Human immunodeficiency virus prevention strategies in China

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Abstract

This paper reviews the current epidemics of human immunodeficiency virus (HIV) infection in China, particularly the globally available prevention strategies developed and implemented. This review focuses on HIV prevention measures in general, such as education, testing, and counseling and in specific responses to transmission modes, such as blood safety, harm reduction for people who inject drugs, and condom promotion to reduce sexual transmission. We also assess newly developed prevention measures, such as prevention treatment, pre-exposure prophylaxis, post-exposure prophylaxis, male circumcision, and promising potential future preventions, including microbicides and vaccines. Based on this assessment, we provide recommendations for their implementation in China. We conclude that there is no magic bullet for HIV prevention, particularly sexual transmission of the disease, but only a combination of these prevention strategies can control the HIV epidemic.

Keywords: Human immunodeficiency virus infection; Epidemic; Prevention strategies; China

Introduction

The epidemic of human immunodeficiency virus (HIV) infection has changed remarkably around the world and domestically in China over the past three decades, with a reduction in new infections and improvements in both the treatment and prevention of the disease.^[1-5] These changes are largely due to the preventive and treatment responses to the HIV epidemic, which have evolved significantly.^[3,6] HIV prevention strategies have shifted from previously focusing on health education, behavioral interventions, and condom promotion, towards a focus on people living with HIV (PLWH) and using biological strategies, such as anti-retroviral therapy (ART) to achieve viral suppression. Anti-retroviral medicines can now be used to eliminate transmissibility, or be provided to those who are not infected but considered high risk to prevent their HIV infection.^[7] Other prevention strategies, such as male circumcision, have been widely used in some African countries; while pre-exposure prophylaxis (PrEP) has been adopted in some developed countries as national control strategies to reduce new HIV infections among people at high-risk of HIV infection.

In China, HIV transmission via blood, including injecting drug use (the primary transmission mode at the initial HIV epidemic stage) has almost been controlled.^[3,8] HIV sexual

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transmission; however, accounted for about 95% of newly diagnosed HIV infections in 2018.^[9] Furthermore, there is no signal that the epidemic is going to slow down. With an increased number of people tested for HIV, the number of newly diagnosed HIV cases is steadily increasing. For the past four years, over 100,000 newly diagnosed HIV cases have been reported each year, climbing to over 148,500 new cases in 2018.^[9,10] Thus, we ask the question, among all newly developed prevention strategies, which are suitable for China? This paper reviews the updated global prevention measures and makes an appropriate assessment of their feasibility to be adopted in China as national strategies.

General Prevention Measures

All prevention strategies are summarized in Table 1.

Educational campaigns

Increasing HIV knowledge and awareness is crucial to improving behavioral risk decisions and stopping the spread of HIV. After 30 years of the fight against HIV in China, most of the public is familiar with HIV and acquired immune deficiency syndrome (AIDS), even though they may not fully understand the disease. In

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Table 1: HIV prevention strategies in China.

General prevention strategies	Specific prevention strategies	Newly developed prevention strategies	Future prevention strategies
Educational campaigns	Safe blood supply	Treatment as prevention	Microbicides
HIV testing and counseling	Harm reduction strategies for people who inject drugs	90-90-90 strategies New social media	Vaccines
	Condom promotion Treatment of sexually transmitted	Detection and treatment of acute infection	
	infections	Pre-exposure and post-exposure	
	Prevention of mother to child	Prophylaxis	
	transmission	Male circumcision	

China, the most powerful AIDS education campaign was the national HIV testing campaign program in 2004 to 2005, targeting former plasma donors and other key populations.^[3, f1, 12] This campaign was directed towards former commercial plasma donors who sold blood plasma in the mid-1990s. The campaign taught them about the risk of selling blood and HIV infection, promoting their need to get tested. In conjunction with this educational messaging, the campaign mobilized different government entities to update national HIV/AIDS policies and improve basic knowledge about HIV/AIDS. Since then, HIV education program has been expanded to the general population and other high-risk groups in collaboration with other international groups such as the United Nations Jointed Program on HIV/AIDS (UNAIDS) and United Nations Population Fund. Subsequently, public knowledge about HIV has been increasing. A general AIDS awareness campaign alone, however, may not be sufficient to control the HIV epidemic and eliminate stigmatization of the disease. More face-to-face education programs in factories, rural areas, schools, and amongst families is needed in China, as studies have found general lower levels of HIV awareness within these groups.^[13] Additionally, though previous efforts focused on providing the correct educational messages grounded in scientific research, we often ignored the target audience's interests and needs, with current messaging potentially only reaching those whom have been impacted by the disease. Though general AIDS educational campaigns can raise overall awareness of the general public, these types of programs have not been evaluated to measure their effectiveness in reducing the number of HIV infections or determining the changes in HIV knowledge in the general population over time. Subsequently, new educational campaigns building on the successes of previous efforts should use messaging that caters to specific audiences in their own language and in familiar settings to be more effective.^[14]

HIV testing and counseling

Voluntary counseling and testing (VCT) has been shown to be one of the most effective strategies in finding and diagnosing HIV+ individuals and is also an important entry point into care and treatment. VCT can reduce risk behaviors and is an important strategy for reducing HIV transmission, as awareness of HIV status has been shown to help increase safer sexual practices.^[15] China adopted VCT as a part of its national HIV programming in 2003 and this program has since been expanded to over 10,000 sites by the end of 2018.^[9] VCT also plays an integral role in finding HIV cases. In 2017, HIV cases diagnosed at VCT sites accounted for 27% of total diagnosed cases in China.^[9] More importantly, the cases diagnosed at VCT centers are usually among individuals whom have yet to progress to late-stage HIV, compared to cases diagnosed in hospital settings. Thus, these patients often initiate ART sooner, giving them a chance to live longer, while also reducing secondary HIV transmission in the community.

