HIV/AIDS in China

Epidemiology, Prevention and Treatment

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Introduction

Over the last three decades, China has experienced rapid social and economic transitions. During this period, China has moved from a closed country to an open country and moved from one of least developed countries in the early 1980s to now having the second largest gross domestic product (GDP) in the world. The rapid developments in aviation domestically and internationally, highways, and railway, including speed trains, have facilitated the movement of large numbers of people internally and externally. Housing in cities has moved from primarily being publicly owned to now completely privately owned. China has shifted from a purely socialist to now a more capitalist-like country. China has risen from being a low-income country (1987–1996) with all its people equally poor to a lower-middle-income country (1997–2009) and today an upper-middle-income country (2010–2017, The World Bank 2018), with many billionaires and millions of poor people. The rich have become richer, and the gap between the rich and the poor has widened significantly.

Social and economic changes have brought large population movements. For example, Shenzhen was once a very small fishing village with less than a thousand people, but thanks to its strategic location on the northern border of Hong Kong, it has developed into one of the richest and most well-developed cities in China with more than 20 million people and many large international companies. Many of China's small cities have become bigger cities. Many of China's youth and young adults have moved from rural villages to urban cities. The social norms and lifestyles of Chinese people have significantly changed. Drug use has returned to China, and the resurgence of traditional opioid drugs has quickly evolved into polydrug use and use of synthetic, stimulant "club drugs" (Sun et al. 2014; Zhao et al. 2004). Promiscuity and risky sexual behavior have also returned—now, almost half of China's population (47% overall, 57% of men and 37% of women) is estimated to have multiple sexual partners in their lifetimes (Huang et al. 2014), 4.5% of women and 11.5% of men reported engaging in noncommercial extramarital sex, and 5.5% of men reported commercial sex in past 12 months (Zhang et al. 2012).

Not surprisingly, dozens of outbreaks of emerging and reemerging infectious diseases have recently occurred in China, including severe acute respiratory syndrome (SARS), coronavirus (Cheng et al. 2007), *Streptococcus suis* (Feng et al. 2014), syphilis (Chen et al. 2011), avian flu (Parry 2013), and severe fever

with thrombocytopenia virus (SFTSV) (Li 2013). Most came fast and disappeared quickly. However, human immunodeficiency virus (HIV) came to China and has not left (Cui et al. 2016; Pisani and Zhang 2017; Zeng et al. 1986).

Unique Epidemics of HIV/AIDS in China

The epidemiology of HIV/AIDS in China is quite unique. Five years after the first cases of acquired immunodeficiency syndrome (AIDS) were reported by the US Centers for Disease Control and Prevention (CDC), the first AIDS case was found in China—a foreign traveler in 1985.

Neither the government officials nor the public believed that HIV/AIDS would become a public health threat in China. However, scientists did not believe that there were no HIV infections in China. Virologists and epidemiologists started to search and finally found the first cases of HIV infection among four patients with hemophilia who had used imported factor VIII from a US pharmaceutical company in 1983 (Zeng et al. 1986). Although this important scientific finding did not change the perceptions of the risk of an HIV epidemic in China, it did highlight the importance of ensuring the safety of blood products, which spurred the Chinese Government to immediately issue a new policy banning the importation of all blood products.

Thus, in the mid-1980s, China was still very "clean"—there was almost no drug use, almost no or at least no visible commercial sex, and no overt homosexual activity. The links between drug use and risky sex and HIV infection were based on US epidemiological data. The Chinese still believed that an HIV epidemic could not possibly happen on their soil. So, when the first HIV outbreak was accidentally found among people who inject drugs (PWID) in Ruili, Dehong Prefecture, Yunnan Province, in 1989, scientists, public health specialists, government officials, and the public were all shocked. On the one hand, it was only 146 cases. On the other hand, 146 was a sudden, huge jump from zero. Either way, the Chinese could not accept it.

After the identification of this first outbreak, two false beliefs that were common among the government officials and public health specialists caused several lost opportunities to control the then-small-scale HIV/AIDS epidemic in its early stages. The first of these was that China was not a drug-consuming country. Rather, police and public security officials believed that China was just another country on the route that smugglers used to traffic drugs from the "Golden Triangle" to the West. This misperception led Chinese officials and public health leaders to believe that only a very small number of people in a very small border region could be affected and, therefore, it should not cause much concern. The second false belief was that the geography where the outbreak occurred would naturally contain it. The 146 HIV cases were found in the far end of the southwest corner of the country in a remote, rural area, where infrastructure was poor and travel over distances was difficult and very slow. People who lived there were generally considered isolated from the rest of China. This misperception led Chinese officials and health and public health leaders to believe that the epidemic would not spread and become a national threat and, similarly therefore, it should not cause much concern.

Unfortunately, these beliefs were wrong. The number of drug users increased rapidly along drug trafficking routes from Myanmar to Dehong, where the outbreak was found, to central Yunnan Province, and to the neighboring provinces, including Guangxi, Sichuan, Guangdong, and others. HIV infection also increased and spread, albeit more gradually, among drug users in these same areas where drug trafficking and drug use were increasing and spreading. By 1995, just 6 years after the outbreak was found, more than 50% of counties in Yunnan had reported HIV infections among PWID. Even worse, HIV infection was being observed among drug users in Sichuan and Xinjiang. From then, the epidemic sped up very quickly and spread through the drug-using population to all provinces in just 5 years. By 2000, China's HIV epidemic among drug users was a nationwide problem.

