



Interventions to improve the HIV continuum of care in China

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Abstract

Purpose of Review To describe HIV epidemic and interventions for improving HIV continuum of care in China.

Recent Findings The reported HIV epidemic has been continuously increasing, partially due to the expansion of active HIV testing campaign. Public health intervention programs have been effective in containing HIV spread among former plasma donors and people who inject drugs (PWID), but more infections occur among heterosexual men and women and young men who have sex with men. Of 1.25 million Chinese people are living with HIV, one-third do not know their status. About two-thirds of diagnosed individuals have used antiretroviral therapy (ART) and two-thirds of those on ART have achieved viral suppression, but some risk groups such as PWID have lower rates. The national free ART program has reduced adult and pediatric mortality and reduced heterosexual transmission.

Summary China faces great challenges to reduce HIV sexual transmission, improve the HIV continuum of care, and close the gaps to the UNAIDS Three “90” Targets.

Keywords HIV · Continuum of care · Testing · Antiretroviral therapy · Viral suppression · China

Introduction

Since the first case was reported in 1985, the HIV/AIDS epidemic and risk factors in China have gone through several phases. The number of reported HIV/AIDS cases nationwide was under 300 each year during 1985–1993 and less than 10,000 from 1994–2002, and most cases were people who inject drugs (PWID) [1, 2]. China shares international borders with two major heroin producing regions in Asia—the “Golden Triangle,” which includes Myanmar, Laos, and part of Thailand, and the “Golden Crescent,” which includes Afghanistan, Iran, and Pakistan. As China opened its borders

for trade, it also became a new destination for drug trafficking in the late 1980s [3]. Heroin and opium were trafficked from the “Golden Triangle” countries to Yunnan and Guangxi provinces in southwestern China, and from the “Golden Crescent” countries to Xinjiang province in northwestern China. Local residents along these trafficking routes in these bordering provinces and in some inland cities became drug users, and the practice of sharing unclean needles and syringes caused rapid spread of HIV among PWID (Fig. 1) [4, 5].

The number of annual reported cases jumped to 21,691 in 2003, and further doubled to 47,676 in 2004 (Fig. 2). The sharp increase was mainly due to the increased HIV screening