PLWH who are unaware of their status rarely actively seek HIV testing. To diagnose cases earlier, the World Health Organization (WHO) issued a guideline to promote provider-initiated HIV testing and counseling (PITC). These guidelines support HIV testing initiated by the provider rather than the patient and emphasized the importance of early diagnosis. The PITC guideline has been adopted by member countries and promotes HIV testing globally.^[16] Since 2011, testing and diagnosing HIV cases have been listed as a priority policy for the national control of HIV in China. Since that time, the number of HIV tests and the number of HIV cases diagnosed at medical care settings has significantly increased, accounting for about 60% of total tests and over 50% of diagnosed HIV cases throughout the country.^[9]

Specific Prevention Measures

Safe blood supply

Globally, transmission of HIV through blood transfusion is relatively uncommon, accounting for a small proportion of HIV infections around the world.^[17] Having experienced an outbreak of HIV among former commercial plasma donors in the mid-1990s,^[18-20] China has made significant improvements in ensuring a safe blood supply to eliminate HIV transmission via blood transfusion.^[9] Since 2015, the Chinese government has scaled-up HIV ribonucleic acid (RNA) testing strategies, to shorten the "window period" of HIV infectiousness, or the time between potential exposure to HIV infection and when the HIV test will provide an accurate result. During this period, a person can be infected with HIV, but test negative for the disease. From approximately 14 to 21 days using 4th generation antigen and antibody tests, to some 10 to 14 days using RNA nuclear acid methods, the widespread use of these newer tests have reduced the risk of HIV infection

via blood transfusion by almost half. Challenges remain; as sporadic cases of HIV infection during this "window period" have been reported in China. Strategically, selfdeferral of men who have sex with men (MSM) from blood donation is a key strategy in protecting the blood supply, as HIV prevalence in this group is much higher than in the general population in China.^[21] Studies have estimated however, that MSM continue to account for a proportion of blood donors, as a large proportion of MSM use blood donation as a means for HIV testing.^[22] The use of their blood may place recipients at a greater risk of HIV infection if transfused during the window period. As more cases of HIV are identified amongst donors, the higher chance of "window period" infections and the higher the risk of HIV transmission via transfusion. To ensure blood safety, laboratory screening is not enough. This should be supplemented with screening of potential high-risk blood donors, including screening for specific behaviors rather than periods of abstinence.^[23] In China, screening of blood donors and improved supervision and management of the blood supply is needed to eliminate the risk of "window period" transfusion.

Harm reduction strategies for people who inject drugs

With the first initial cases of HIV in China among injection drug users, strategies to control the spread of HIV amongst this group were at the forefront of prevention efforts. Harm reduction programs for preventing HIV transmission among people who inject drugs include opioid substitution therapy and needle and syringe exchange programs. Since 2004, about 200,000 clients have participated in such harm reduction strategies for people who use opiates and for people who inject drugs^[3] in China. Ten years after implementation, the HIV epidemic among drug users has considerably declined. The HIV incidence among clients enrolled in methadone maintenance treatment programs has decreased from 1% in 2006 to 0.03% in 2018, almost eliminating new HIV infections amongst this group. The proportion of HIV cases acquired via injecting drug use has also declined, from 44.2% in 2005 to less than 3% in 2018. While the number of newly diagnosed HIV cases via injection drug use peaked at almost 20,000 per year in 2005, it has since reduced to less than 4000 cases in 2018.^[9] Subsequently, due to the success of these harm reduction interventions, HIV transmission via injecting drug use is no longer a major route of HIV transmission in China. However, the lessons from the US and UK^[24,25] warn us that these strategies must be sustained to avoid future outbreaks of HIV amongst this key population.

Condom promotion

Research and global programs over the past three decades have supported the recommendation that condoms can effectively reduce HIV transmission, if they are used appropriately at the community level.^[26] Communitybased condom promotion can raise awareness and result in increased condom use, leading to reduced sexually transmitted infections (STIs) or HIV transmission.^[27] Though efforts have been made to promote condom use among high-risk groups, including MSM, HIV continues to spread among these groups globally, as well as in China.^[28] HIV infected individuals whom do not use condoms or do not use condoms consistently are major reasons why HIV continues to spread via sexual transmission.

Since 2004, China has promoted condom use in female sex workers and MSM for the prevention of HIV sexual transmission. Sentinel surveillance results from 2015 showed that 77% of sex workers and 53% of MSM reported condom use during the last sexual episode.^[29] From 2006 to 2015, the HIV prevalence among female sex workers consistently remained below 1%, while the prevalence of HIV among MSM increased from 1% to 8% during the same period time. Therefore, promoting condom use only is not an effective method for eliminating HIV sexual transmission. It must be combined with other prevention measures.^[30] Additionally, long-term and routine condom use and promote higher availability of condoms, should be implemented to address these ongoing concerns.