In the meantime, a catastrophic outbreak of HIV infection was suddenly identified among commercial blood plasma donors in China in 1995 (Wu et al. 1995). Unsafe blood collection practices had resulted in the exposure of thousands of poor rural farmers to HIV. The magnitude of the HIV outbreak among former plasma donors (FPD) seemed so enormous that many Chinese officials scared into inaction. Little effort was made in the early stages to truly understand the actual extent of the epidemic. It was only known that HIV infections were being found in all provinces where commercial plasma collection was prevalent.

There was only one epidemiological study of HIV infection among FPD conducted in the years following the outbreak. It was found that the prevalence of HIV infection was associated with the frequency of plasma donation (Wu et al. 2001). The complete and true picture of the outbreak of HIV infection among FPD was not made public until 2005, 10 years after the outbreak was identified. The Chinese Government launched a nationwide HIV testing campaign among FPD from 2004 to 2005 during which some one million FPD were interviewed and tested for HIV infection. It was estimated that about 69,000 people had become infected.

Unlike the HIV/AIDS epidemics of the neighboring countries, HIV infection among female sex workers (FSW) never really took off in China. Based on international experience, an outbreak among this important key population had been expected but never really materialized. Rather, over the past 30 years, HIV prevalence among FSW has remained less than 1%. Only in some areas, where there were female injecting drug users involved in commercial sex, had the HIV prevalence in this risk group exceeded 1%. This very low prevalence among FSW has helped slow the growth of China's HIV epidemic.

Similarly, international experience indicated that an outbreak among men who have sex with men (MSM) was imminent. However, this was not observed until 2005, almost 20 years after the first reported HIV infection and 16 years after the first outbreak in China. The slow start of HIV among MSM indicated that there had been almost no interaction between the MSM and PWID risk groups or, at least, there had been very limited crossover. This has been supported by virology studies that have found different HIV viral subtypes among the PWID population compared to the MSM population, suggesting that HIV was not brought into the Chinese MSM community by Chinese PWID but rather via interaction with the

Westerners. Because of the lack of effective control strategies, HIV spread very fast among MSM in China. National sentinel surveillance data showed that the HIV prevalence in this group increased from 1% in 2005 to 8% in 2017.

Responding in the Chinese Way

China's response to its HIV/AIDS epidemic has gone through three stages—from initial denial to very conservative and now to innovative and positive. China is very different from most of the countries in developing world. Once the Chinese Central Government has decided to do something, it is done quickly and on a national scale. This working style has been particularly important for public health since program coverage is critical in controlling an epidemic.

When the first few cases of HIV infection were diagnosed among FPD in early 1995 (Wu et al. 1995), field observation suggested that the contamination in the process of plasma collection may have caused a potential outbreak of HIV infection in this population. In response to this finding, the Chinese Government immediately and vigorously shut down all commercial plasma collection centers across China within just a few weeks.

Harm reduction programs, including methadone maintenance treatment (MMT) and needle and syringe exchange programs (NSEP), were not initiated until 15 years after the first HIV outbreak was identified among PWID in 1989. In the 1990s, the concept of harm reduction was new. The officials in the Ministry of Health were very supportive. However, the officials in the Ministry of Public Security were against harm reduction. The Asia and Pacific Regional Offices of the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the United Nations Office on Drugs and Crime (UNODC) played a significant role in policy advocacy for harm reduction. Health officials and police officials were invited to attend advocacy workshops together, which helped improve the communication between these largely separate government departments. They also traveled on joint study tours to learn about harm reduction programs in other countries, such as Australia and the Netherlands. These events were critically important for Chinese public security and law enforcement officials to see that harm reduction strategies for drug users were well accepted by their counterparts in other countries. Over the course of many years, hardline conservative attitudes toward harm reduction softened, and finally, harm reduction strategies were adopted and written into the first Chinese State Council-issued National Five-Year Action Plan (2001–2005).

In 2004, China established its first eight MMT clinics and then very quickly scaled up MMT nationwide in just a few years. By 2006, the original eight clinics had expanded to 320 and by 2007 to over 500. By 2010, all counties that had at least 500 drug users had set up an MMT clinic. The NSEP also expanded very quickly. While MMT is led and supervised by the Ministry of Health, the Public Security Bureau, and the Food and Drug Administration but is operated by the local health departments, the NSEP is operated by the local health departments as well with the support of the drug users themselves. The combination of MMT and NSEP, plus

other intervention and treatment programs, has successfully controlled the HIV epidemic among China's drug-using population.

HIV testing is the first step for people living with HIV (PLWH) to have a chance to be diagnosed and to have an opportunity to access healthcare. Promoting HIV testing was very difficult in the early stages of China's epidemic. Even after the massive outbreak of HIV infection among FPD was identified in 1995, large-scale testing programs were still not established. It was not until nearly 10 years later in 2004–2005 that the numbers of people receiving testing began to approach an appropriate magnitude. Although criticisms came from both domestic and international sources, China engaged in active HIV testing campaigns targeting high-prevalence areas (i.e., Henan Province, Yunnan Province) and key, high-risk populations (i.e., PWID, FPD, FSW). Since 2005, the HIV testing has been expanded quickly, particularly after the World Health Organization (WHO) issued a new guideline on provider-initiated testing and counselling (PITC). The numbers of HIV tests performed and the number of HIV infections diagnosed in clinical settings have significantly increased. In 2017, the annual number of HIV tests provided in China exceeded 200 million. In some provinces, such as Yunnan, about 40% of the population has been tested for HIV.

