# **Prevention and control of HIV/AIDS in China: lessons from the past three decades**

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#### Abstract

In the past 37 years, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) has undergone various major transmission routes in China, with the world most complex co-circulating HIV-1 subtypes, even the prevalence is still low. In response to the first epidemic outbreak of HIV in injecting drug users and the second one by illegal commercial blood collection, China issued the Anti-Drug Law and launched the Blood Donation Act and nationwide nucleic acid testing, which has avoided 98,232 to 211,200 estimated infections and almost ended the blood product-related infection. China has been providing free antiretroviral therapy (ART) since 2003, which covered >80% of the identified patients and achieved a viral suppression rate of 91%. To bend the curve of increasing the disease burden of HIV and finally end the epidemic, China should consider constraining HIV spread through sexual transmission, narrowing the gaps in identifying HIV cases, and the long-term effectiveness and safety of ART in the future.

Keywords: Human immunodeficiency virus; Acquired immunodeficiency syndrome; Antiretroviral therapy; Transmission route; HIV-1 subtype

#### Introduction

There are few diseases that have struck the world as suddenly as human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and had a dramatic impact on global health policies, social economics, population behaviors, and academic research. Because of the multiple routes for HIV transmission, including sexual (heterosexual and homosexual intercourse), blood (injection drug use and blood transfusion), and mother-to-child, neither high-income countries nor middle- and low-income countries have been immune to the pandemic.

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Since the discovery of its first HIV case in 1985,<sup>[1]</sup> China has been a notable participant in the global fight against HIV/AIDS. However, the country is home to 18% of the world population and has been facing complex challenges as it attempts to control the disease across its diverse landscape ranging from remote rural areas to modern megacities.<sup>[2]</sup> The mode of HIV transmission varies considerably by region and has continued to evolve over the past three decades. China has experienced several HIV outbreaks that have greatly accelerated the spread of the disease. These include an outbreak among injection illicit drug users (IDUs),<sup>[3]</sup> similar to those that have occurred in

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developed countries (e.g., the United States),<sup>[4]</sup> and an outbreak related to blood transfusion,<sup>[5]</sup> similar to those that have occurred in underdeveloped countries (e.g., Kenya).<sup>[6]</sup> China experiences in addressing its HIV/AIDS epidemic are therefore relevant to many countries around the world.

China has made remarkable achievements in HIV prevention and control during the past three decades. The Joint United Nations Programme on HIV/AIDS (UNAIDS) previously estimated that the number of HIV-infected individuals in China could reach 10 million by 2010;<sup>[7]</sup> however, China has been able to limit the epidemic to <0.1% of HIV prevalence as of the end of 2017.<sup>[8,9]</sup> And by October 2020, there were 1.045 million people actually reported living with HIV/AIDS across China.<sup>[10]</sup> The political commitment, social engagement, and international support that are jointly responsible for this remarkable achievement have rarely been evaluated or reviewed.

The aim of this review is to evaluate the national plans and actions taken by China to prevent and control HIV/AIDS during the past three decades, and to provide a foundation for policy and practice improvements to achieve UNAIDS 95-95-95 targets (95% of all people living with HIV will know their HIV status; 95% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy [ART]; 95% of all people receiving ART will have viral suppression). We employed a narrative literature review of both published and grey literature [Supplementary materials A, http://links.lww.com/CM9/A815] as well as interviews with policymakers and care practitioners.

#### **Overview of the epidemic**

There have been three phases to the HIV epidemic in China: (1) sporadic cases (1985-1988), including 24 cases imported from overseas and four cases as a result of imported infected blood products; (2) endemic outbreaks (1989–1994), including outbreaks among IDUs in several border areas of the Yunnan province; and (3) expansion phase (1995 to present day), characterized by an increasing prevalence and expanded geographic reach. Since then, the number of HIV/AIDS cases grew rapidly. The annually newly reported HIV/AIDS cases in China increased 15 times from 2705 cases in 2005 to 42,406 in 2019. While the number of HIV/AIDS-related death only increased 25% from 40,711 in 2005 to 51,250 in 2019. From January to October 2020, there were 112,000 diagnosed living with HIV/AIDS cases and by October 2020, 1.045 million actually reported living HIV/AIDS cases in China, equating to a prevalence of <0.075%.<sup>[10]</sup> Since 1998, HIV cases have been discovered in all 31 provinces of the Mainland of China; however, the prevalence across provinces varies widely, from 0.01% in Shanxi to 0.21% in Yunnan.