Treatment of STIs

STIs have been recognized as a major public health threat in China since they re-emerged in the early 1980s.^[31] Importantly, HIV and other STIs have been spreading from high-risk groups to the general population, leading to the high rates of sexual transmission of HIV in the country. People suffering from STIs can have ulcers in their genital areas, which cause tears in the surface of skin or mucosa, therefore increasing the risk of HIV transmission, infectiousness, and susceptibility. Thus, efforts to address the timely diagnosis and treatment of STIs helps lesson the impact of these ulcers and reduces potential HIV transmission. Health education messaging and structural interventions to increase condom use can help prevent STIs. Additionally, early detection and treatment of individuals infected with STIs via clinical and partner notification services and screening programs, can help reduce potential transmission.^[31] However, studies have shown that treatment of STIs may not reduce HIV at the community level.^[32] In areas with high rates of STIs and high prevalence of HIV sexual transmission, treatment of STIs reduces HIV transmission. However, in areas where rates of STIs are low, treatment of STIs will not have an impact nor slow down HIV sexual transmission. Therefore, treatment of STIs is an effective strategy to control HIV sexual transmission where STIs are common and HIV is primarily transmitted via sexual intercourse. Unfortunately, STI care services are not well managed in China, with no current national strategy for the management of STIs in the country. Strategies to reduce stigmatization of those with STIs and HIV, as well improving the linkage between outreach services and clinical care are needed to improve control and management of HIV/STIs.

Prevention of mother to child transmission

Mother-to-child transmission, also known as "vertical transmission," occurs when HIV is transmitted from an HIV-positive mother to her child during pregnancy, childbirth, and breastfeeding. Without ARV treatment, the likelihood of a positive pregnant woman passing the virus to her child is 15% to 45%.^[33] Prevention of mother-to-child transmission (PMTCT) programs offer a range of services for women to help maintain their health during pregnancy and stop their infants from acquiring HIV. More than one million HIV infections among children have been prevented between 2010 and 2018 due to the implementation of PMTCT interventions.^[33] In 2017, 80% of pregnant women living with HIV were receiving ART, but in the same year, almost 90,000 children were newly infected during breastfeeding.^[33]

In 2015, the World Health Organization (WHO) developed Option B+, recommending that all pregnant women living with HIV be immediately provided ART, regardless of CD4 count. This guideline has been adopted by numerous countries, leading to the elimination of mother-to-child transmission in places such as Cuba, Thailand, and Malaysia.^[33]

PMTCT is also a key component of China's national HIV/ AIDS strategy. In 2005, China started its first PMTCT program in eight cities throughout the country. This program provided free HIV testing and treatment as a standardized part of HIV antenatal care.^[34] China's Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis, and Hepatitis B program was later launched in 2010 and extended nationwide in 2015. As a result, more than 99% of HIV-infected pregnant women were tested and 90% received treatment in 2017. In the same year, the mother-to-child transmission rate of HIV was 4.9%, falling from 12.8% in 2005.^[35] The key components of China's PMTCT program, including (1) routine, provider initiated, opt-out HIV screening during pregnancy, delivery, and post-partum, (2) maternal ART, (3) infant prophylaxis, and (4) follow-up testing for infants and children, have played critical roles in reducing motherto-child transmission of HIV. Since implementing the PMTCT program, HIV testing rates among HIV-positive mothers and the number receiving ART have both increased, though challenges still remain. Improved collaboration efforts and quality of services are needed to achieve total elimination of mother-to-child transmission in China.

Newly Developed Prevention Measures

Treatment as prevention

As early as the year 2000, researchers have found that when HIV viral load was lower than 400 copies per milliliters, the virus was not transmissible.^[36] However, this study was not immediately translated into prevention policy. It was not until a randomized trial demonstrated that treatment of PLWH whose CD4 cell count was above 500 could reduce 96% of HIV sexual transmission among sero-discordant couples that treatment as prevention began to gain notoriety.^[37] Additional trials have also reported that when viral load was reduced to undetectable levels, the HIV transmission diminished among sero-discordant couples in both heterosexual and homosexual relationships.^[38] In 2014, an ongoing trial of heterosexual and homosexual

sero-discordant couples in which the HIV positive partner was taking ARVs, found no transmission of the virus. Additionally, in 2017, another trial among homosexual sero-discordant couples also reported zero cases of transmission in over 16,000 acts of condom-less anal sex.^[39] Thus, treatment as prevention is a key intervention to reducing the transmission of HIV worldwide.

Observational studies in China have also observed that treatment as prevention can significantly reduce HIV sexual transmission among couples.^[40] Subsequently, treatment as prevention policies among sero-discordant couples was adopted in China in 2011, and have since significantly reduced HIV transmission, from 2.6% in 2011 to 0.68% in 2017.^[9] A few recent studies have also addressed the programmatic conditions affecting the implementation of treatment as prevention across China. It was found that early initiation of ART as prevention for HIV is highly feasible given current guidelines. The success of treatment as prevention; however, is highly dependent upon adherence to ART therapies. Thus, successful adoption of a national treatment as prevention strategy must place great importance on promoting good adherence and monitoring of viral load among those initiating treatment.

90-90-90 strategies

Theoretical, mathematical modeling studies have shown that once the proportion of HIV infections diagnosed, treated, and achieving viral suppression reaches a certain level, the HIV epidemic may be eliminated.^[41] Additionally, research has identified that when coverage of ART is high, the incidence of HIV infection is low.^[42] Therefore, in 2014, the UNAIDS announced a new global control strategy that 90% of people infected with HIV know their status, 90% of diagnosed PLWH receive ART, and 90% receiving ART achieve viral suppression.^[43] The 90-90-90 strategy has been adopted by many counties globally, with actions being taken to achieve such targets. As a result, great progress has been made across the world. As of 2016, 70% of PLWH know their status, 77% of those diagnosed are on treatment, and 82% on treatment were found to be virally suppressed.^[44] This progress is not constant across regions; however, particularly in Western and Central Africa and the Middle East and North Africa, where substantially far fewer people are aware of their status and initiated treatment.^[44] Many other countries have already achieved or nearly achieved these targets. In British Columbia, rapid scale-up of treatment has resulted in reduced new transmission of HIV infections.^[45] China too has adopted these targets as a part of the 13th 5-year action plan, with improvements already being seen. A nationwide survey carried out in 2015 found that 68% of PLWH in China were diagnosed, 67% among those diagnosed were receiving ART, and 65% were virally suppressed.^[46] Improved linkage to care, including streamlining HIV screening and diagnosis, along with immediate initiation of ART, could help China achieve the 90-90-90 targets.