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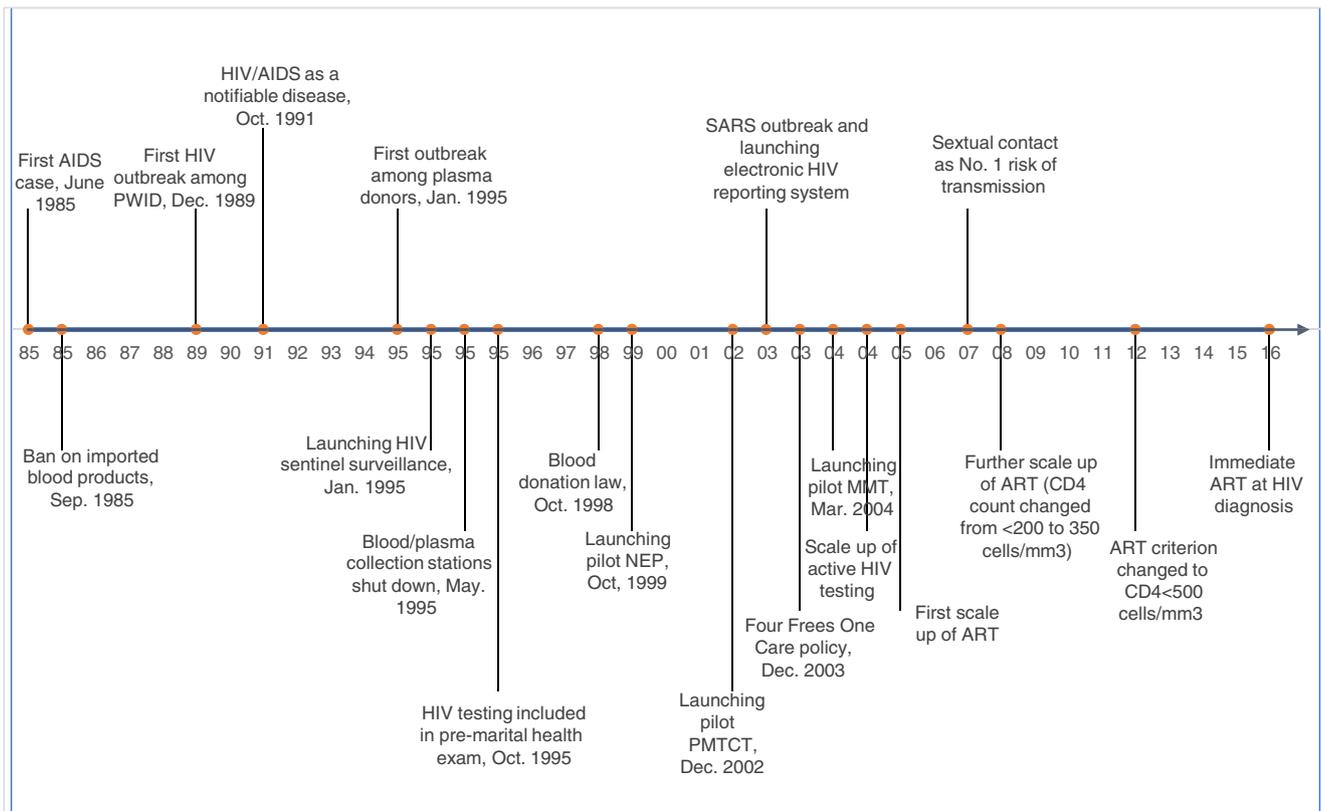


Fig. 1 Important events of HIV/AIDS epidemic and policy development in China, 1985–2018. PWID, people who inject drugs; NEP, needle exchange program; PMTCT, prevention of mother-to-child transmission; MMT, methadone maintenance treatment; ART, antiretroviral therapy

