilitated large numbers of people being tested for HIV and a high proportion of people living with HIV (PLWH) being diagnosed. Moreover, a large number of people diagnosed with HIV have received free ART. The case-fatality rate of PLWH has dropped by over 70% in the past 30 years. However, the HIV/AIDS epidemic is not yet under control. The epidemic has shifted almost exclusively to expansion via sexual transmission. The number of newly-diagnosed HIV cases continues to increase and the number of deaths among PLWH has remained unacceptably high. To take control of the HIV/AIDS epidemic, China faces tremendous challenges and needs to develop new strategies.

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Z. Wu et al. (eds.), *HIV/AIDS in China*,
https://doi.org/10.1007/978-981-13-8518-6_35

35.1 The Many Challenges of China's HIV Epidemic

China's HIV epidemic continues to evolve. It started with injecting drug use in the late 1980s, it expanded quickly via contaminated plasma collection in the early- to mid-1990s, and then, increased further via mother-to-child transmission (MTCT; Pisani and Zhang 2017; Chaddah and Wu 2017). Today, the HIV epidemic in China has shifted from multiple transmission modes to now almost exclusively sexual transmission (Wu 2018). Unfortunately, however, our understanding of the epidemic has not become simpler.

The proportion of newly diagnosed people living with HIV (PLWH) who reported sexual contact as their infection route increased in just 5 years from less than 90% in 2013 to over 95% in 2017—heterosexual contact has accounted for 66.2–69.5% of all sexually-acquired infections and homosexual contact for 19.1–28.2% (National Center for AIDS/STD Control and Prevention 2017, 2018). Over the next 5 years, the epidemic is predicted to continue to evolve with an increase in the proportion of infections attributed to heterosexual contact, perhaps approaching 75%, and a decrease in the proportion attributed to homosexual contact, perhaps declining to 20%.

Although heterosexual transmission is clearly the largest driver of new HIV infections in China, HIV prevalence among female sex workers (FSW) and male attendees of sexually transmitted infection (STI) clinics remains consistently below 1%. How then, should we interpret the observed increase in heterosexual transmission of HIV? This is a typical case when population size is huge, even a typical case when population size is huge, even a very low prevalence still produces a considerably large number of HIV infections. This mode of HIV epidemic makes control extremely difficult.

HIV infections acquired via heterosexual transmission are concentrated primarily in rural areas where the initial HIV outbreaks occurred and first spread including, for example, Yunnan, Guangxi, Xinjiang, and Sichuan. Newly diagnosed men who report their route of infection as being heterosexual contact tend to report acquiring their infections from FSW. By contrast, newly diagnosed women most commonly report acquiring their infections from extra-marital, non-commercial partners (National Center for AIDS/STD Control and Prevention 2018).

In the context of commercial sex, a small number of FSW usually provide sexual services to a large number of male clients. Thus, intervention programs targeting FSW should have a significant positive impact and successfully slow down the epidemic. However, there are tremendous barriers to delivering effective HIV interventions to Chinese FSW. Firstly, low-tier FSW (i.e., those who charge low fees and are usually independent and street-based) are at the highest risk of acquiring and transmitting HIV and other STIs (compared to mid- and high-tier FSW) yet are the most difficult to approach. This very large, and very high-risk subgroup of FSW are typically scattered across rural regions and outer reaches of city suburbs, and deliberately hide their occupation and move frequently for fear of harsh societal stigma and discrimination as well as police "crackdowns" and incarceration. Secondly, with increased mobile device use and increased cellular network and wireless internet coverage as well as rapid adoption of mobile applications for

geospatial social networking, FSW have changed the way they seek potential clients, which further contributes to the "hidden" nature of Chinese FSW and challenges in approaching this vulnerable group with HIV prevention, testing, treatment, and care services.