New social media

Social media is now a daily part of people's lives, even impacting how individuals find and connect with potential sexual partners. Due to this rapid and widespread use of social media, innovative prevention programming is being integrated into these tools to provide needed health and HIV services to users.^[47-49] In China, there are over 3300 social media applications for special populations. For example, over 100 social applications are designated for MSM, of which; the most popular is called Blued. Building on their widespread popularity, Blued developed interventions aimed at preventing AIDS amongst MSM. Through their application, AIDS awareness messaging is disseminated, while also encouraging users to get tested for HIV. The Blued application has become an important platform for controlling HIV among MSM communities in China.

Detection and treatment of acute infection

HIV progression can be divided into the following stages: acute infection, asymptomatic phase, and clinical symptomatic phase. Individuals experience different levels of infectiousness depending on their stage of HIV progression. Mathematical modeling studies show that if individuals are diagnosed at later stages, it can be much harder to control HIV at the community level.^[50] Additionally, individuals at the early, acute stage of HIV tend to have high viral load and be very infectious. Acute infection can be defined as the period between HIV acquisition and emergence of specific antibodies,^[51] representing a period of increased transmission efficiency. Thus, immediate diagnosis and treatment of acute HIV infection can significantly reduce new cases of HIV. Optimal clinical and public health strategies for acute infection are lacking; however. There are currently not specific guidelines regarding diagnostic strategies or ART for persons with acute infection in China. This is particularly worrisome, as acute infection may compro-mise the effectiveness of PrEP.^[51] Early treatment initiation can avert damage to the immune system and shrink latent viral reservoirs.^[51] Kroon and colleagues, for example, found that diagnosis and treatment of acute HIV infection among the MSM community could reduce 88% of new HIV infections.^[52] The period of acute HIV infection, however, is very short and its role in HIV transmission is limited.^[53] In addition, diagnosis of acute HIV infection is very difficult and hard to implement in many developing countries. We do not believe it could be used as a national prevention strategy in China.

Pre-exposure and post-exposure prophylaxis

PrEP refers to HIV medication that is taken by HIVnegative people to reduce their risk of infection. Currently, Truvada is the only drug approved for the use of PrEP globally. PrEP works by stopping the viral replication of HIV and if used consistently, can overwhelmingly reduce the risk of HIV transmission. Drug resistance has also been found to be very low (<0.1%),^[7] while observational studies have found that the impact of PrEP on kidney toxicity is also very low.^[54]

Generally, PrEP is recommended for those in serodiscordant relationships and homosexual men. Randomized control trials have demonstrated that among MSM,^[55-57] heterosexual high-risk groups^[58,59] and people who inject drugs,^[60] the daily use tenofovir disoproxil fumarate/emtricitabine can significantly reduce HIV infection, potentially preventing 90% of infections. In MSM, studies have shown that PrEP can reduce 52.4% of HIV transmission, though this is highly dependent upon the compliance rate of those taking the therapy.^[61] Though many studies have proven the effectiveness of PrEP in various study populations, there still remains debate among doctors and target populations about the use of PrEP.^[62] In China, various studies have reported a very low acceptance rate of PrEP among different popula-tions,^[63,64] as taking a daily pill or taking ART just before and after having sexual intercourse were found to be inconvenient. As a result, compliance remains low. Injectable, long-term releasing or implanted ARVs which slowly release the medicine and remain effective for a few months^[65] are now being considered as a method for the prevention and control of HIV. This could serve as a future prevention strategy in China. Campaigns that emphasize the impact of PrEP on HIV prevention, including promoting understanding of the intervention and its side effects, could help improve acceptability.

Post-exposure prophylaxis (PEP), or taking ART after potential exposure to HIV, has been widely used for occupational exposures over the past decades. PEP is often used in emergency cases to prevent HIV, with research showing it can reduce the risk of infection by 80%.^[66] In Nigeria, an observational study observed that of 115 health professionals who were exposed to HIV over a 12year period, no single HIV infection was transmitted when the professionals took PEP.^[67] In China, about 700 to 1000 episodes of occupational exposures occur each year, during which PEP has been used in a timely manner and no single HIV infection has been reported.^[68] National and international guidelines regarding PEP use are quite common across the globe, though simplified strategies and improved adherence and retention rates while on PEP are necessary.

Literature regarding non-occupational PEP is limited, though some countries have developed guidelines on non-occupational PEP to assist people when needed.^[69] At present, PEP is highly requested among MSM communities in China. It has not become a national strategy however, as PEP therapy is quite expensive in the country.

Male circumcision

Over the last 10 years, male circumcision has been identified as a prevention method to reduce HIV sexual transmission for men, particularly for heterosexual males.^[70] Evidence has suggested that medical male circumcision can reduce the risk of female to male sexual transmission by approximately 60%.^[71] Thus for the last decade, the WHO and UNAIDS have recommended voluntary medical male circumcision as a key strategy for the prevention of HIV. This method has primarily been used and found to be effective in African countries,^[72] though studies have reported varying outcomes relating to the impact of male circumcision in reducing HIV transmission among MSM.^[73] A recent systematic review;

however, did identify that male circumcision was associated with a 24% decreased odds of HIV infection among MSM in low and middle-income countries.^[74] With support from the Major Research Project on Prevention and Treatment of Major Infectious Diseases including AIDS and Viral Hepatitis, China has pilot-tested male circumcision among MSM. Unfortunately, the acceptability of this intervention was found to be very low.^[64] Given very low prevalence of HIV infection, about eight per ten thousand, we do not believe male circumcision is an effective strategy to reduce transmission of HIV in China.