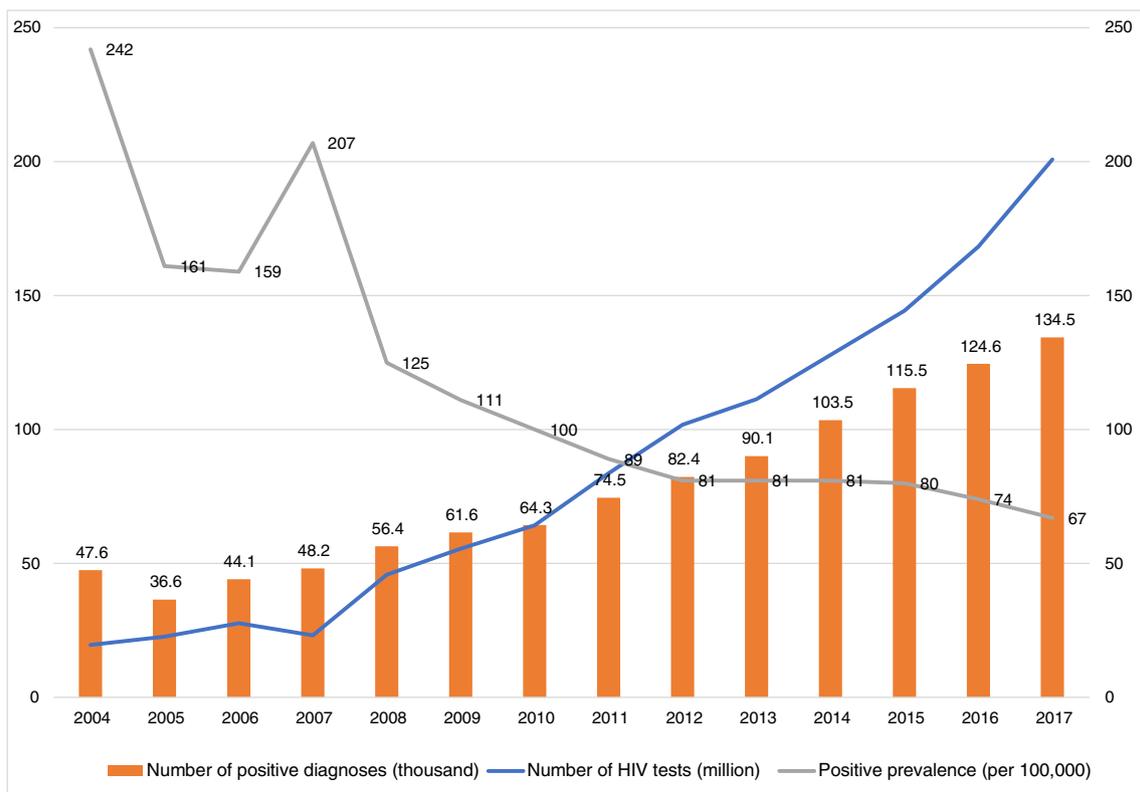


Fig. 2 Number of HIV tests and positive diagnoses and prevalence in China, 2004–2017

among former plasma donors (FPD) in central China in 2003 and scale up of active HIV testing across the country in 2004 (Fig. 1) [2]. During 1994–1997, many blood/plasma collection stations were operated in the rural regions in Henan and surrounding provinces. Poor farmers sold bloods to make money, and the donations of same blood types were pooled in an unsterilized container. After plasma was extracted, the red blood cells were re-infused to the donors, so that the donors could reduce anemia and increase the frequency of blood donation. This unhygienic practice caused a rapid spread of blood-borne diseases including HIV (Fig. 1) [4, 6, 7]. These plasma donors who contracted the virus in the 1990s were largely detected during 2003–2005 (Fig. 3). By 2005, FPD accounted for 10.7% of estimated 650,000 people living with HIV (PLWH) [8].

HIV started to spread to the spouses of PWID and FPD through sexual transmission in the 1990s [9, 10]. National HIV sentinel surveillance showed that HIV prevalence among commercial sex workers increased dramatically from 0.02% in 1995 to 2% in 2000, and increased prevalence was also observed among sexually transmitted disease (STD) patients and low-risk women at pre-natal clinic visits [11]. Since the beginning of twenty-first century, homosexual transmissions of HIV have become increasingly common. Studies showed that HIV prevalence rates among men who have sex with men (MSM) ranged from 2.5% (2001–2008) [12] to 9.9% (2010) [13] compared with 0.05–0.06% in the general population (2003 to 2009) [8]. Since 2006, a significant portion of new HIV/AIDS cases have been contributable to sexual transmissions. Heterosexual contact replaced injecting drug use (IDU) for the first time as the most common transmission route in 2007, and it contributed to nearly 70% reported new cases in

2017. Homosexual contact has become an increasingly significant risk factor, and the proportion of homosexual transmissions rose from 3.4% in 2007 and 25.5% in 2017. Meanwhile, IDU-associated transmissions have significantly reduced, and other risk factors contributed to only a small number of newly reported infections (Fig. 3). Compared with 47,676 reported cases in 2004, it took about 10 years to be doubled to 90,119 by 2013, and only additional 4 years to be tripled to 134,512 by 2017, and sexual transmission is the main driving force for the continuing growth of HIV epidemic in China (Figs. 2 and 3).

HIV Prevention Interventions

In response to the HIV/AIDS epidemic, the Chinese government has made tremendous progress though it also made mistakes in the early years. During the 1980s and 1990s, its preventive strategies were focused on stopping HIV from entering the country, such as banning import of blood products, restricting the entry and residence of people with HIV from other countries, and cracking down drug trafficking across the borders [14, 15]. Laws against drug abuse and prostitution were also enforced with attempts to stop transmission within the country, including detaining drug users and sex workers and isolating HIV-positive individuals [16–18]. These containment policies proved to be little effective and even counter-effective, as they probably drove people with risk behaviors to hide their risk activities and discouraged them to seek health care [19].