#### **Transmission routes**

Several major modes of HIV/AIDS transmission have been identified in China during the past 37 years. In the 1980s, the first HIV/AIDS outbreak occurred among IDUs in Dehong Prefecture, Yunnan Province along the southwest border of the world largest illicit drug production and

distribution center, the so-called "Golden Triangle."<sup>[11]</sup> The epidemic steadily spread from Yunnan to neighboring provinces and eventually to all 31 provinces of the China.<sup>[12]</sup> In the early 1990s, the second HIV/AIDS outbreak occurred alongside the emergence of illegal commercial blood collection stations in rural areas of central China, mainly concentrated in the provinces of Henan, Anhui, Shaanxi, Hebei, Shandong, and Guiz-hou.<sup>[13]</sup> Successful efforts to curb injection drug use and illegal blood collection have led to the emergence of sexual transmission, both heterosexual and homosexual, as the major route for HIV infection in recent years.<sup>[9]</sup> In 2019, there were 71,204 newly infected HIV/AIDS cases in China, among whom, nearly zero HIV infection through blood transfusion were reported; the mother-to-child transmission rate decreased to minimal levels, and >95% we are through sexual behaviors.<sup>[14,15]</sup> Between 2006 and 2020, the proportion of cases resulting from homosexual transmission increased from 2.5% to 33.4%, and about eight out of every 100 men who have sex with men (MSM) lived with HIV/AIDS; as well as the proportion resulting from heterosexual transmission increased from 30.6% to >66.5% [Figure 1].<sup>[15,16]</sup> Currently, homosexual transmission is the primary route of infection in the east and central China provinces, accounting for 62.4% to 77.88% of newly reported cases.<sup>[14]</sup> In the south-western regions of China, heterosexual transmission predominates, accounting for 50% to 70% of new cases.<sup>[15,17]</sup>

#### Virologic characteristics

China is among the countries with the most complex cocirculating HIV-1 subtypes in the world. Between the late 1980s and early 1990s, multiple HIV strains, including subtype B, Thai-B(B'), subtype C, and CRF01\_AE HIV-1, were introduced to Yunnan province.<sup>[3,18-20]</sup> At present, six subtypes, 20 circulating recombinant forms (CRFs), and 117 unique recombinant forms (URFs) of HIV-1 strains have been detected in China compared with 11 subtypes and 14 CRFs in Cameroon, according to the records of the Los Alamos national database.<sup>[12]</sup> The most commonly identified CRFs are CRF07\_BC<sup>[21]</sup> and CRF08\_BC<sup>[22]</sup> among IDUs and CRF55\_01B<sup>[23]</sup> and CRF59\_01B<sup>[24]</sup> among MSM. For CRF01\_AE, multiple strains have been independently introduced into China, including at least seven co-circulating lineages [Figure 2].

The strains of HIV in China have become more and more complex in recent years. A large number of recombinant viruses strongly suggest that high-risk populations infected with multiple co-circulating HIV subtypes have become "incubators" and "accelerators" for HIV diversification. recombinants, such as CRF07\_BC<sup>[21]</sup> New and CRF08\_BC,<sup>[22]</sup> replaced their parental strains (subtypes B and C) soon after they were produced.<sup>[25,26]</sup> Seven CRFs, 41 URFs, and multiple second-generation recombinant viruses have been identified from heterosexuals.<sup>[12]</sup> Similarly, six CRFs and 27 URFs have been identified among Chinese MSM, with the recombination types reflecting all combinations of major strains (literature search and analysis were shown in Supplementary materials section "Selection criteria", http://links.lww.com/CM9/A815).





### Disease burden

The disease burden of HIV/AIDS in China has been growing but is still at a relatively low level. Compared with 0.08 per 100,000 population in 1990, the mortality rate of HIV in China has reached 2.23 per 100,000 population in 2019, which accounted for 0.3% of the overall deaths for

all causes and 71.34% of the overall deaths of the China Notifiable Diseases.<sup>[2,10,14]</sup> This is much lower than the average level over the world (a mortality rate of 9.10 per 100,000 population that accounted for 1.53% of overall deaths in 2019).<sup>[27]</sup> Similar results can also be found with respect to disability-adjusted life years (DALYs)—in 2019

HIV/AIDS caused 139 DALYs per 100,000 population accounting for 0.37% of total DALYs in China, in comparison to 1.88% of total DALYs over the world.<sup>[27,28]</sup>