Changes in social norms and perceptions of sex have greatly changed Chinese sexual life. Casual sex has become more popular than ever. More people are accepting of the idea of having sex with friends, colleagues, or even strangers. This increase in acceptability of extra-marital, non-commercial sex explains the majority of HIV infections acquired through heterosexual contact among women and about 40% heterosexually-acquired infections among men (National Center for AIDS/STD Control and Prevention 2018). All PLWH, whether diagnosed or undiagnosed, may be engaging in this type of risky behavior, potentially transmitting HIV to their sexual partners. This means that there are no "focal points" to be targeted by outreach programs, making prevention intervention very difficult.

Male-male sexual contact is the major mode of transmission driving the HIV epidemic in urban areas and in northern China (National Center for AIDS/STD Control and Prevention 2018). In the capital cities of all 31 provinces, homosexual transmission accounted for over 50% of newly reported HIV infections among men. However, men who have sex with men (MSM) are thought to account for less than 5% of the entire male population in China. Thus, Chinese MSM clearly experience a disproportionate burden of disease. However, this group is actually quite diverse and is similarly hidden and difficult to reach with interventions for several reasons. Firstly, a majority of newly diagnosed HIV infections attributed to male-male sexual contact are reported among male youths and young adults. However, middle-aged and older Chinese men are known to practice risky homosexual behavior as well and therefore are at similar risk of HIV infection. Thus, it is thought that the age distribution of PLWH who are MSM is skewed young because of deliberate miss-reporting of infection route by adult males who do not want their male-male sexual activity exposed. Over-reporting of heterosexual contact and under-reporting of homosexual contact transmission routes among Chinese men living with HIV helps explain the observed differences in patterns of HIV infection between men and women but highlights major barriers to intervention—it is unclear which men need what kinds of intervention services and how these men can best be approached. Secondly, a considerable proportion of MSM also have sex with women (MSMW), and many are married. Extreme societal pressure to marry and produce an heir to carry on the family name combined with persistent stigma and discrimination against MSM combine to encourage this practice. Furthermore, many MSM and MSMW do not self-identify as homosexual or bisexual and therefore messaging on the risks of HIV and the importance of protecting oneself and one's partners in the context of a particular sexual orientation yields suboptimal results. Female partners of MSMW are particularly vulnerable to HIV infection as they are often unaware of their male partners' homosexual behavior. This may also help explain the observed differences in patterns of HIV infection between men and women—men acquire HIV infection from men and pass their infection on to women. However, this also similarly highlights major barriers to intervention as it becomes difficult to know who needs what kinds of services and how best to deliver them.

One possibility for solving some of these issues has been the development and broad adoption of mobile applications tailored to men seeking men for dates and sex. These virtual communities provide a range of different modes of communication (e.g., person-to-person texting, group chatting, message boards, advertising) combined with geospatial locating capabilities that enable men to easily seek and find other men in a relatively hidden and safe environment. Research is only now just beginning to uncover how these tools can be used to deliver HIV prevention, testing, and treatment interventions in a way that is relevant and effective for MSM in China. Early results are promising, and this work must be expanded.

Two additional groups of people require special attention if China is to bring its HIV epidemic under control. The first is students. Over the past 5 years, the number of students newly-diagnosed with HIV infection has significantly increased. Now, over 3000 students are diagnosed with HIV infection each year, and over 80% of them report having become infected via male-male sexual contact. The second is senior male adults over 60 years of age. Less than 5000 new infections among men over 60 were diagnosed in 2010, but just 7 years later in 2017, almost 20,000 new infections were found among this group. This represents a doubling in the proportion of all cases reported annually—from 7.4% to 14.7% (National Center for AIDS/STD Control and Prevention 2018). Although traditionally, men over the age of 60 tend to be less sexually active, modern medicine has changed that—erectile dysfunction drugs such as Viagra have extended their sexual capability well into old age. These senior men most likely visit low-tier FSW, thereby exposing themselves to the risk of HIV and other STIs.

While it appears China's HIV epidemic has perhaps grown simpler over time with now nearly all cases caused by a single transmission route, the many above-described issues, as well as others that are perhaps not yet recognized, underscore the complicated nature of China's current HIV/AIDS epidemic. China must re-commit itself to developing a deeper understanding of its current epidemic and applying that understanding to innovative interventions.