With the emerging scientific evidence on effective prevention interventions and communicating with international

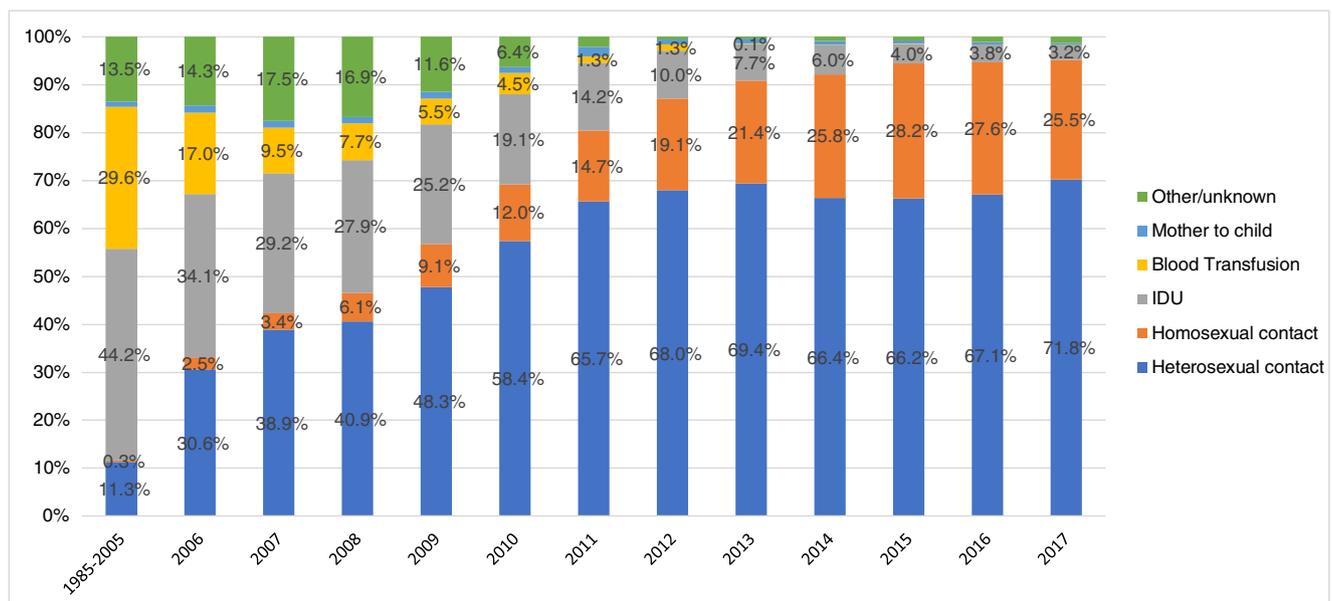


Fig. 3 Transmission routes of newly reported HIV/AIDS cases in China, 1985–2017

communities about their successful experiences, Chinese policymakers gradually shifted their attitudes and adopted pragmatic policies [18]. The Blood Donation Law took effect in 1998, illegal blood/plasma collection stations were closed, and HIV transmission among rural donors was largely stopped in rural central China [4, 20], though the secondary transmissions from infected FPD to their spouses and children have been reported in some communities [21–23]. Two large harm reduction programs—needle/syringe exchange program (NEP) and methadone maintenance therapy (MMT)—have been launched and scaled up since 1999 and 2004, respectively, and have significantly reduced HIV risk among PWID [24, 25].

Although China has successfully contained HIV epidemics among PWID and FPD, it is facing greater challenges than ever before in preventing sexual transmission. PWID and FPD, the previously main high-risk populations, were most confined to limited geographical regions in southwestern/northwestern or central China, and they were relatively easy targets for the prevention intervention programs to focus on. In recent years, the transmission modes have shifted to heterosexual and homosexual contacts, which means that the prevention intervention programs must reach the hidden populations like female sex workers (FSW) and MSM. Sexual transmission may also mean diffusing of high-risk behaviors among the general population, which poses challenges of focusing interventions.