Although highly active antiretroviral therapy (HAART) became available internationally in 1996, PLWH in China were not able to access to HAART due to its unaffordably high cost. In 2003, the Chinese Government made a promise to provide free antiretroviral therapy (ART) to all people with AIDS in rural areas and people with AIDS living below the poverty line in urban areas. Rather than waiting for patients come for ART, the health workers actively approached the patients and convinced them to initiate ART. However, health facilities in rural areas were unable to provide ART services. Thus, this capability needed to be quickly scaled-up. Providing free ART to those who became infected with HIV via unsafe plasma collection practices during the early to mid-1990s was treated as a public health emergency. Health workers in county hospitals were sent to rural villages to work in short-term, 3-month rotations. At the same time, rapid training courses on ART provision were offered to health workers at township health centers and rural health clinics. Multiple strategies were used to have all diagnosed PLWH who were FPD on ART in less than 6 months. Since 2006, annual targets for the number PLWH initiated on ART have been set in order to promote increases in ART uptake. In 2017, more than 130,000 patients had newly enrolled into the government's free ART program. The rapid roll out of the National Free ART Program has significantly reduced the case-fatality rates among PLWH in China.

Prevention of mother-to-child transmission (PMTCT) of HIV infection was initiated in 2005. However, the program was small scale and expanded very slowly. On World AIDS Day 2009, Premier Wen Jiabao chaired a panel meeting in Ditan Hospital with top AIDS experts, community-based organization leaders, UNAIDS and WHO technical officers, and Chinese Government officials. Premier Wen was provided with evidence showing that PMTCT was the most cost-effective of all HIV prevention strategies. He then promised to provide PMTCT to all pregnant women starting in the next year. Since 2010, the Ministry of Health has implemented PMTCT for HIV, syphilis, and hepatitis B virus (HBV) infection nationwide.

Milestones

Over the past three decades, there have been many milestones along China's HIV/AIDS response journey. Among the many important initiatives, a few milestones, in particular, were critical to the development of important national programs and facilitated considerable forward progress.

The first outreach program targeting FSW in real-world community settings (i.e., not in closed settings such as detention centers) was launched in 1996 (Wu et al. 2007). This pilot project was supported by the World Bank. The study demonstrated an effective approach to significantly increase the knowledge of FSW about HIV and other sexually transmitted infections (STIs) and the benefits of increased condom use. This pilot study provided a foundation for developing the first national guideline on condom promotion for FSW in China.

The first intervention workshop on HIV/AIDS was organized in Beijing by the Chinese Academy of Preventive Medicine, now renamed as Chinese Center for Disease Control and Prevention (China CDC), in 1997. The workshop was extremely controversial at that time. The main focus of the workshop was to discuss strategies for preventing or reducing HIV transmission among key populations, including FSW, PWID, and MSM. Although the distribution of the workshop's proceedings was banned, the presentations and ensuing discussions and debates were very encouraging.

In 1998, the vice minister of Health, Dr. Dakui Ying, visited FSW in an entertainment establishment in Chengjiang County, Yunnan Province. It was a demonstration study site, supported by the WHO, for the promotion of condom use, frequent health checkups, and treatment uptake for reproductive tract infections (RTIs) among establishment-based FSW. At that time, the interventions targeting FSW were still very sensitive. Dr. Ying talked with the women and was happy to learn that the project had helped them understand HIV/AIDS and other STIs and the importance of consistently using condoms and getting regular reproductive health checkups. His visit signaled great support for this sensitive but effective program, an endorsement that was a key milestone in China's HIV/AIDS response.

In 2001, an important policy paper, "China's Action Plan for Reducing and Preventing the Spread of HIV/AIDS (2001–2005)," was issued by the State Council Office (State Council Office 2001). This new central government policy described the most effective HIV prevention measures, such as condom use promotion, opioid substitution therapy, and needle social marketing (i.e., equivalent to NSEP), and a plan for the implementation of these prevention measures with specific measurable targets. Most importantly, this policy and plan were matched with appropriate funds meant to facilitate the achievement of the targets.

In 2003, Vice Premier Wen Jiabao visited Ditan Hospital in Beijing. This was the first time that a top government official had appeared publicly and shown care for PLWH and the health professionals providing services to PLWH. This public show of support and acknowledgment of the HIV/AIDS epidemic was a critical next step toward a more vigorous, coordinated, and comprehensive response.

In another such significant event, President Hu Jingtao visited You'an Hospital in Beijing in 2004. This was the first time the nation's top leader had publicly shown that he cared for PLWH and endorsed HIV/AIDS prevention and treatment programs. His visit showed lower-level government officials and China's people that HIV/AIDS would be dealt with in all seriousness and determination and that he and China would prioritize control of the epidemic and elimination of the negative impacts upon people infected and affected. This visit changed the perceptions and attitudes of the public toward PLWH.

In 2004, another important policy paper, the "Notice of the State Council on Conscientiously Strengthening HIV/AIDS Response," was issued by the State Council (State Council 2004). This was the very famous "Four Frees and One Care" policy, whereby the Chinese Central Government promised to provide free HIV testing, free ART for PLWH in rural areas and those in urban areas who were under the poverty line, free PMTCT to all pregnant women, and free schooling for children infected and affected. This policy completely changed the landscape of China's HIV/AIDS response, had a huge positive impact on its HIV/AIDS epidemic, and brought much-needed hope to its people.

In 2005, Vice Minister Longde Wang chaired a first meeting among MSM. At that time, male-male sexual behavior and the presence of MSM in Chinese society were taboo topics. Although the meeting was very small (a few officials and only eight MSM were invited) and lasted only about 3 hours, it had a significant impact and contributed to the successful launch of national response efforts among MSM.

In 2006, a third important policy paper was issued by the State Council, the "Regulations on AIDS Prevention and Treatment" (State Council 2006). With this policy, all effective HIV prevention, intervention, and treatment measures, including harm reduction strategies, anti-stigma strategies, and others, were protected by the law.