35.2 Challenges in Controlling the Sexual Transmission of HIV

China's sexually driven HIV/AIDS epidemic is shaped by social and cultural norms about sex. Shifts in these norms toward increasing tolerance and acceptance of multiple sexual partners, homosexual and bisexual behaviors, casual sex, and extra-marital sex are unlikely to change in the near future. Thus, it is expected that the sexual transmission of HIV infection will continue in China as well. Making matters worse is the rapid increase in synthetic drug use, particularly among China's youth and young adult populations, is further contributing to riskier sexual behaviors that facilitate HIV sexual transmission.

In general, people are presumed to think rationally. In the case of PLWH, it is assumed that they simply did not have sufficient HIV/AIDS knowledge, did not know the risks, and/or did not understand how to prevent it. Furthermore, it is

assumed that once people have such knowledge, they should able to take actions to prevent HIV infection. This is the typical belief among the Chinese public, and it is true for most infectious diseases, particularly food- or water-borne digestive infections and diseases that are preventable with vaccines. However, it is not true in the case of HIV.

One of the authors that contributed to this volume asked one question of over 100 students who had been diagnosed with HIV within the prior 3 years. The question was: "if you could go back 5 years and live them over again with your current HIV/AIDS knowledge, are you confident you would prevent your HIV infection?" Very, unfortunately, none answered "yes." Some people engage in high-risk sexual behaviors even though they know they could become infected with HIV because of economic factors, some because they cannot, or choose not, to control themselves, and some because they simply do not care. Clearly, knowledge alone is insufficient for HIV prevention.

If used appropriately, condoms are very effective tools for preventing HIV infection via sexual transmission. So, why have condoms not stopped China's sexually-driven HIV epidemic? In general, people believe that the use of a condom is not difficult and therefore, once people learn how to use condoms and that condoms can protect them from HIV infection, they will henceforth easily choose to consistently use condoms to protect themselves. Unfortunately, this is not the case in real life. In real life, consistent condom use is very difficult.

Many years ago, a peer educator from San Francisco was invited to appear on a nationally syndicated television talk show in the United States. When asked why he worked so diligently to spread the message on safe sex among MSM communities and at the same time he, himself, was continuing to engage in risky sexual behavior, he replied that he was good at his job, but that he was also a human being—a regular homosexual man. His answer surprised audiences. Clearly, risky sexual behavior is not linearly associated with HIV/AIDS knowledge and perceived HIV/AIDS risk.

To understand how Chinese MSM communities perceive the HIV epidemic, a very small focus group discussion was held in Beijing in 2015, with representatives of MSM communities from selected cities (e.g., Beijing, Tianjin, Guangzhou, Qingdao, Chengdu). A total of ten men were invited. One man said that once a person used a 0.03 mm condom, he would never use a 0.05 mm condom again, and once he used a 0.01 mm condom, he would never use a 0.03 mm condom again. One man, who was employed as a surgeon at a famous university-affiliated hospital said that he had not used a single condom in the past 3 years. All in attendance were shocked by this—it was unbelievable that a well-educated health professional continued to engage risky sexual behavior. He replied that the risk was worth it to him to have the enhanced pleasure he experienced having sex without using a condom. This phenomenon of passion and gratification overcoming rationality is very hard to understand, but it is a real-world issue.

Taken together, these findings suggest reliance on education and condom promotion only will not be enough to slow down the sexual transmission of HIV. More must be done. Biological (rather than behavioral) strategies must be employed to effectively confront the challenges associated with preventing the spread of HIV in

China via sexual contact. Many biologically-based prevention technologies and strategies have been developed, tested, and found to be safe and effective in preventing HIV transmission among different risk groups and in different settings.

Treatment of STIs is an effective strategy for reducing sexual transmission of HIV and has been used in most countries. Studies have shown that in areas where STIs are prevalent and HIV is primarily transmitted via sexual contact, treatment of STIs significantly reduces HIV incidence. STIs are prevalent in China, and controlling STIs, particularly syphilis, has been adopted as a national strategy for HIV control in China. However, it is not well and fully implemented and thus, has so far had very limited impact on China's HIV epidemic.