#### Efforts and achievement

#### Political commitment

The Chinese government has devoted a great deal of time and effort to HIV/AIDS prevention and control, taking full advantage of its national system. It continues to maintain its firm commitment to HIV control by ensuring equal rights and interests for all individuals with HIV/AIDS, providing HIV/AIDS treatment to all individuals in need, and aiming to achieve the UNAIDS 95-95-95 target for prevention and control. China has developed a total of 30 main national laws, regulations, policies, and plans (both medium- and long-term) related to HIV/AIDS. At the central government level, China established the State Council AIDS Working Committee in 2004, which is led by the incumbent Vice-Premier [Supplementary materials B, http://links.lww.com/ CM9/A815]. Currently, the Committee involves the heads of 34 ministries and 11 key provinces [Figure 3]. At the local government level, community leader responsibility for AIDS prevention and control was implemented, and leaders who fail to meet their responsibility will be called to account. From 1995 to 2015, the annual growth rate of China total expenditures on HIV/AIDS prevention and control was 10.1%, tripling the global level of 3.1%<sup>[29]</sup> and reaching 6.104 billion Chinese yuan (RMB, 995.8 million US dollar <sup>[30]</sup> in 2014, and 6.959 billion RMB (1.137 billion USD) in 2017. Nearly all (98.8%) of this investment in AIDS prevention and control came from the Chinese government. To resolve challenges in ART for 127 key counties with high HIV prevalence, the China Comprehensive AIDS Response (CARES) Program was established (panel 2).<sup>[31]</sup> Collectively, China targeted efforts for HIV/AIDS prevention and intervention have helped control the risk of HIV transmission through IDUs, blood transfusion, and mother-to-child as well as significantly reduced HIV/AIDS-related mortality. Additionally, the national web-based Comprehensive HIV/ AIDS Information System was established to collect realtime data to support the monitoring of HIV testing, prevention, and treatment [Supplementary materials C, http://links.lww.com/CM9/A815].<sup>[32]</sup>

### **CARES** program

In 2003, the Chinese Ministry of Health launched the CARES Program (China CARES). By 2013, the China CARES had explored a set of comprehensive mechanisms for HIV control and prevention that addressed local outbreaks and conditions, which covers a total of 32 provinces, 309 county-level areas, which included >5397 townships, and a total population of 170 million.<sup>[33]</sup>

The China CARES endows three powerful strategies: (1) A mechanism for collaboration between government leadership and responsible departments was established. State leaders clarified the responsibilities of each department (e.g., public security, justice, finance, publicity, radio and television, family planning, civil affairs, education, agriculture, women federation, and communist youth league). China CARES also promoted the revision and development of national and local laws and regulations; 106 state-level documents and 3609 countylevel documents were prepared.<sup>[34]</sup> (2) Central and local governments provided special funds to support China CARES. On average, each CARES site received 4.3 million RMB (614,000 USD) from the central government and an equivalent amount from the local provincial, prefecture, and county governments, in addition to funds from other sources. (3) A monitoring and evaluation plan was established to ensure activities were carried out as planned. At the national level, joint on-site supervisory visits were organized once a year for selected program sites. Through 2007, a total of 73 visits occurred nationwide.<sup>[34]</sup>

China CARES also takes action in the following fields: (1) Enhance the awareness of HIV/AIDS in China by publicity and education. From 2004 to 2008, 67.9 million



Figure 3: Governance of HIV/AIDS prevention and control in China. HIV/AIDS: Human immunodeficiency virus/acquired immunodeficiency syndrome.

informational documents on HIV/AIDS were distributed across the country, with an average of 2.8 per family and 1.1 per person. A total of 247 televisions and radio stations broadcast information on AIDS prevention programs, with a monthly average of 175 programs at each China CARES site. HIV/AIDS awareness improved significantly across China CARES sites, increasing from <30% in 2004 to 86% in 2008. High levels of HIV knowledge were demonstrated by 86% of rural adults, 92% of urban adults, 76% of grade 7 to 9 students, and 91% of grade 10 to 12 students; the national average was 68%.<sup>[34]</sup> (2) The high-risk behaviors intervention reached 89.4% of highrisk entertainment venues and 88.6% of commercial sex workers. A total of 159 methadone maintenance clinics were set up in 309 CARES areas by 2013. There were 1226 free sites established for HIV voluntary counseling and testing.<sup>[33]</sup> (3) Specific medical institutions were designated for the treatment and management of HIV-infected patients. By the end of 2013, 547 designated hospitals provided antiretroviral treatment in China CARES. Collectively, the CARES sites treated 62,755 AIDS patients, which accounted for 22.6% of total patients in treatment nationwide. (4) The "Four Free and One Care" policy was implemented in first-round China CARES program sites, and it had a profound impact on national and local HIV/AIDS control and prevention work. Through China CARES, national policies on HIV/AIDS control and prevention were developed and tested through implementation. The 295 institutions established at China CARES sites cared for 11,116 HIV/AIDS patients (approximately 37.7% of those in treatment nationwide). All HIV orphans at China CARES sites benefited from the "Two Free and One Subsidy" policy. By March 2008, the number of patients receiving subsidies reached 23,497 (approximately 79.7% of patients at China CARES sites). In 2013, the number of people living with HIV or AIDS who were below the minimum living standard and HIV orphans or lonely old people at China CARES sites was 32,473, and 33,022 of them received assistance.<sup>[34]</sup>