In the early 2000s, most national HIV/AIDS projects were supported by international donors, including The Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund), the United Kingdom's Department for International Development (DFID) AIDS Project, the US CDC Global AIDS Project (GAP), the World Bank Health IX Project, and others. Each project collected their own data for documentation and evaluation, as did all domestically funded projects, resulting in enormous burden on the field workers and huge inefficiencies in data collection, entry, checking, maintenance, and reporting. Thus, China launched its unified, web-based National HIV/AIDS Comprehensive Response Information Management System (CRIMS) in 2008 (Mao et al. 2010). CRIMS collects and monitors HIV testing and treatment data, data on outreach and intervention among key populations, harm reduction program data, and surveillance data. CRIMS generates monthly, quarterly, and annual national HIV implementation reports and provides vital data for the evaluation national HIV/AIDS programs.

The "Notice of the State Council on Further Strengthening HIV/AIDS Response" was issued by the State Council at the end of 2010 (State Council 2010). The policy was an important milestone in the further development of China's HIV/AIDS response as it emphasized the expansion of all HIV testing, prevention, and

treatment programs and focused on the creation of effective strategies to provide sufficient coverage of these programs in order to bring the HIV/AIDS epidemic under control.

Faster Movement from Science to Policy Implementation

One of the most unique advantages of China is its ability to quickly move from scientific results to policy implementation. This is extremely important for public health programs, such as national HIV/AIDS prevention or treatment programs. Here, we provide two typical examples to illustrate this point.

When a remarkable 96% reduction in HIV transmission between PLWH on ART and their serodiscordant partners was reported by an American scientist in 2011 (Cohen et al. 2011), Chinese scientists also began investigating the possibility that treatment itself could act as a prevention measure. Similar results were observed in an observational cohort study conducted from 2008 to 2010 (He et al. 2013). These findings were immediately translated into national policy and implemented. In 2011, a national workshop on the so-called "treatment-as-prevention" (TasP) strategy was held in Shenzhen. All known serodiscordant couples and all newly diagnosed PLWH who had serodiscordant partners were approached and encouraged to initiate ART regardless their CD4 cell counts. As a result of this effort, the number of serodiscordant couples being managed by the TasP strategy increased from 65,795 in 2011 to 141,435 in 2017. The HIV seroconversion rate among serodiscordant couples dropped from 2.72% in 2011 to 0.68% in 2017 (National Center for AIDS/STD Control and Prevention 2018).

After many years of scaling up ART, the number of HIV/AIDS-related deaths had remained unacceptably high. Each year, about 20,000 PLWH were dying. It was difficult for the officials and policymakers to understand why ART was not reducing mortality. Then, scientists in China finally discovered that over 70% of PLWH who had died had not actually initiated ART at all. This finding was very surprising. Further analysis revealed that most of those who died were diagnosed in a late stage of HIV disease. The diagnosis procedure was too complicated and too long, and the services were fragmented—several different agencies located in different places were involved in multiple steps. Scientist and health and public health experts proposed a simplified structural intervention to shorten the period from diagnosis to initiation of ART. The intervention was called the "One4All" strategy. In this strategy, all tests for diagnosis, clinical staging, and ART preparation are performed at the same time, and treatment is initiated immediately for all diagnosed individuals regardless of CD4 count, all in one healthcare setting and all in a very compressed span of time. Scientists have used a before-and-after study design in two demonstration counties to evaluate the 12-month case-fatality rate and found a 62% reduction (Wu et al. 2015). Scientists then used a cluster-randomized controlled trial design to evaluate testing completeness, ART initiation, viral suppression, and mortality. Those who received the One4All intervention experienced 20-fold increased odds of testing completeness within 30 days, three-fold greater odds of ART initiation within 90 days, and a 56% reduction in 12-month mortality

(Wu et al. 2017). This new simplified procedure has immediately been adopted as a new national policy and has been written into the 13th Five-Year Action Plan for Prevention and Treatment of HIV/AIDS in China (2016–2020).

In summary, China has progressed from a position of denial to a position of leadership with respect to its HIV epidemic and response. It has, in a relatively short time, developed and implemented one of the most effective HIV/AIDS control programs in the world. This book documents that remarkable journey.

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Contents

Part I

Epidemiology

Evolution of HIV/AIDS Epidemics in China

1

Yan Cui, Liyan Wang, Jennifer M. McGoogan, and Elizabeth Pisani

Abstract

China is vast, diverse, complex, and dynamic, and its HIV epidemic reflects these features. The surge of political, economic, and social change that came after the founding of the People's Republic of China in 1949 set the stage, and the departure from isolationist policies and movement toward participation in the global economy in the 1970s opened the door. HIV came to China in an outbreak among people who inject drugs in the southwest region in the late 1980s and again in a major outbreak among former commercial plasma donors in the mid-1990s. Over the past 30 years, China's HIV epidemic has expanded to other key populations (e.g., commercial sex workers, men who have sex with men) and all regions. The count of 146 people diagnosed in 1989 has grown to an estimated 1.25 million people as we enter 2019. The epidemic has steadily grown and expanded and has evolved into two parallel epidemics, one heterosexual and the other among men who have sex with men. This chapter documents the evolution of China's HIV epidemics—their general features, epidemiology, and impact.

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1.1 Introduction

After the People's Republic of China was established in 1949, the country and its peoples became isolated. Foreigners and foreign businesses disappeared from urban settings, the education system shut down, and the land was given back to the peasants. Primary health services spread to rural areas, healthy living was actively promoted, and behaviors including drug use, prostitution, and same-sex relationships were considered immoral and were strongly discouraged and, in many cases, criminalized. The development of extremely conservative social mores contributed, for example, to a precipitous decline in sexually transmitted infections (STIs).