Future Prevention Strategies

Microbicides

Microbicides are new products being studied that contain drugs that prevent vaginal or rectal transmission of HIV via sexual exposure. These microbicides can take the form of vaginal rings, gels, films, inserts, or enemas, aimed at preventing HIV or STIs. Several studies over the past decade have examined the safety and efficacy of such preventative measures. A clinical trial conducted in 15 sites across Southern and Southeastern Africa showed that a vaginal ring which continually released the ART drug Dapivirine, provided a modest level of protection against HIV infection in women.^[75] Similar trials testing the safety and efficacy of a Dapivirine ring found overall effectiveness to be around 31%.^[75] Further studies are being established which examine the effectiveness of rectal microbicide gels to reduce the risk of HIV transmission through anal sex.

Microbicide development research in China was launched in 2008 under the National 11th Five-Year Plan on HIV. Thus far, studies in China have been focused on pre-clinical development, addressing the mechanism of mucosal HIV infection, though few outcomes have thus far been reported. Microbicides provide a new and unique opportunity for HIV prevention without requiring a daily pill such as PrEP. Thus, this discreet, long-acting method may be a new strategy to reduce sexual transmission of HIV in China.

Vaccine

A vaccine is the most effective strategy to controlling viral infectious epidemics. However, 35 years have passed since the first isolation of the HIV virus, and no vaccine has yet to be developed. Since 1987, more than 30 HIV candidate vaccines have been tested, though only one has shown positive results.^[76] The RV 144 trial performed in Thailand found that the HIV infection rate was 31.2% lower in the group receiving the vaccine compared to the group receiving the placebo.^[76] Though efforts to find an effective vaccine for preventing HIV infection continue, there remain great challenges given the rapid mutation of the HIV virus.^[77] It seems unlikely that we would have a vaccine to control the epidemic in the next 10 years.

Conclusions

Sexual transmission of HIV accounts for 95% of infections in China, with the number of newly diagnosed cases

continuing to increase year by year. Subsequently, controlling HIV sexual transmission faces great challenges. At the macro level, increased HIV sexual transmission is largely due to changing social norms and social environments. Social media, for example, connects people in an easier and faster manner, providing better opportunities for quickly finding a sexual partner. MSM in particular have become the most important mode of HIV sexual transmission in urban cities in China. As the population of China is quite large, a tiny change in HIV incidence or prevalence translates into a large number of HIV cases. Thus, controlling the HIV epidemic requires consideration of these macro level factors.

There is no magic bullet for controlling the sexual transmission of the HIV epidemic. Though there are a few, new prevention strategies developed in recent years, unfortunately none can be used alone to stop the epidemic. Cases in African countries or parts of China have demonstrated that implementation of combined interven-tions can achieve epidemic control.^[78] Controlling the HIV epidemic, particularly the sexual transmission of HIV, should focus on three critical areas: infectious cases, transmission mode, and the susceptible population. Prevention must consider fully implementing all strategies listed in the 13th 5-year action plan. We need to prioritize the key areas and key populations, and develop specific implementation plans for execution. Yunnan can serve as role model for the rest of China, as the province has developed its own annual plan for setting specific targets to achieve the 90-90-90 targets by 2020. Only when we work hard to implement all planned strategies in targeted populations can the number of new HIV infections be reduced.

Disclaimer

The views and opinions expressed herein belong to the authors alone, and do not represent the official policy, or endorsement of their affiliated institutions.

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Conflicts of interest

None.

References

- 1. Wu Z, Rou K, Cui H. The HIV/AIDS epidemic in China: history, current strategies and future challenges. AIDS Educ Prev 2004;16 (3 Suppl A):7–17. doi: 10.1521/aeap.16.3.5.7.35521.
- 2. Cui Y, Liau A, Wu ZY. An overview of the history of epidemic of and response to HIV/AIDS in China: achievements and challenges. Chin Med J 2009;122:2251–2257. doi: 10.3760/cma.j.issn.0366-6999. 2009.19.013.
- 3. Wu Z. HIV/AIDS in China-beyond the Numbers. Singapore: People's Medical Publishing House and Springer Nature; 2017.
- 4. Murray CJ, Ortblad KF, Guinovart C, Lim SS, Wolock TM, Roberts DA, *et al.* Global, regional, and national incidence and mortality for

HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384:1005–1070. doi: 10.1016/S0140-6736(14)60844-8.