Male circumcision has been found to be effective in reducing HIV infection among heterosexual males and has been used in some of the African countries where HIV prevalence is high. Although China's HIV epidemic continues to expand, the overall national HIV prevalence is only 0.06% (National Center for AIDS/STD Control and Prevention 2018). Furthermore, a pilot test of male circumcision among MSM was conducted and although participants' reported intention was high, their actual acceptance rate was less than 1%. Low prevalence combined with low acceptance suggests a low probability of success for this intervention and therefore, male circumcision has not been advanced as a national strategy in China.

Pre-exposure prophylaxis (PrEP) using antiretroviral (ARV) drugs has been tested in heterosexual and homosexual populations internationally and found to be safe and effective, resulting in several nations' health authorities approving ARVs for HIV PrEP. In general, PrEP must meet following criteria to be effective: (1) it must be affordable, (2) it must target uninfected men in areas that have a relatively high HIV incidence (e.g., at least 3%), (3) it must target groups willing to take it, and (4) it must include medical monitoring for side effects. In China, the overall incidence of HIV prevalence is very low. The only group that may meet these criteria for PrEP is MSM. A first pilot study of PrEP was conducted in China from 2008 to 2011, but results were disappointing—the intention to use PrEP was low (19%) and actual uptake of PrEP was even lower (2.5%; Ding et al. 2016). A second study of PrEP, conducted from 2012 to 2015, demonstrated that it could be effective in reducing HIV incidence if the compliance rate was high (Zhong 2018). An ongoing qualitative study indicated that MSM are unlikely to take PrEP for HIV prevention—risk perception is low, belief in PrEP as an effective prevention strategy is low, and worry about PrEP side effects and drug resistance is high. Thus, government provision of free PrEP is currently difficult to justify. Furthermore, the only ARV medicine that has been studied for PrEP in China is tenofovir disoproxil fumarate (TDF), which costs about 15 USD per month when manufactured in China as a generic. Truvada, a dual medicine for PrEP manufactured by the Gilead, costs some 300 USD a month in China. Without assistance, Truvada is unaffordable for many people in China. Perhaps in the future, the Chinese Government should consider partial coverage of the cost of PrEP by including it in state-provided health benefits. However, at the present time, PrEP has not been included as a national prevention strategy.

Post-exposure prophylaxis (PEP) has been used for many years in China as a prevention strategy for health, public health, and other professionals occupationally exposed to HIV. Each year, about 700–1000 HIV exposure events occur in China, with a majority of those being among health professionals, and some among law enforcement officers. PEP has been provided to all professionals who report occupational exposure to HIV and none have become infected. Request for the non-professional use of PEP mainly comes from MSM communities. Services for providing PEP to MSM based on request only operate in a few cities, such as Beijing, Guangzhou, and Shanghai, with individuals requesting PEP bearing the costs themselves. However, PEP has not been expanded and implemented as a national prevention strategy yet.

HIV treatment as prevention (TasP) is a strategy based on the fact that PLWH, the only sources for producing new HIV infections, can be made less infectious through effective treatment. To take full advantage of this strategy, PLWH must be diagnosed as quickly as possible after they become infected and must be initiated on effective treatment as soon as possible after they are diagnosed. Studies have shown that early diagnosis and immediate initiation of ART can reduce onward HIV transmission considerably. The TasP strategy has been implemented in China since 2011 among serodiscordant couples. In 2011, there was a total of 65,795 known serodiscordant couples in China, 58% of PLWH within these couples received ART, and the HIV seroconversion rate was only 2.6% (National Center for AIDS/STD Control and Prevention 2018). In 2017, there were 141,435 known serodiscordant couples nationwide, ART coverage had increased to 81% and the HIV seroconversion had fallen to 0.68% (National Center for AIDS/STD Control and Prevention 2018). Clearly, this strategy works, but the number of new HIV infections remains unacceptably high.