When HIV came to the world's attention in the early 1980s, China was in the beginning of yet another period of rapid social and economic change. The nation had adopted an "open door" policy in the late 1970s, welcoming foreign investment, expertise, and tourists. Foreign products appeared in Chinese shops, and foreign businesses entered Chinese markets. Interaction between Chinese nationals and foreigners increased dramatically. When the first few cases of HIV were detected in China—among foreign nationals, Chinese citizens who had returned from abroad, and people who had been treated with imported blood products—the government reacted swiftly. The import of blood products was stopped, travel bans were put in place, and foreigners wishing to reside in China were required to undergo HIV testing. In addition, information campaigns vociferously denounced the risk behaviors known to spread the virus. These campaigns were promoted most actively in the increasingly cosmopolitan cities of the eastern seaboard, where it was thought the risk of people adopting such behaviors was greatest (see Chaps. 17 and 18 for more information).

Initially concentrated among people who inject drugs (PWID) in the southwest (Ma et al. 1990; Wu et al. 2004) and then appearing among former commercial plasma donors (FPD) in rural areas in central China (Wu et al. 1995, 2001, 2008), HIV spread across the land, entered urban centers, and today affects all of China's provinces, prefectures, counties, and districts. The epidemic has evolved over time and has become more generalized and is now driven predominantly by the sexual transmission route—heterosexual sex and, increasingly, sexual contact between men who have sex with men (MSM). Infection by sexual contact now accounts for more than 95% of newly diagnosed cases each year (Wu 2018).

This evolution has been shaped in part by HIV prevention and control programs, which have been successful in limiting the continuing spread of HIV in many of the key populations first affected or threatened by the virus. However, as has been the case in most countries, public health officials and policymakers were not always able to anticipate the course of the epidemic. Thus, while the evolution of the epidemic was influenced by China's response, China's response was also influenced by the evolution of its epidemic.

1.2 The HIV Outbreak Among People Who Inject Drugs

The first domestic outbreak of HIV was detected in 1989 in an extremely remote, rural area of southwestern China's Yunnan province (Ma et al. 1990; Shao et al.

1991; Zhang et al. 1991, 1994). It took Chinese authorities and most other observers by complete surprise. A local public health worker investigating hepatitis C virus (HCV) among PWID in Yunnan province, close to the Myanmar border, found that while 95% of the blood samples she collected tested positive for HCV, a shocking 40% also tested positive for HIV. After an exhaustive investigation by specialists from central government health authorities, 146 cases of HIV infection were confirmed (Pisani and Zhang 2017).

Although opium use had been commonplace in this region for many generations, the drug had traditionally been smoked. Heroin, refined in the so-called Golden Triangle and intended for export to Western markets, began to trickle across the Myanmar border after China began to open its borders to foreign trade. Once the HIV outbreak among PWID was identified in 1989, stored serum samples that had been drawn between 1986 and 1988 for HCV testing were re-tested for HIV. No HIV infection was found, suggesting that HIV had been discovered very soon after it first arrived in China (Zhang et al. 1994; Zhao et al. 1991).

By 1995, the HIV epidemic among PWID remained concentrated in the southwest region, primarily in southwestern Yunnan province (Wu et al. 2004). However, despite efforts to control the heroin trade, HIV spread along corridors established by drug traffickers who were intent on exporting the drug to Hong Kong for onward sale to America or Europe. The geographic expansion of both heroin supply and HIV infection accelerated when improvements in road infrastructure and air travel facilitated the movement of people over previously very difficult terrain. Areas with high concentrations of ethnic minority populations, including the large and sparsely populated northwestern Xinjiang Uygur Autonomous Region (Xinjiang), were disproportionately affected by the increase in heroin use. Thus, just 5 years later in 2000, HIV had already spread to neighboring Sichuan and Guangdong provinces and Guangxi Zhuang Autonomous Region (Guangxi), as well as Xinjiang (Fig. 1.1; Wang et al. 2015).

HIV prevalence among PWID, predominantly male PWID, in these five most-affected provinces peaked in 1999 at 30%, whereas in all other provinces (besides these five), HIV prevalence peaked in 2003 at 5%. However, PWID using heroin were not the only drug users affected. Individuals who used other drugs (e.g., methamphetamine, ketamine) by other means (e.g., smoking) were also becoming infected with HIV. For these non-PWID, (or non-injecting drug users [IDU]) HIV prevalence was also greatest in the five provinces, peaking at 6% in 2005, while always remaining below 1% in all other provinces (Fig. 1.2; Wang et al. 2015).

Risky drug injecting behavior, namely, sharing drug injecting equipment, continued to dominate as the major risk factor for HIV infection in the early years of China's epidemic. This was in part because PWID were more likely to be tested for the virus than anyone else. Testing was beginning to be scaled up in the early 2000s—mandatory HIV testing (MHT) was implemented in closed settings such as compulsory detoxification centers, reeducation-through-labor camps, and reform-through-labor prisons and voluntary counseling and testing (VCT) also began to be offered. However, relatively few cases were found compared to estimates of the true number of cases. Thus, in 2004 Yunnan conducted a 4-month testing campaign during which 425,000 individuals were offered testing, 99% accepted, and 13,500