- 5. GBD 2015 HIV Collaborators. Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980–2015: the Global Burden of Disease Study 2015. Lancet HIV 2016;3:e361–e387. doi: 10.1016/S0140-6736(16)31012-1.
- Zhao Y, Poundstone KE, Montaner J, Wu ZY. New policies and strategies to tackle HIV/AIDS in China. Chin Med J (Engl) 2012;125:1331–1337. doi: 10.3760/cma.j.issn.0366-6999.2012.07. 025.
- Riddell J, Amico KR, Mayer KH. HIV preexposure prophylaxis: a review. JAMA 2018;319:1261–1268. doi: 10.1001/jama.2018.1917.
- Cui Y, Shi CX, Wu Z. Epidemiology of HIV/AIDS in China: recent trends. Global Health J 2017;1:26–32. https://doi.org/10.1016/ S2414-6447(19)30057-0.
- National Center for AIDS/STD Control and Prevention, China CDC. Annual Report of China National HIV/STD/HCV Comprehensive Prevention and Treatment Programs in 2018. Beijing: National Center for AIDS/STD Control and Prevention, China CDC; 2019.
- Wu Z. Characteristics of HIV sexually transmission and challenges for controlling the epidemic in China (in Chinese). Chin J Epidemiol 2018;39:707–709. doi: 10.3760/cma.j.issn.0254-6450.2018.06.002.
- 11. Wu Z, Sun X, Sullivan SG, Detels R. Public health. HIV testing in China. Science 2006;312:1475–1476. doi: 10.1126/science. 1120682.
- 12. Wu Z, Sullivan SG, Wang Y, Rotheram-Borus MJ, Detels R. Evolution of China's response to HIV/AIDS. Lancet 2007;369:679–690. doi: 10.1016/S0140-6736(07)60315-8.
- Liu H, Li M, Jin M, Jing F, Wang H, Chen K. Public awareness of three major infectious diseases in rural Zhejiang province, China: a cross-sectional study. BMC Infect Dis 2013;13:192. doi: 10.1186/ 1471-2334-13-192.
- 14. Humana People to People China. Progress reports in infectious disease control in Yuexi, Sichuan Province. Available from: http:// www.hppchina.org.cn/article/index/index/?lang=Cn&id=273. [Accessed September 5, 2019]
- Fonner VA, Denison J, Kennedy CE, O'Reilly K, Sweat M. Voluntary counseling and testing (VCT) for changing HIV-related risk behavior in developing countries. Cochrane Database Syst Rev 2012;9: CD001224. doi: 10.1002/14651858.CD001224.pub4.
- Kennedy CE, Fonner VA, Sweat MD, Okero FA, Baggaley R, O'Reilly KR. Provider-initiated HIV testing and counseling in lowand middle-income countries: a systematic review. AIDS Behav 2013;17:1571–1590. doi: 10.1007/s10461-012-0241-y.
- Takei T, Amin NA, Schmid G, Dhingra-Kumar N, Rugg D. Progress in global blood safety for HIV. J Acquir Immune Defic Syndr 2009;52 (Suppl 2):S127–S131. doi: 10.1097/QAI.0b013e3181baf0ac.
- Wu Z, Liu Z, Detels R. HIV-1 infection in commercial plasma donors in China. Lancet 1995;346:61–62. doi: 10.1016/s0140-6736(95) 92698-4.
- Wu Z, Rou K, Detels R. Prevalence of HIV infection among former commercial plasma donors in rural eastern China. Health Policy Plan 2001;16:41–46. doi: 10.1093/heapol/16.1.41.
- 20. Li N, Wang Z, Sun D, Zhu Q, Sun G, Yang W, et al. HIV among plasma donors and other high-risk groups in Henan, China. J Acquir Immune Defic Syndr 2010;53 (Suppl 1):S41–S47. doi: 10.1097/ QAI.0b013e3181c7d717.
- Lee SS, Lee CK, Wong NS, Wong HY, Lee KCK. Low compliance of men having sex with men with self-deferral from blood donation in a Chinese population. Blood Transfus 2014;12:166–171. doi: 10.2450/2013.0103-13.
- 22. Lu J, Xu J, Reilly KH, Li Y, Zhang CM, Jiang Y, *et al.* The proportion and trend of human immunodeficiency virus infections associated with men who have sex with men from Chinese voluntary blood donors: a systematic review and meta-analysis. Transfusion 2015;55:576–585. doi: 10.1111/trf.12871.
- Goldman M, Yi QL, Ye X, Tessier L, O'Brien SF. Donor understanding and attitudes about current and potential deferral criteria for high-risk sexual behavior. Transfusion 2011;51:1829– 1834. doi: 10.1111/j.1537-2995.2011.03078.x.
- Peters PJ, Pontones P, Hoover KW, Patel MR, Galang RR, Shields J, et al. HIV infection linked to injection use of oxymorphone in Indiana, 2014–2015. N Engl J Med 2016;375:229–239. doi: 10.1056/NEJMoa1515195.