Even though there has been no cure for eliminating the transmission source and no vaccine for protecting susceptible individuals, there are evidence-based, effective strategies for preventing sexual transmission of HIV. Antiretroviral therapy can reduce viral load in the body of HIV-infected individuals and therefore reduce sexual transmission. This treatment as prevention (“TasP”) strategy has been supported by the evidence from randomized clinical trials among serodiscordant heterosexual couples and homosexual male couples [26–28]. Analysis of Chinese national HIV treatment data also showed ART could prevent HIV transmission in serodiscordant heterosexual couples. The updated Chinese guidelines for diagnosis and treatment of HIV/AIDS (2018) recommend early initiation of ART for HIV prevention. Post-exposure prophylaxis (PEP) can reduce the likelihood of infection in those with a recent HIV exposure [29], and this has been mainly used for occupational prophylaxis in China. Pre-exposure prophylaxis (PrEP) can reduce the risk of contracting the virus for HIV-negative persons who have high-risk behaviors [30, 31], but it has very limited use in China, as the Chinese government prioritizes its ART programs on treating those who are already infected. Male circumcision can significantly reduce heterosexual transmission; [32–34] China could greatly benefit from the scale up of this intervention, as few Chinese men are circumcised. More research is needed to evaluate the actual uptake versus stated willingness for use among Chinese men

and to evaluate its efficacy among MSM [35–39]. With advent of these newly developed strategies, the “ABC” HIV prevention principles, namely abstinence, being faithful, and condom use, are no longer emphasized as much as in the early era of HIV epidemic. However, a mathematical model showed condom use is the most effective single intervention for mitigating the rising trend of HIV among MSM in Beijing [40]. As casual sex and multiple sexual partnership are common among Chinese high-risk and general population, a modified version of ABC principles should be incorporated in HIV prevention programs, in which abstinence could mean no sex for lifetime or avoiding sex with an individual with unknown HIV status, and being faithful could mean having one sexual partner for lifetime or only having one partner at a time. These more practical principles may be easier for targeted populations to accept and comply with. As no single intervention is 100% effective, combination interventions have been evaluated recently [40–43], which showed a synergistic effect on HIV prevention. This strategy should be incorporated into Chinese HIV prevention programs.

HIV Testing Interventions

China has scaled up active HIV testing programs over the past 15 years (Fig. 1). From 2004 to 2017, HIV screening tests increased ten folds from approximately 20 to 200 million, while newly diagnosed HIV infections increased nearly three folds from 47,606 to 134,512. The positive testing rate declined from 242 to 62 per 100,000 tests (Fig. 2), as more low-risk people might take a test as the testing campaign expanded. Meanwhile, newly reported HIV infections have increased rapidly in this period, and the expanded testing may partially explain for the increase.

HIV testing is offered through various venues in China. China has a nationwide network of more than 3000 Centers for Disease Control and Prevention (CDCs) at the national, provincial, city, and district/county levels, and almost all CDCs have an HIV voluntary counseling and testing (VCT) clinic providing free testing and pre- and post-test counseling [18]. Free testing is also offered at blood banks and detention centers such as prisons and jails, or through public health or research surveys. People may also pay for a test when they have a surgery or blood transfusion or when they undertake a pre-marital and pre-natal health examination. Of 200 million tests in 2017, about 59% were completed in hospitals, 16% during pre-marital and pre-natal health examinations, 13% for voluntary or commercial blood donations, and only 1.3% in VCT clinics. Compared with low HIV-positive rates in pre-marital/pre-natal examinations and blood donations—13 and 11 per 100,000 tests, respectively—it was as high as 1343/100,000 in VCT clinic tests (Table 1). People may actively seek a test at VCT clinics when they have high-risk