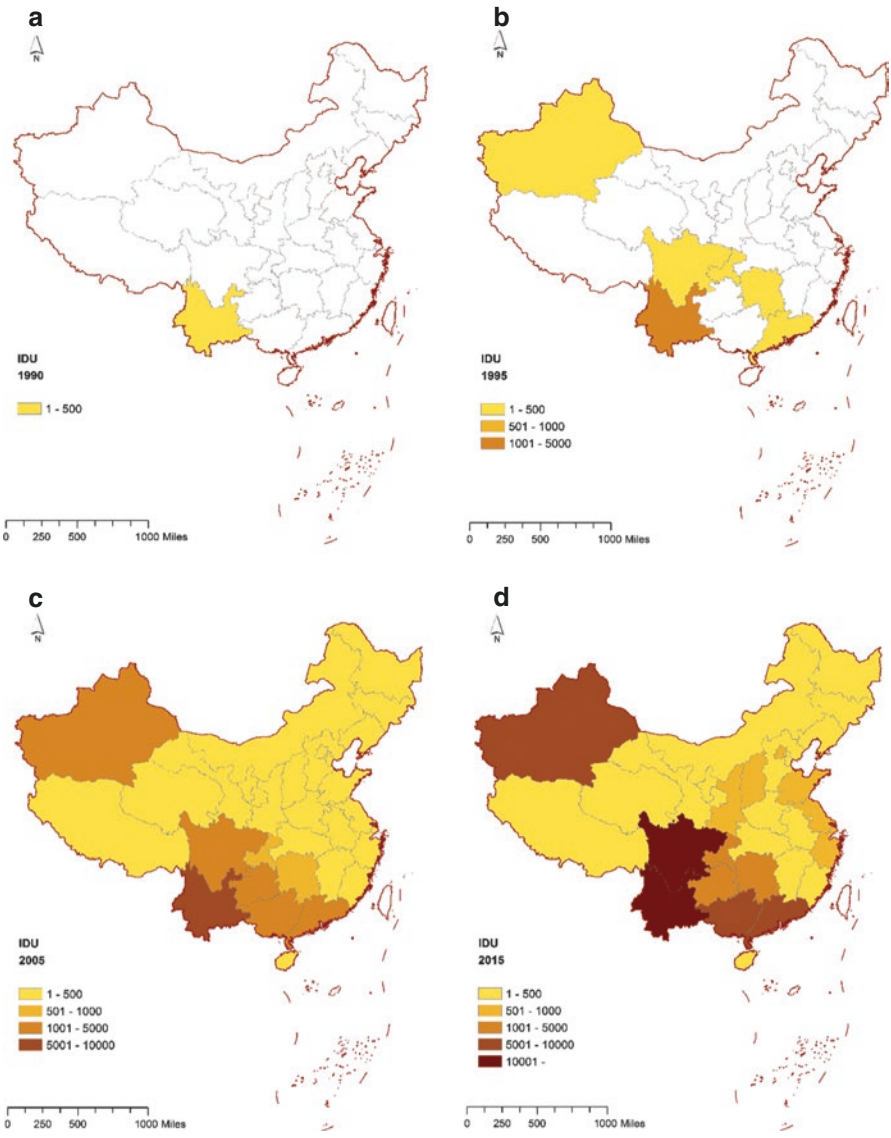

Fig. 1.1 Geographic distribution of the absolute number of HIV/AIDS cases identified among PWID in the years 1990 [panel a], 1995 [panel b], 2005 [panel c], and 2015 [panel d]. Color variation indicates numbers of cases by county. Lines within the map mark province borders

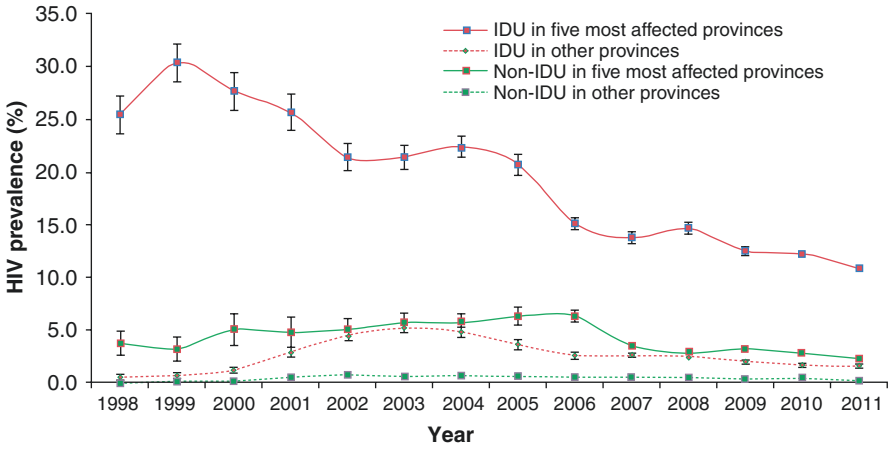

Fig. 1.2 Graph showing changes in HIV prevalence over time for PWID and non-PWID (i.e., people who use drugs by means other than injection) in the five most affected provinces (i.e., Yunnan, Sichuan, Guangdong, Guangxi, and Xinjiang) and all other provinces. Bars for each data point indicate the 95% confidence interval. Data originated from the HIV sentinel surveillance system. Figure adapted with permission from Wang et al. (2015)

new cases of HIV infection were found, many of whom were PWID (see Chap. 12 for more information).

Transmission via unsafe injecting behavior among PWID also drove the early epidemic in part because, for many years, very few PWID had access to services that might help them to reduce the harms associated with their drug-taking behaviors. Harm reduction strategies that are intended to reduce the negative consequences of drug use, in this case HIV infection, include opioid substitution therapies and provision of sterile injecting equipment. Substantial evidence of the effectiveness of these strategies in curtailing the spread of HIV among PWID populations already existed by this time (early 2000s) in other settings. Nevertheless, the idea of giving opioids (i.e., methadone) and needles and syringes to PWID was met with very strong opposition by government officials at all levels, particularly within the Public Security Bureau, and by civil society. Drug use and HIV infection were viewed as scourges and both PWID and people living with HIV (PLWH), and even more so, PWID who also had HIV infection, faced severe stigma and discrimination (see Chaps. 18 and 19 for more information).