- McAuley A, Palmateer NE, Goldberg DJ, Trayner KMA, Shepherd SJ, Gunson RN, *et al.* Re-emergence of HIV related to injecting drug use despite a comprehensive harm reduction environment: a crosssectional analysis. Lancet HIV 2019;6:e315–e324. doi: 10.1016/ S2352-3018(19)30036-0.
- Koff A, Goldberg C, Ogbuagu O. Condomless sex and HIV transmission among serodifferent couples: current evidence and recommendations. Ann Med 2017;49:534–544. doi: 10.1080/ 07853890.2017.1320423.
- 27. Malekinejad M, Parriott A, Blodgett JC, Horvath H, Shrestha RK, Hutchinson AB, *et al.* Effectiveness of community-based condom distribution interventions to prevent HIV in the United States: a systematic review and meta-analysis. PloS One 2017;12:e0180718. doi: 10.1371/journal.pone.0180718.
- 28. Hughes AJ, Saxton PJ. Thirty years of condom-based HIV prevention by gay men in New Zealand. N Z Med J 2015;128:19–30.
- National Center for AIDS/STD Control and Prevention, China CDC. China National HIV/Syphilis/HCV Surveillance Report in 2015. Beijing: National Center for AIDS/STD Control and Prevention, China CDC; 2015.
- 30. Liu H, Su Y, Zhu L, Xing J, Wu J, Wang N. Effectiveness of ART and condom use for prevention of sexual HIV transmission in serodiscordant couples: a systematic review and meta-analysis. PloS One 2014;9:e111175. doi: 10.1371/journal.pone.0111175.
- Chen XS, Peeling RW, Yin YP, Mabey DC. The epidemic of sexually transmitted infections in China: implications for control and future perspectives. BMC Med 2011;9:111. doi: 10.1186/1741-7015-9-111.
- Stillwaggon E, Sawers L. Rush to judgment: the STI-treatment trials and HIV in sub-Saharan Africa. J Int AIDS Soc 2015;18:19844. doi: 10.7448/IAS.18.1.19844.
- Avert. Prevention of mother-to-child transmission (PMTCT) of HIV. https://www.avert.org/professionals/hiv-programming/prevention/ prevention-mother-child. Accessed December 21, 2019.
- 34. Zeng H, Chow EPF, Zhao Y, Wang Y, Tang M, Li L, et al. Prevention of mother-to-child HIV transmission cascade in China: a systematic review and meta-analysis. Sex Transm Infect 2016;92:116–123. doi: 10.1136/sextrans-2014-051877.
- 35. Wang A, Qiao Y, Dou L, Wang Q, Wang X, Su M, et al. Challenges of eliminating mother-to-child transmission of HIV, syphilis and hepatitis B in China: a cross-sectional survey. Poster Abstract. Lancet, Published Online October 26, 2018. https://www.thelancet. com/pdfs/journals/lancet/PIIS0140-6736(18)32684-9.pdf. Accessed December 21, 2019.
- 36. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, *et al.* Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med 2000;342:921–929. doi: 10.1056/ NEJM200003303421303.
- Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al.* Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493–505. doi: 10.1056/NEJMoa1105243.
- Rodger AJ, Cambiano V, Bruun T, Vernazza P, Collins S, van Lunzen J, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. JAMA 2016;316:171–181. doi: 10.1001/jama.2016.5148.
- 39. Bavinton BR, Pinto AN, Phanuphak N, Grinsztejn B, Prestage GP, Zablotska-Manos IB, *et al.* Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. Lancet HIV 2018;5:e438–e447. doi: 10.1016/S2352-3018(18)30132-2.
- 40. He N, Duan S, Ding Y, Rou K, McGoogan JM, Jia M, et al. Antiretroviral therapy reduces HIV transmission in discordant couples in rural Yunnan, China. PloS One 2013;8:e77981. doi: 10.1371/journal.pone.0077981.
- Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet 2009;373:48–57. doi: 10.1016/S0140-6736(08)61697-9.
- 42. Tanser F, Barnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. Science 2013;339:966–971. doi: 10.1126/science.1228160.

- 43. UNAIDS. 90-90-90 an ambitious treatment target to help end the AIDS epidemic. Available from: http://www.unaids.org/sites/default/ files/media_asset/90-90-90_en_0.pdf. [Accessed November 12, 2015]
- 44. Ghys P. AIDS by the Numbers: Where Do We Stand with 90-90-90? https://www.iapac.org/909090-workshop/presentations/ 909090tw17-Sa1200-Ghys.pdf. Accessed on December 21, 2019.
- 45. Montaner JS, Lima VD, Barrios R, Yip B, Wood E, Kerr T, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet 2010;376: 532–539. doi: 10.1016/S0140-6736(10)60936-1.
- 46. Ma Y, Dou Z, Guo W, Mao Y, Zhang F, McGoogan JM. The human immunodeficiency virus care continuum in China: 1985-2015. Clin Infect Dis 2018;66:833–839. doi: 10.1093/cid/cix911.
- 47. Schnall R, Travers J, Rojas M, Carballo-Dieguez A. eHealth interventions for HIV prevention in high-risk men who have sex with men: a systematic review. J Med Internet Res 2014;16:e134. doi: 10.2196/jmir.3393.
- 48. Muessig KE, Nekkanti M, Bauermeister J, Bull S, Hightow-Weidman LB. A systematic review of recent smartphone, Internet and Web 2.0 interventions to address the HIV continuum of care. Curr HIV/AIDS Rep 2015;12:173–190. doi: 10.1007/s11904-014-0239-3.
- Hightow-Weidman LB, Muessig KE, Bauermeister JA, LeGrand S, Fiellin LE. The future of digital games for HIV prevention and care. Curr Opin HIV AIDS 2017;12:501–507. doi: 10.1097/COH. 000000000000399.
- 50. Powers KA, Ghani AC, Miller WC, Hoffman IF, Pettifor AE, Kamanga G, *et al.* The role of acute and early HIV infection in the spread of HIV and implications for transmission prevention strategies in Lilongwe, Malawi: a modelling study. Lancet 2011;378:256–268. doi: 10.1016/S0140-6736(11)60842-8.
- Rutstein SE, Ananworanich J, Fidler S, Johnson C, Sanders EJ, Sued O, *et al.* Clinical and public health implications of acute and early HIV detection and treatment: a scoping review. J Int AIDS Soc 2017;20:21579. doi: 10.7448/IAS.20.1.21579.
- 52. Kroon E, Phanuphak N, Shattock AJ, Fletcher JLK, Pinyakorn S, Chomchey N, *et al*. Acute HIV infection detection and immediate treatment estimated to reduce transmission by 89% among men who have sex with men in Bangkok. J Int AIDS Soc 2017;20:21708. doi: 10.7448/IAS.20.1.21708.
- Suthar AB, Granich RM, Kato M, Nsanzimana S, Montaner JS, Williams BG. Programmatic implications of acute and early HIV infection. J Infect Dis 2015;212:1351–1360. doi: 10.1093/infdis/ jiv430.
- 54. Marcus JL, Hurley LB, Hare CB, Nguyen DP, Phengrasamy T, Silverberg MJ, *et al.* Preexposure prophylaxis for HIV prevention in a large integrated health care system: adherence, renal safety, and discontinuation. J Acquir Immune Defic Syndr 2016;73:540–546. doi: 10.1097/QAI.00000000001129.
- 55. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010;363:2587–2599. doi: 10.1056/NEJMoa1011205.
- 56. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet 2016;387:53–60. doi: 10.1016/S0140-6736(15)00056-2.
- 57. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015;373:2237–2246. doi: 10.1056/ NEJMoa1506273.
- Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med 2012;367:399–410. doi: 10.1056/ NEJMoa1108524.
- Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, *et al.* Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med 2012;367:423–434. doi: 10.1056/NEJMoa1110711.
- 60. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2013;381:2083–2090. doi: 10.1016/S0140-6736(13)61127-7.