### Prevention against IDU-related outbreaks and transmission

In 1989, the first HIV outbreak among heroin drug users occurred along China southwest border and quickly spread among other IDUs in neighboring provinces. In response, China enacted its first national anti-drug law in 1990: Decision of the Standing Committee of the National People Congress on Drug Detoxification.<sup>[35]</sup>

The Chinese Ministry of Public Security has cooperated with the Ministry of Health to gradually improve drug rehabilitation regulations over time. The regulations on AIDS prevention and treatment issued in 2006 and the Anti-Drug Law issued in 2008 allowed healthcare institutions to provide methadone maintenance treatment (MMT) and clean needles to drug addicts for the purpose of reducing HIV transmission through needle-sharing behavior. By June 2016, there were 33,486 participants in needle exchange programs and 161,975 IDUs receiving MMT. From 2006 to 2017, HIV incidence among individuals involved in MMT decreased from 0.95 per 100 person-years to 0.03 per 100 person-years. Moreover, results from a clean needle exchange intervention showed that the proportion of

2803

needles being shared in the intervention group was lower than that in the control group (35.3% *vs.* 62.3%). At the Guangdong site, the HIV incidence of the intervention group was significantly lower than that of their counterparts (12.9% *vs.* 33.3%, P < 0.011).<sup>[36]</sup>

These comprehensive measures effectively controlled the HIV epidemic in the Chinese IDU population. For example, the number of nationally annually reported new HIV/AIDS cases decreased 44.5% between 2012 and 2017.<sup>[37]</sup> And according to the calculation of a mathematical model, an estimated 98,232 to 211,200 new HIV infections and secondary transmission events were prevented between 1990 and 2015 [Supplementary materials D, http://links.lww.com/CM9/A815].

# Prevention against blood product-related outbreaks and transmission

After the initial HIV outbreak in commercial plasma donors in the early 1990s, the Chinese government banned commercial blood collection stations.<sup>[38]</sup> In the 1998 Blood Donation Act, China implemented voluntary blood donation and encouraged the active participation of all its citizens.<sup>[39]</sup> This regulation immediately removed the financial incentives associated with illegal blood collection and cut the supply, effectively ending this route of HIV transmission in China.

Concerns regarding blood safety were again raised as a result of the increasing proportion of voluntary blood donations from MSM (from 10.3% in 2001–2005 to 47.6% in 2010–2012).<sup>[40]</sup> Because MSM are a high-risk group and there is a window after infection before HIV can be detected by enzyme-linked immunosorbent assay, the Chinese government implemented nucleic acid testing at blood banks in 2010. Pilot programs for nucleic acid testing were conducted at 15 blood stations in 12 provinces in 2010,<sup>[12]</sup> and in 2014, the central government invested one billion RMB to establish capacity for nucleic acid testing at all blood stations within three years. With this investment, China narrowed the window for HIV detection by 50%<sup>[41,42]</sup> and became one of only four developing countries worldwide to implement nucleic acid testing for blood donation.<sup>[41]</sup> Among the 62,167 newly reported HIV/AIDS cases in China in 2020, nearly zero were reported to infect HIV/AIDS as a result of blood transfusion or the use of infected blood products.<sup>[14]</sup>

### Prevention against sexual transmission

Although commercial sex work remains illegal in China, the government has taken bold steps to implement behavioral interventions among female sex workers (FSWs) and male sex workers. Drawing on the experience of Thailand, China launched a pilot program to promote condom use and conduct health education among FSWs in Yunnan from 1996 to 1997. In 2004, the Ministry of Health, along with seven other ministries, created the High-Risk Behavior Intervention Work Guidance Program. This pilot program enlisted public health professionals to conduct outreach, peer education, condom promotion, HIV testing, and counseling to FSWs and MSM. High-risk population intervention teams were