Table 1 HIV testing in China in 2017

Venue of testing	No. of tests, <i>n</i> (column proportion %)	No. of HIV positives, <i>n</i> (prevalence per 100,000)	No. of HIV late diagnosis (CD4 < 200 cells/mm ³), <i>n</i> (prevalence %)
Hospitals ¹	118,811,773 (59.2)	72,667 (61.2)	27,468 (37.8)
Pre-marital/pre-natal clinics ²	31,299,640 (15.6)	4056 (13.0)	603 (14.9)
Blood banks ³	26,190,960 (13.0)	2767 (10.6)	406 (14.7)
Surveys ⁴	4,889,290 (2.4)	3101 (63.4)	586 (18.9)
VCT clinics ⁵	2,693,766 (1.3)	36,177 (1,343.0)	9117 (25.2)
Detention lefts ⁶	2,183,542 (1.1)	4194 (192.1)	687 (16.4)
Entertainment ⁷	1,337,130 (0.7)	400 (29.9)	53 (13.2)
Others ⁸	13,314,818 (6.6)	11,150 (83.7)	2375 (21.3)
Total	200,720,919 (100.0)	134,512 (67.0)	41,295 (30.7)

¹ Including HIV testing before surgery and blood transfusion

² Including pre-marital and pre-natal health examinations

³ Including blood donation and commercial collection of blood or blood products

⁴ Including public health surveys or research projects

⁵ Including voluntary counseling test (VCT) clinics at Disease Control and Prevention (CDCs) and community-based organizations (CBOs)

⁶ Including prisons, jails, and drug detention centers

⁷ Including health examination for staff working in dancing hall, Karaoke bars, game rooms, billiard halls, etc

⁸ Including all other or non-classified venues

behaviors or because their partners are infected with HIV. It is suggested that VCT could be a productive way of detecting new infections, and people should be encouraged to undertake voluntary HIV testing. Moreover, about 38% HIV-infected people diagnosed in hospitals had CD4 count < 200 cells/mm³ compared with 31% in all cases, suggesting later diagnosis in hospital settings (Table 1).

The National Health Commission of the People's Republic of China estimated that 1.25 million Chinese people lived with HIV at the end of 2018, and about two-thirds knew their HIV status. It is far below the first target of the UNAIDS Three "90"s. People should be encouraged to take voluntary testing considering the history data showing a higher productivity of detecting HIV in VCT clinics. There are numerous noteworthy characteristics of HIV/AIDS epidemic in 2017: about 70% reported cases were heterosexual transmissions and 25% were homosexual transmissions; the proportion of infections among older men aged 60 or above doubled from 7.4 to 14.7% from 2010 to 2017; students accounted for 19% cases in youth cases aged 15–24 years; 82% infections among students were contracted via homosexual contact. It is suggested HIV testing campaigns should be tailored for people with high risks of sexual transmission, especially FSW and their clients, MSM, elder men, and college students.

A meta-analysis showed the prevalence rates among Chinese FSW in high- and low-tier entertainment venues during 2000–2011 ranged from 0.59 to 1.10% [44], but the estimated prevalence might be several-fold higher [45]. A 2014 survey by the Chinese Center for Disease Control and Prevention (China CDC) estimated that about 60% male