Although seemingly simple and easy, this strategy has several important challenges. First, a large proportion of PLWH in China remain undiagnosed and/or present late to testing and care. A majority of new infections are probably transmitted by PLWH who do not know they are infected. Thus, HIV testing has been scaled up very quickly, particularly in the past 15 years. The more HIV tests performed, the more PLWH are diagnosed—in 2004, 20 million tests were provided, yielding 23,100 diagnoses while in 2017, 200 million tests were performed and 134,512 diagnoses were made (Wu et al. 2017a, b; National Center for AIDS/STD Control and Prevention 2018). Although a majority of HIV tests were conducted, and a majority of HIV diagnoses were made, in healthcare settings (62% of tests and 54% of diagnoses in 2017), a disproportionately large number of these PLWH were diagnosed only after they had progressed to advanced HIV disease or AIDS. These "late presenters" have had HIV infection for years and not known it, likely passing on their infection to multiple sexual partners. More must be done to encourage early and frequent HIV testing uptake. Second, detection of acute or early stage of HIV infection (i.e., the first, short window of time when infectiousness is at its peak) requires sophisticated laboratory technology and is not feasible to be implemented on a nationwide scale. With testing uptake already sub-optimal, scaling up capacity for HIV detection in acute early infection is unlikely to have a meaningful impact on China's HIV epidemic. Third, there

continues to be "leakage" from China's HIV care continuum—PLWH are lost with every step from screening HIV-reactive, to confirmed diagnosis, to clinical assessment and initiation of ART (Ma et al. 2018). Service fragmentation has historically caused the process of becoming diagnosed and starting treatment to be too slow, difficult, and complicated—wait times were too long, notifications were late or incomplete, and follow-up for migrants or mobile populations was nearly impossible. A new patient path from screening to treatment has been developed that substantially streamlines, simplifies, and accelerates this process and results in trials have been very impressive, resulting in its adoption already as national policy (Wu et al. 2017a, b). However, implementation is still ongoing.

35.3 Future Directions

China's ultimate goal, the elimination of HIV, is large and daunting, and to some perhaps, seemingly impossible. However, it can easily be broken up into many smaller goals, which may form an outline of future directions. For example, it is possible to eliminate HIV from certain geographic areas, or among specific group of people.

Dehong prefecture, Yunnan province, is a likely geographic candidate for HIV elimination. Comprehensive responses to HIV have been implemented in Dehong since 2003. These included condom use promotion among FSW, harm reduction among PWID, large scale HIV testing programs both within healthcare settings and in the broader community, and ART for all diagnosed PLWH. Now, 15 years later, these efforts are paying off—the number of newly diagnosed cases has dropped from roughly 1500 annually in 2003 to only 300 cases in 2017, probably as a result of these intensive interventions. Continuation of these programs, alone, could result in a further reduction to less than 100 per year in the next 5 years. Further expansion or addition of new, innovative strategies may result in even faster elimination.

Elimination of HIV MTCT is also possible in China. Since 2010, China has implemented a nationwide program targeting all pregnant women for the prevention of HIV, syphilis, and hepatitis B virus (HBV) transmission to their infants. As a result of this program, the overall HIV MTCT rate has reduced from 8% in 2009 to 5.2% in 2017, and in urban areas to less than 2%. To completely eliminate this HIV transmission route, further data analysis is needed. Public health specialists need to understand the following questions: Are MTCT events concentrated in certain areas or are they distributed across the whole country? Why are MTCT events still occurring under the universal PMTCT program? Did PMTCT program services not reach these mother-infant pairs in a timely fashion? Or, is the program not effective at blocking this route of HIV transmission? Asking these questions and others and seeking the answers through analysis of routinely collected data is an important activity necessary for improving the PMTCT program, and eventually eliminating this transmission mode.