established at each level of China Centres for Disease Control and Prevention (CDC) to implement HIV intervention activities and report progress quarterly. In 2008, HIV-related intervention activities reached 329,000 FSWs per month and 49,000 MSM per month. By 2014, these figures increased to 440,000 FSWs per month and 252,000 MSM per month. These represent an increase in the nationwide coverage of the intervention between 2008 and 2014 from 30.9% to 81.0% among FSWs and from 8.6% to 78.5% among MSM. Among FSWs, the proportion undergoing HIV testing increased from 35.8% to 39.0%, and the proportion reporting persistent condom use in the last month increased from 56.9% to 70.7%. Similar results were found in the MSM population, with the HIV testing rate increasing from 29.1% to 49.7%, and the persistent condom use rate in the last six months increasing from 41.3% to 46.2%. Meanwhile, Truvada<sup>®</sup> is approved by the Chinese National Medical Products Administration for pre-exposure prophylaxis (PrEP) in combination with safe sexual practices to reduce the HIVinfected risk of adults and adolescents (at least 35 kg) through high-risk sexual behaviors in August 2020. And the Chinese Center for Disease Control and Prevention has issued the Technical Guidelines for Post-exposure HIV Prophylaxis to promote the full implementation of postexposure prophylaxis (PEP) in China since October 2020. Despite these improvements, sexual transmission is the main route of HIV transmission. In recent years, 95% of the newly reported cases have been sexually transmitted, with heterosexual transmission accounting for about 70%. National data show that about 8 out of every 100 MSM are infected with HIV.<sup>[15,16]</sup> Therefore, continued observation of Chinese FSWs and MSM is needed to determine the ultimate effectiveness of current intervention efforts.

### Prevention against mother-to-child transmission

China launched prevention of mother-to-child transmission of HIV (PMTCT) programs in 2003, <sup>[43,44]</sup> then promulgated "the Implementation Plan for Prevention of Mother-to-Child Transmission of AIDS, Syphilis and Hepatitis B." PMTCT programs consist of a range of interventions, including free HIV counseling and testing for pregnant women, free antiretroviral drug prophylaxis for HIV positive pregnant women and newborns. According to national data, the rate of mother-to-child transmission reduced from 7.1% in 2012 to 4.9% in 2017,<sup>[36]</sup> aiming at reducing HIV/AIDS mother-to-child transmission rate to 3% in 2025 according to "Health China 2030 plan." As a province with a high incidence of HIV-infected pregnant women in China, the mother-to-child transmission rate in Yunnan province had dropped to 2.83% in 2017,<sup>[45]</sup> which was close to the global elimination of mother-to-child transmission standards (<2%).<sup>[46]</sup>

#### Infection detection

China has established an HIV testing network that covers 98% of county-level areas. The over 30,000 HIV screening laboratories and 600 confirmatory laboratories are widely distributed across hospitals, CDCs, blood stations, maternal healthcare centers, judicial administrations, customs administrations, and military health systems. In some areas, such as Yunnan province, rapid HIV tests are even provided at village clinics.

Various HIV testing strategies have been implemented in China over the past decade. Provider-initiated HIV testing and counseling became the mainstay in 2009. In 2015, hospitals performed 72% of HIV testing nationwide and diagnosed 52.2% of HIV-infected cases. Voluntary counseling and testing (VCT) sites have multiplied over time, and in 2015, the 8849 sites in China conducted 1.7% of all HIV testing and diagnosed 28.9% of HIV-infected cases. A total of 45,509 primary screening laboratories and 691 confirmation laboratories throughout the country continue to promote voluntary counseling and testing of high-risk groups, expansion of screening of medical institutions, mobilization of social organizations testing, self-testing of key population groups, etc. China explores the comprehensive intervention of "Internet plus" in the prevention and treatment of AIDS and innovates the application of molecular network technology to guide accurate intervention. Large-scale HIV screening has also proven helpful. In 2004, tens of thousands of commercial plasma donors and IDUs and other people in high HIV infection risk were screened for HIV; within the span of a few months, 23,000 cases were identified in Henan, and 13,500 were identified in Yunnan. The number of HIV tests performed in China has continued to grow, increasing from about 100 million in 2012 to 200 million in  $2017^{[37]}$ ; China currently accounts for about one-third of global HIV testing, aiming at achieving the first 90% early.