participants contracted HIV through commercial sexual activity [45]. Studies have shown increasing HIV prevalence among older men and college students [46–49], and high incidence among MSM [47, 50, 51]. However, HIV testing rates are low among FSW [52, 53], FSW male clients [54], and MSM [55, 56]. The common barriers for seeking a test among FSW include misunderstandings about HIV, low perceived risk of HIV, mistrust of free VCT service, and fear of a positive result [57]. Perceived severity of HIV infection, perceived benefits of HIV testing, and perceived self-efficacy are associated with uptake of HIV testing among FSW male clients [54]. The barriers among MSM include stigma and discrimination related to HIV and homosexuality, limited HIV knowledge, inconvenient clinic times, not knowing where to get a free test, fear of positive diagnosis or nosocomial infection, low perceived service quality, low perceived HIV risk, fear of disclosure, and concerns/doubts about HIV services [55]; these are also the barriers for college students [58–60]. HIV testing and counseling is the gateway to HIV care, and frequent testing may reduce the risk of HIV infection [61]. Interventions for promoting HIV testing should be tailored to address prevalent stigma, low perceptions about HIV risk and self-efficacy, and other personal, social, and structural barriers among these high-risk groups. In recent years, innovative techniques and strategies have been used for increasing HIV testing, including use of social media platforms WeChat (Chinese version of Facebook), online chatroom, text messages, and MSM-friendly Blued [62–69]. Leveraging social media platforms may be particularly useful for young MSM [70]. Strategies such as peer-led intervention, crowdsourcing

intervention, rapid testing, and home-based self-testing have demonstrated effective for increasing uptakes of HIV testing [71–75].

Linkage-to-Care Interventions

Linkage to care, which is the start of engagement in HIV care, includes two steps: one is to link HIV screening positives to confirmatory test and the second is to link confirmed positives to HIV care. In China, routine linkage to care service is embedded in the testing procedures. There are ten thousands of screening labs in CDC clinics, blood donation stations, and hospitals [76]. When an individual has a positive result of a venue-based screening test, clinic staff will collect a venous blood sample and send to a confirmatory lab; if confirmed positive, the person will be asked to come back to the clinic to receive the testing result and post-test counseling. It is mandated that HIV-positive individuals provide their national identification number, and all newly diagnosed cases be reported via a nationwide real-time web-based HIV/AIDS case reporting system [77]. All HIV-infected individuals are evaluated for eligibility for free ART at local CDCs, and referred to obtain ART at designated infectious disease (ID) hospitals. There are multiple steps where people may drop out of the linkage chain: taking a confirmatory testing, obtaining the testing result, being evaluated for ART eligibility, and going to a designated hospital for treatment and care.

An analysis of 388,496 newly identified HIV cases during 2006–2012 in China found that an average 57% received baseline CD4 test within 6 months of diagnosis, and it increased from 20% in 2006 to 77% in 2012 [78]. Delaying in CD4 test was associated with older age, low education level, injection or sexual routes of transmission, HIV diagnosis in a hospital or in a detention center, and being a migrant worker [78]. Another study among MSM in 15 Chinese cities found that 21% of 4063 men with a positive screening test did not receive confirmatory testing and 34% of 3024 newly diagnosed MSM did not receive a CD4 test within 12 months of diagnosis [79]. Barriers for linkage to care among MSM may include discrimination, lack of guidance, fear to disclosure, and time or location inconvenience, and facilitators may include peer referral and peer counseling, free or standardized HIV care, and extended involvement [80].

It might be unlikely to remove some social and legal obstacles in near future, such as stigma and discrimination and requirement for providing national identification number; novel interventions could enhance linkage. Some CDC clinics and ID hospitals hire MSM peer counselors, and peer support has been proven efficacious for both promoting testing and linkage [81]. Testing and linkage service in gay-friendly community-based organizations (CBO) is also acceptable and feasible [71, 74]. The collaboration between CDCs, ID hospitals,

and gay-friendly CBO can ensure the testing and linkage interventions to reach the hard-to-reach populations. Streamlining HIV screening and confirmatory tests, CD4 and viral load tests, and fast diagnosis has shown to be cost-effective for improving linkage [82, 83].

Although home-based screening test strategy has advantages of reducing stigma and fear of disclosure and increasing uptake of a test, it poses challenges of linking positive screening individuals to get a venue-based confirmatory test and HIV care. Reimbursing the testing cost may help screening positive individuals to take a confirmatory test [74]. A social entrepreneurship testing model has been proven feasible, in which CDC staff interpret the screening test results via an online platform and provide referral to CBO staff, who subsequently contact the individuals and provide counseling, confirmatory test, and linkage to care [84].