PWID is likely the first high-risk population that would be a reasonable candidate for eliminating HIV in China. After 15 years of harm reduction, the HIV

epidemic among China's PWID population has been well controlled. The proportion of all newly diagnosed HIV cases among PWID fell from 44% in 2004 to less than 4% in 2017. At the peak of China's HIV epidemic among PWID, 16,000 cases were newly identified in 2006. Only 4000 cases were found in 2017. Hopefully, the total number of new infections among PWID could fall further to less than 1000 in next 5 years, but in order for that to happen, further epidemiological analysis is required to guide precise responses to the gaps in current harm reduction programs.

Elimination of HIV transmission among serodiscordant couples is another good target. The HIV seroconversion rate in this key, the high-risk group has already fallen to less than 1% as a result of TasP strategies. However, coverage is currently only approximately 80% and no special guidance, counseling, or support are provided to couples who want to have a child. In order to eliminate HIV transmission among serodiscordant couples, coverage must be made universal and services must be expanded.

Although not reasonable yet to consider elimination, the sexual transmission route must be addressed quickly and comprehensively so that the trajectory with which China's HIV epidemic is expanding may be changed and brought toward control. MSM is the group most hit by the HIV epidemic in China now and that will continue for a long time. Great effort, focus, prioritization, and funding must be dedicated toward prevention of HIV transmission in the contexts of both heterosexual contact and homosexual contact. Prevention strategies targeting transmission events during commercial sex should continue to concentrate on FSW, including condom use promotion, regular STI check-ups, and timely treatment, and HIV testing. In the context of non-commercial heterosexual contact, it is important to increase sexual health knowledge, HIV/AIDS knowledge, encourage correct and consistent condom use, and early and frequent testing. For MSM, all current, effective programs, including condom promotion, HIV testing, and ART must continue and be further expanded. New prevention strategies need to be tried and implemented on a national scale. The most promising new prevention strategies include PrEP and PEP, but more study will be required to understand how best to implement and promote PrEP and PEP among MSM communities. Furthermore, more effort should be put into developing MSM-friendly community-based organizations that can help with the design, implementation, and evaluation of future interventions among MSM.

HIV testing is one of the most important HIV epidemic control strategies. However, despite China's massive expansion of HIV testing via a range of testing format options, people still have low rates of testing uptake and still tend to not be diagnosed until they have already entered late-stage disease. Considerable effort has been made to understand the unique compliments of barriers to HIV testing experienced by high-risk groups, and still, not much progress in this area has been made in recent years. One reason is that stigma toward HIV and PLWH is persistently severe. It is the single most important barrier for Chinese people to seek and obtain an HIV test. This is particularly true among already-marginalized groups, such as MSM, FSW, PWID, and others. One of the future strategies for improving rates of first-time and repeat HIV testing is HIV self-testing. Self-testing protects privacy

and confidentiality, is convenient and easy, and offers results very quickly. This strategy is very promising. Making self-test kits more readily available, cheaper, simpler, easier to use, and more reliable and accurate is of critical importance. More supportive national policies for promoting HIV self-testing and linking self-testers to further diagnosis and treatment services are needed.

Finally, social media applications, such as WeChat, MOMO, and Blued, are new tools that have been rapidly adopted by people in China, allowing them to make social connections, communicate regularly, and find friends and dates. WeChat is one of the most popular apps being used in China. It was launched in 2011. It is currently being used by 94% of all mobile phone devices in China and already has 800 million users. MOMO is one of the most popular apps being used by heterosexuals to make friends and find sexual partners. It was also launched in 2011 and already has 300 million users. Blued is the most popular mobile app being used by MSM in China. Estimates suggest that almost 80% of all MSM in China use Blued. All of these apps represent important new platforms for approaching people with HIV/AIDS information and prevention interventions. This must be part of the solution in the future if China is going to bring its HIV/AIDS epidemic successfully under control.

In summary, there is a great need to innovate and implement multiple new combinations of strategies in order to take China's comprehensive HIV/AIDS response into the next decades. Looking backward, it is clear that China has made major strides toward the ultimate goal of HIV elimination. However, looking forward, it is clear that more, and more difficult, challenges lie ahead. China must gather its resolve and confront these challenges directly and pragmatically, yet aggressively because the next major strides required will be even more difficult to achieve.

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