### Antiretroviral treatment

Since 2003, the Chinese government has provided free combination ART to HIV-infected patients through the National Free Antiretroviral Treatment Program. This program has ensured the successful treatment of infected individuals through the following measures: (1) Establishing a special fund for purchasing drugs, which has grown from 16.07 million RMB in 2003 to 184.97 million RMB in 2006.<sup>[47]</sup> In 2017, the funding has been increased to 1654.38 million. (2) Issuing a series of medical assistance policies that mandate the coordination and cooperation among government departments in relation to healthcare investments. (3) Reducing the drug prices through national centralized procurement. (4) Supporting free CD4+ T cell count, viral load, and drug resistance testing for every patient; as a result, CD4+ T cell testing has increased from 20% in 2005 to 86% in 2013. (5) Formulating guidelines for the diagnosis and treatment of HIV/AIDS that reflect national conditions in China and establishing 12 training centers to strengthen patient management capabilities among clinical professionals across the country. (6) Establishing a CDC-hospitalcommunity model for patient management to promote collaboration among all levels of the healthcare system. (7) Exploring the advanced case management model in which patients receive a comprehensive range of services (e.g., testing, counseling, guidance, treatment, and referral) at one institution; this proved effective in increasing rates of drug compliance and treatment retention.<sup>[48]</sup>

Despite limited financial investment and a lack of drug options, China has achieved ART rates that rival those of

developed countries. From 2007 to 2012, the annual expenditure for antiretroviral drugs per patient was 706 USD in China, compared with 9489 USD in the US.<sup>[49]</sup> During the past 15 years, highly active ART coverage among individuals infected with HIV in China has expanded from 25% to 80% in 2017, with a viral suppression rate of 91%.<sup>[37]</sup> HIV mortality decreased to 3.6% by 2017, and the proportion of pre-treatment drug resistance has remained lower than that of developed countries (3.6% *vs.* 8.4%).<sup>[49-52,50-53]</sup>

## Social engagement

Educational institutions, community-based organizations (CBOs), media, and celebrities have also played an important role in enhancing public awareness of HIV/ AIDS and reducing related discrimination. Sex education related to HIV prevention has been strengthened in primary, secondary, and high schools as well as in colleges. In addition to a series of classroom activities and specific lectures related to HIV prevention, a number of provinces (e.g., Yunnan, Liaoning, and Zhejiang) track knowledge of HIV/AIDS within the AIDS Prevention Teachers' Network and AIDS prevention information in local textbooks.<sup>[54]</sup> A study of 16 provinces revealed that 86% of 7851 college students had received school-based sex education.<sup>[12,55]</sup> The AIDS, sex, and health online credit course had been audited by nearly 140,000 students from 259 colleges and universities within 1 year.<sup>[56]</sup>

CBOs in China have been playing an increasingly important role. CBOs focused on HIV/AIDS began appearing in 2000, and as of 2015, there were 789 registered AIDS-related CBOs.<sup>[57]</sup> Chinese Association of STD and AIDS Prevention and Control, the largest government-led society organization in China, serves as a bridge between the government and social forces in HIV/ AIDS response. It is not only an important supporter of grassroots CBOs but also have concentrated their efforts on the promotion of academic exchange, holding five national AIDS conferences attended by thousands of participants and publishing the only AIDS-related academic journal in China, *Chinese Journal of AIDS and* STD.<sup>[58,59]</sup> CBOs also had achieved success among hardto-reach groups, such as MSM, IDUs, and sex workers.<sup>[60]</sup> For example, the AIDS care China CBO has focused on providing targeted services for patients with AIDS and their relatives to improve treatment adherence and to strengthen patients' societal connections. This organization was honored with the 2006 Red Ribbon Award by the United Nations Development Programme.<sup>[61,62]</sup>

A team of nearly 30 celebrities, known as Ambassadors for HIV/AIDS Prevention, Control, and Caring, has become an important force in disseminating basic knowledge and proper attitudes to the public. These Ambassadors have provided HIV/AIDS-related training, lectures, and assistance as well as participated in advertisements, movies, and documentaries. China's first lady, Peng Liyuan, has begun advocating for HIV/AIDS prevention and control in 2006 and visited most of the high-epidemic rural areas of China and attended a camp for AIDS orphans each year.<sup>[63]</sup> She has also been an appointed WHO Goodwill Ambassador for Tuberculosis and HIV/AIDS since 2011.<sup>[64]</sup> As China's first lady, she has been sharing China experiences in the fight against AIDS with the world since 2013. In recognition of her remarkable contributions to the global response to HIV, UNAIDS presented Mrs. Peng with their Award for Outstanding Achievement.<sup>[65]</sup>

The prevention and control of HIV/AIDS in China has involved active participation from citizens across the nation devoted to the promotion of public understanding and elimination of discrimination. AIDS awareness among high-risk populations, including migrant workers, FSWs, and MSM, has increased from 73.6% to 79.7% in 2008 to 82.8% to 92.8% in 2014.<sup>[66]</sup> Among college students, awareness increased from 69.7% to 82.2% after health education.<sup>[67]</sup> Social prejudice and discrimination against individuals with AIDS have slowly been reversed in China. An investigation showed that 45% of teenagers had an improved attitude toward people infected with HIV after a conference on a nationwide AIDS awareness initiative. Moreover, most individuals surveyed after watching the anti-discrimination movie, "Together," reported a willingness to maintain their associations with HIV-positive individuals.[68]