International studies have shown some effective interventions including on-site linkage among HIV testing institutes [85], service support (e.g., case management) [86, 87], peer navigator or HIV system navigation [88, 89], intensive outreach [90], and providing incentives [91]. These evidences could be considered during developing Chinese intervention programs.

Treatment and Care Interventions

The most impactful program might be the “Four Frees and One Care” program—free VCT, free ART, free prevention of mother to child transmission, free education to AIDS orphans, and financial assistance and social support to people living with HIV. This program was launched in 2003 mainly for FPD and their families; the free ART program was first scaled up in 2005 so that any HIV-infected individuals with $CD4 < 200$ cells/mm³ were eligible to receive treatment; it was further scaled up in 2008 and the CD4 criterion for starting ART was lifted to 350 cells/mm³; by 2016, any infected individuals can start ART regardless of CD4 count (Fig. 1). The national ART program has significantly reduced adult and pediatric mortality [92–94], and has reduced HIV transmission [95]. However, there are still significant gaps to the 2nd and 3rd targets of the UNAIDS Three “90”s. An estimate by China CDC showed that 67% diagnosed individuals started ART and 65% ART users achieved viral suppression in 2015 [96]. People who were infected via blood products had the highest rates (92% and 74%, respectively), followed by heterosexuals (70% and 46%) and homosexuals (71% and 43%), and PWID with the lowest rates (41% and 24%) [96].

The ultimate goal of HIV care is to achieve viral suppression, and people with suppressed viral load may live a healthy life, and those with undetectable viral load are unlikely to transmit the virus [97]. There is limited data on why Chinese HIV-infected individuals fail to initiate and adhere to ART and to achieve viral suppression, and the cause might be multi-

facets. Comorbid drug and alcohol abuse and mental health illness are associated with a lower rate of ART and poorer adherence [96, 98, 99]. Lack of ART knowledge, high perceived psychological and behavioral barriers to ART adherence, and low adherence self-efficacy may lead to poor adherence [100]. Other reasons for failure to achieve viral suppression may include outdated regimens and side effects of antiretroviral drugs, poor adherence, and drug resistance [101]. The most common regimens in the Chinese free ART program include stavudine (d4T), zidovudine (AZT), and tenofovir (TDF) along with lamivudine (3TC), the ritonavir-boosted lopinavir (LPV/r) regimen, as the World Health Organization (WHO) recommends for use in resource-limited settings, should be promoted as a key second-line antiretroviral therapy (ART) to mitigate drug resistance problem [102].

To close the gap to the 3rd UNAIDS target, comprehensive strategies should be implemented. Patients should be educated to initiate ART early and adhere to ART-based care. More potent antiretroviral drugs should be made available to patients for reducing side effects and improving treatment efficacy. Drug resistance should be routinely monitored to guide the use of ART. International experiences of improving access to treatment and retain patients in care include systematic monitoring, health service support (e.g., case management and peer navigation), and intensive outreach [103]. As comorbid disorders are common among HIV-infected individuals, integrated care with primary care, mental health services, substance abuse treatment, and other chronic disease management may improve HIV care outcomes [104–106].

Conclusions

HIV epidemic continues to grow in China, though the Chinese government has made significant achievements in containing its spread among FPD and IDU. With implementation of the expanded HIV testing campaigns over the past 15 years, two-thirds of infected individuals know their HIV status. The national free ART program has treated two-thirds of diagnosed patients and helped two-thirds of treated patients to achieve viral suppression. Innovative interventions should be developed and implemented to prevent HIV sexual transmission and improve voluntary HIV testing among sex workers and their clients, MSM and college students, and older people who live in rural regions. Expanding antiretroviral regimens for national free ART program and integrated HIV care will help improve initiation and adherence of ART and close the gaps to the three targets of the UNAIDS Three “90”s.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors

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