Yet, with persistence, research, and eventually small pilot trials, the National Methadone Maintenance Treatment (MMT) Program was launched in 2005, and China's Needle and Syringe Exchange Programs were scaled up the same year (Sullivan and Wu 2007). Today, less than 4% of all individuals newly diagnosed with HIV report having acquired the infection via injecting drug use (National Center for AIDS/STD Control and Prevention 2017) (see Chaps. 9 and 10 for more information).

1.3 HIV Spread Among Plasma Sellers

The economy in China's coastal provinces began to boom in the late 1980s, driven by overseas investment and manufacturing exports. However, China's central provinces did not benefit from this investment. While their economies remained centered on agricultural production, poverty was widespread, and many households began to look for ways to supplement their income.

In the meantime, a brand-new domestic market for blood products emerged in the wake of the central government's ban on foreign imports. High demand and low supply combined with initially very few competitors meant that the domestic blood product business was extremely lucrative. Peasants in the central provinces were thought to be an inexpensive and safe source for plasma because of their conservative cultural values and their remote location. Thus, many plasma collection stations opened all over rural Henan, Anhui, and neighboring provinces. But unfortunately, like in many new industries that spring up quickly, government regulation and oversight lagged (Chaddah and Wu 2017).

When a Shanghai-based blood product company performed a random quality assurance survey in the autumn of 1994, they found that plasma collected from a 41-year-old female donor in Anhui had tested positive for HIV-1 antibodies (Wu et al. 1995). By the spring of 1995, detailed epidemiological investigations had gathered compelling evidence pointing to unsafe plasma collection practices as the means of transmission (Wu et al. 2001, 2008). Furthermore, a molecular and phylogenetic investigation into the HIV virus found among former commercial plasma donors (FPD) discovered that it was the same subtype as had been circulating among the PWID community in southwestern China (Nerurkar et al. 1998). This evidence signaled the high probability that, at some point, one or more infected PWID sold plasma in central China, thereby introducing HIV into the broader blood plasma seller population (Nerurkar et al. 1998).

Epidemiologists investigating HIV transmission among FPD found that many donated with extremely high frequency. This practice was facilitated by personnel at the collection stations—donated blood would be centrifuged on the spot and red blood cells re-injected into donors allowing them to donate again more rapidly. To keep costs down, the blood was centrifuged in batches. This meant that any pathogens in the blood taken from one individual would be mixed into the blood taken from many others and then distributed to the larger group when the pooled red blood cells were divided up and re-injected into the donors. This proved to be a very effective way of spreading HIV (Chaddah and Wu 2017; Wu et al. 2001, 2008).

As soon as this practice and its harmful consequences came to light, central government authorities put in place strict controls on blood collection centers. However, by this time, blood collection had already become an important contributor to the economies of otherwise poor counties, and local officials did not always enforce the new regulations. Moreover, some companies attempted to get around the new regulations by going out to small villages to harvest blood, rather than collect it in collection centers based in the larger district towns. This compounded the difficulty of controlling HIV transmission by unsafe blood plasma collection

practices. Although it was more common for women to sell blood than men, the legacy of a cultural belief that women's blood was, because of menstruation, more "dispensable," onward transmission to sex partners meant that the epidemic in central China quickly acquired the characteristics of a heterosexual epidemic (Chaddah and Wu 2017).

Although local authorities were in some cases slow to respond on a sufficient scale to the outbreak of HIV among FPD in central China in the mid-1990s, some data indicate that the health system actually identified the outbreak fairly early. Blood product company records and retrospective testing of blood samples collected between 1992 and 1994 by public health authorities in the central provinces found no HIV infection prior to late 1994, the same time as infections were first attributed to unsafe plasma collection practices by epidemiologists from the Chinese Academy of Preventive Medicine (renamed the China CDC in 2002).

Nevertheless, the full extent of this tragic outbreak became apparent nearly a decade later, by which time many of those infected had died. In 2004, Henan, one of the worst affected provinces, took the bold step of trying to understand just how many households and individuals had acquired HIV through selling blood. A door-to-door census was conducted to determine how many in each household sold blood in the mid-1990s. Supported by a promise of access to free care and treatment made by China's leaders at the United Nations General Assembly, health workers then offered free HIV testing. Some 280,300 people in Henan province reported having sold blood during the period in question, and 92% of them agreed to take an HIV test. Among the 258,237 people tested, 23,157 were newly diagnosed with HIV infection, for a prevalence of 9.9% (Wu et al. 2006). In just 3 months, Henan identified six times as many infections as had been reported in the province in the preceding 10-year period (Wu et al. 2017).

In subsequent years, seeing that those diagnosed were indeed given free care and support services, many other FPD came forward. HIV prevalence among these "late self-identifiers" was much higher at 16%. A number of other provinces also followed Henan's lead (Wu et al. 2017). A study by Dou et al. (2010) of the spatiotemporal expansion of the HIV epidemic among China's FPD found that the epidemic was strongly focused in Henan province, but did also affect all neighboring provinces as well as, more mildly, a few provinces further afar (Fig. 1.3).

As a part of this same study, estimated dates of infection were calculated for approximately 26,000 FPD with known plasma donation dates. This analysis found that the HIV transmission events in some counties in Henan and northern Anhui actually peaked as early as 1992. Although diagnosis rates and treatment initiation rates were substantial in the 2002–2007 timeframe, the analysis by Dou et al. found that the median time from estimated date of seroconversion to death for these FPD was roughly 13 years. This meant that many of those affected by this outbreak were never identified (Fig. 1.4; Dou et al. 2010).