### International support

International organizations have provided important funding and methodologic support, which have been essential for the management of HIV/AIDS in China, particularly during the early stages. Large organizations, including the Joint United Nations Programmeon HIV/ AIDS (UNAIDS) and World Health Organization (WHO), have used their experiences and novel technologies to assist with the development of national policies and guidelines.<sup>[69]</sup> For example, in 2000, China initiated a VCT pilot program with the support of WHO, United Nations Population Fund (UNFPA), and the China-UK program. VCT quickly became a national strategy in 2004 and expanded to 7335 sites by 2009.<sup>[70]</sup> The Global Fund, one of the largest international programs, contributed 324 million USD to China between 2003 and 2013,<sup>[71]</sup> and it made notable progress in fighting HIV/AIDS at different stages. The Global Fund first effectively addressed the issues surrounding second-line drug availability and affordability for children in seven provinces of central China. The organization later implemented intervention service platforms for IDUs and commercial sex workers, including MMT clinics, needle exchange points, and VCT in seven high-prevalence provinces. The Global Fund also facilitated domestic CBO engagement in interventions among MSM to help combat the increasing numbers of sexually transmitted infections in this high-risk group.<sup>[72]</sup>

International CBOs have also made outstanding contributions. For example, the Gates Foundation donated >50 million USD to China for HIV/AIDS control,<sup>[73,74]</sup> supporting cooperation between the Chinese government and community organizations on a project to expand HIV prevention among those at highest risk of infection as well as to provide treatment and care for those living with HIV [Supplementary materials E, http://links.lww.com/CM9/A815].<sup>[74,75]</sup>

#### **Challenges and recommendations**

To bend the curve of the increasing burden of HIV in China, and finally end the epidemic, China must conquer the following challenges in transmission control, infection detection, and patient treatment.

## To constrain the spread from high-risk subgroups to the general population

According to international experiences, sexual transmission is the dominant model of HIV infection. The spread of HIV from high-risk subgroups to the general population is a concern that China is currently facing. To prevent this, more attention should be paid to these high-risk subgroups, particularly MSM.

The heterosexual route has become the primary HIV transmission route in China. To make things worse, there are various factors that promote heterosexual route HIV transmission. First, the proportion of synthetic drug abusers showed a rapidly increasing trend in national registered illicit drug abusers, which increased from 6.70% in 2005 to 57.14% in 2015 [Supplementary materials F, http://links. lww.com/CM9/A815]. Second, the infection mode of reported heterosexual route infected cases was mainly through non-married heterosexual sexual contact, which increased from 78.2% in 2008 to 88.2% in 2014.<sup>[76]</sup> Lastly, seeking casual sex partners through the Internet was as high as 13.4% among the 15- to 24-year-old youth population.<sup>[77]</sup> All the above three factors will fuel the speed of the HIV epidemic spread through the heterosexual route.

Additionally, the incidence of HIV among MSM in China was two times higher than that in Western countries (5.5 per 100 person-years vs. 2.1 per 100 person-years),<sup>[78]</sup> and it continues to rise during 2005 to 2014.<sup>[79]</sup> By comparison, the incidence of HIV in commercial sex workers in China was 1.4 per 100 person-years.<sup>[80]</sup> Because of the stigma associated with homosexuality, the proportion of MSM who also engage in sex with women is high in China, with estimates ranging from one-third to one-half of the MSM popula-tion,<sup>[81,82]</sup> which was pretty high relative to in England (10.6%).<sup>[83]</sup> These men engaging in bisexual behavior have a higher HIV prevalence than those having sex exclusively with men (5.4% vs. 3.8%).<sup>[82]</sup> Only 7% of bisexual MSM with HIV disclosed their positive test results to all of their sexual partners.<sup>[84]</sup> Moreover, bisexual MSM are less likely to use condoms when they engage in sexual intercourse with women than with men (28.1% *vs.* 36.6%).<sup>[81,85]</sup> Notably, HIV infections among college students also need worthy attention.<sup>[86]</sup> The number of college students infected with HIV has increased by 35% annually from 2011 to 2015<sup>[87]</sup>; 81.8% of these students were infected through homosexual intercourse in 2017. The number of newly diagnosed college students has seen an annual growth rate ranging from 30% to 50% over the past several years.<sup>[88]</sup> Among Chinese students, there is a high rate of condom-less sexual intercourse and a low level of knowledge about safe behavior,<sup>[89]</sup> leaving young students vulnerable to infection.<sup>[90]</sup>

The intervention of HIV transmission through heterosexual behavior should be further strengthened, the education and intervention of synthetic drug abuse, multiple sexual partner behavior, and seeking casual sex partners through the Internet should be reinforced through both traditional media including television and newspapers as well as new media, including Internet and social dating applications.