- 61. Zong X. Practice and challenges in pre-exposure prophylaxis research to prevent HIV infection. A presentation made at 2018 Academic Conference of National Center for AIDS/STD Control and Prevention, China CDC. Beijing, 2018
- 62. Karris MY, Beekmann SE, Mehta SR, Anderson CM, Polgreen PM. Are we prepped for preexposure prophylaxis (PrEP)? Provider opinions on the real-world use of PrEP in the United States and Canada. Clin Infect Dis 2014;58:704–712. doi: 10.1093/cid/ cit796.
- 63. Liu C, Ding Y, Ning Z, Gao M, Liu X, Wong FY, *et al.* Factors influencing uptake of pre-exposure prophylaxis: some qualitative insights from an intervention study of men who have sex with men in China. Sex Health 2018;15:39–45. doi:10.1071/SH17075.
- 64. Ding Y, Yan H, Ning Z, Cai X, Yang Y, Pan R, *et al.* Low willingness and actual uptake of pre-exposure prophylaxis for HIV-1 prevention among men who have sex with men in Shanghai, China. Biosci Trends 2016;10:113–119. doi: 10.5582/bst.2016.01035.
- 65. Krakower DS, Mayer KH. Pre-exposure prophylaxis to prevent HIV infection: current status, future opportunities and challenges. Drugs 2015;75:243–251. doi: 10.1007/s40265-015-0355-4.
- World Health Organization. Post-exposure prophylaxis to prevent HIV infection. Fact sheet - 1 December 2014. https://www.who.int/ hiv/topics/prophylaxis/info/en/. Accessed on December 21, 2019.
- 67. Abubakar S, Iliyasu G, Dayyab FM, Inuwa S, Tudun Wada RA, Sadiq NM, et al. Post-exposure prophylaxis following occupational exposure to HIV and hepatitis B: an analysis of a 12-year record in a Nigerian tertiary hospital. J Infect Prev 2018;19:184–189. doi: 10.1177/1757177417746733.
- Ma C, Qiu M. Wu ZWY, Detels R, Buterys M, McGoogan JM. Preventing occupational exposure. HIV/AIDS in China- Epidemiology, Prevention and Treatment Singapore: Springer; 2019.
- Benn P, Fisher M, Kulasegaram R. UK guideline for the use of postexposure prophylaxis for HIV following sexual exposure (2011). Int J STD AIDS 2011;22:695–708. doi: 10.1258/ijsa.2011.171011.
- Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet 2007;369:657–666. doi: 10.1016/S0140-6736(07)60313-4.
- World Health Organization. Voluntary medical male circumcision for HIV prevention. Fact sheet: July 2012. https://www.who.int/hiv/ topics/malecircumcision/fact_sheet/en/. Accessed December 21, 2019.
- Wambura M, Mahler H, Grund JM, Larke N, Mshana G, Kuringe E, et al. Increasing voluntary medical male circumcision uptake among adult men in Tanzania. AIDS 2017;31:1025–1034. doi: 10.1097/ QAD.000000000001440.
- 73. Goodreau SM, Carnegie NB, Vittinghoff E, Larke N, Mshana G, Kuringe E, *et al.* Can male circumcision have an impact on the HIV epidemic in men who have sex with men? PloS One 2014;9:e102960. doi: 10.1371/journal. pone.0102960.
- 74. Yuan T, Fitzpatrick T, Ko NY, Cai Y, Chen Y, Zhao J, *et al.* Circumcision to prevent HIV and other sexually transmitted infections in men who have sex with men: a systematic review and meta-analysis of global data. Lancet Glob Health 2019;7:e436–e447. doi: 10.1016/S2214-109X(18)30567-9.
- 75. Nel A, van Niekerk N, Kapiga S, Bekker LG, Gama C, Gill K, et al. Safety and efficacy of a Dapivirine vaginal ring for HIV prevention in women. N Engl J Med 2016;375:2133–2143. doi: 10.1056/ NEJMoa1602046.
- 76. Rerks-Ngarm S, Pitisuttithum P, Nitayaphan S, Kaewkungwal J, Joseph Chiu J, Paris R, *et al.* Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand. N Engl J Med 2009;361:2209–2220. doi: 10.1056/NEJMoa0908492.
- Robinson HL. HIV/AIDS vaccines: 2018. Clin Pharmacol Ther 2018;104:1062–1073. doi: 10.1002/cpt.1208.
- Anderson SJ, Cherutich P, Kilonzo N, Cremin I, Fecht D, Kimanga D, et al. Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. Lancet 2014;384:249–256. doi: 10.1016/S0140-6736(14) 61053-9.

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