Specific strategies to reduce the transmission of HIV from MSM to their female sexual partners are needed. First, China should further strengthen campaigns focused on reducing discrimination against HIV; the prior experiences of publicity ambassadors could be helpful with this endeavor. Second, HIV PrEP and research on preventive vaccination should be better promoted to reduce the possibility of transmission.<sup>[91]</sup> Third, CBOs and social network applications for MSM should be explored given their promise for disseminating HIV knowledge, promoting safe sexual behaviors, and conducting targeted interventions. Fourth, China could consider amending laws related to disclosure of HIV-positive test results to partners and call for compulsory partner notification, similar to actions taken by countries such as Italy, Sweden, and Estonia.<sup>[92]</sup> Fifth, institutions of higher education should hold public courses on safe sex practices and sexual health to ensure students know how to protect themselves and others from HIV.

#### To narrow the gaps in identifying HIV cases

Detection is the biggest challenge in China mission to achieve the UNAIDS 95-95-95 target. It has been estimated that approximately 30% of infections remain undetected. This likely, in part, reflects the low proportion of high-risk individuals who actively seek testing for HIV. Only 47% of MSM in China have voluntarily visited HIV testing centers,<sup>[66]</sup> compared with 86.4% in Australia.<sup>[93]</sup> The disjointed process for HIV diagnosis could also play a role and contribute to losses to follow-up of potential infection cases. It has been reported that about 30% of HIV-positive cases who undergo initial screening do not return to clinics to confirm the diagnosis.<sup>[94]</sup> Notably, the gaps in infection detection not only result in infected individuals not receiving treatment but also could jeopardize patient treatment outcomes as a prior study showed that 34% of cases were first diagnosed during the middle or final stages of the disease.<sup>[95]</sup>

Several approaches are recommended to address these issues. First, China should consider promoting standardized HIV self-detection. Currently, rapid HIV test strips are widely available for purchase online. For example, there are 279 online retailers in Taobao (Chinese public online shopping site) selling these tests, and they fulfilled 55,558 orders in September 2018. Despite their promise, these products require further validation, and self-testing should be a part of a guided process to ensure people receive accurate results and understand how they can get help. Second, further screening initiatives should be considered. Well-conducted screening projects targeted at high-risk populations or high-risk areas have been proven effective in identifying formerly hidden cases of HIV. Such screening projects also have the advantage of promoting immediate HIV treatment and care for infected individuals. The projects could be strengthened by new strategies incorporating the HIV molecular transmission network and online social networks.<sup>[96]</sup> Third, the process for HIV detection should be simplified and the duration between initial screening and diagnosis confirmation should be reduced. One promising model is the "One4All" strategy, which promotes fast and complete diagnosis as well as provides immediate ART to eligible patients. A cluster-randomized trial of this strategy showed improved management outcomes for patients in the intervention.<sup>[97]</sup>

#### To enhance the long-term effectiveness and safety of ART

China should take precautions to limit potential issues in treatment, particularly increased drug resistance, narrow pharmaceutical options, and scarce evidence. First, the vast majority of AIDS treatment in China is undertaken by hospitals specializing in infectious diseases, and these institutions often lack the capacity to provide multidisciplinary clinical management for disease complications. Second, drug resistance is a growing problem that requires immediate attention despite the current rarity of such events. The rate of drug resistance among MSM has reached 5% in some Chinese cities, and reverse transcriptase-related transmitted drug resistance has been identified in an increasing proportion of newly diagnosed HIV/AIDS patients.<sup>[98]</sup> Third, the only treatments currently available for HIV in China are nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors. However, treatment failures after the use of second-line drugs have become more common, already reaching 5% in Xinjiang and Fujian.<sup>[99,100]</sup>

### **Conclusion and perspectives**

While navigating the complicated epidemic of HIV, China has made substantial efforts to achieve the 95-95-95 target for HIV control. National actions have successfully slowed the spread of HIV at several crucial stages. Political commitment, social engagement, and international support have all played critical roles in China achievements. Nevertheless, challenges in transmission control, infection detection, and patient treatment demand further attention and prompt solutions now and in the future. Never has there been a moment in time when international collaborations mattered. In addition to being open to international experience and support, China can share its own experiences and serve as a model for other countries. China has embraced a more active role to end the epidemic by 2030.

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#### **Conflicts of interest**

None.

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