Overall, some 40,000 HIV cases have been identified among plasma sellers to date, although this number clearly does not capture the tens of thousands who likely died of AIDS in the decade before the mass testing campaigns began. An additional 13,000 HIV cases have been reported among people who received HIV-contaminated

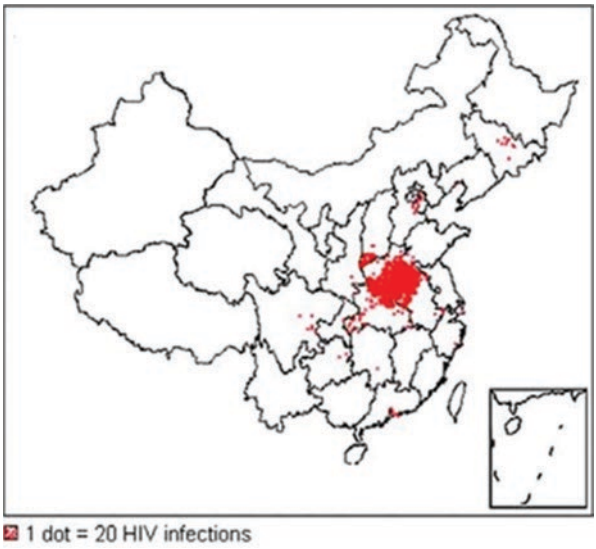

Fig. 1.3 Geographic distribution of the 36,110 HIV/AIDS cases among FPD included in the Dou et al. study (2010). Red dots each denote 20 PLWH. Figure adapted and reproduced with permission (Dou et al. 2010)

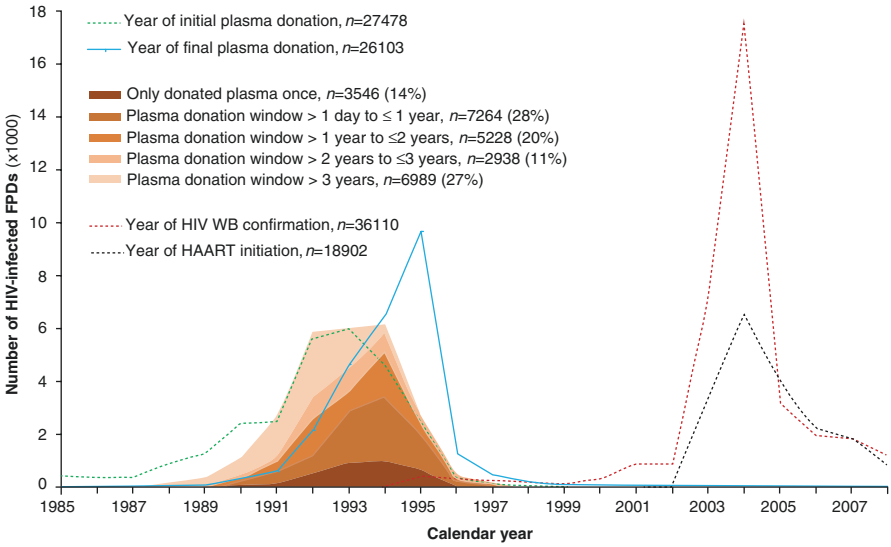

Fig. 1.4 Graph of the distribution of estimated dates of infection among a subset of 26,000 FPD with known plasma donation dates. Graph also shows the temporal distribution of subsequent diagnosis (infection confirmed by Western blot [WB]) and treatment initiation (with highly active antiretroviral therapy [HAART]). Figure reproduced with permission from Dou et al. (2010)

blood products, since it was not until the Blood Donation Law became fully effective in 1998 that stringent screening procedures were universally applied across the country (see Chaps. 6 and 12 for more information).

1.4 Transmission via Heterosexual Contact

In some other Asian nations, most notably Thailand, an HIV epidemic that first surfaced among male PWID was followed very quickly by a rapid increase in HIV prevalence among female sex workers (FSW) and their clients. From the clients of FSW, HIV there has been transmitted onward to their wives or regular female partners. Although this in turn carries the possibility of onward transmission into wider heterosexual networks, this has not been observed in industrialized countries or in many other developing nations. Generally, the wives of men who buy sex do not themselves have other concurrent partners to whom they could pass on HIV.

For the first few decades after the establishment of the People's Republic of China, commercial sex is believed to have been very rare, but by the late 1980s, commercial sex began to reappear, especially in busy border areas where there was a lot of movement of people and goods. These were some of the same areas in which drug use was most common. Some women were not only selling sex but also injecting drugs. Not surprisingly, HIV prevalence among this dual-risk sub-population was relatively high.

However, widespread HIV transmission via heterosexual commercial sex is only possible when the proportion of FSW infected with HIV is relatively high, client turnover is high, and condom use is low. The spread of HIV is further accelerated if the prevalence of other sexually transmitted infections (STIs) is also high, especially if those infections go untreated. None of these conditions are the rule in China. Client turnover among Chinese FSW depends heavily on fees charged and venues worked—it tends to be higher among lower-priced, street-based FSW than among FSW who find their clients in nightclubs or over the Internet. A large majority of the FSW in China is the latter. Condom use also varies with fee, but overall, rates of condom use in commercial sex are extremely high. In addition, there is a very high turnover rate among FSW in China—women report engaging in sex work for a median of just 6 years according to behavioral surveillance data (Chen et al. 2015; Wang et al. 2009).

Together, these factors combine to keep HIV prevalence among FSW in China low. Although HIV prevalence among FSW in areas with historically high rates of drug injection (i.e., Yunnan, Sichuan, Guangdong, Guangxi, and Xinjiang) was four times higher than in other areas of China, FSW in areas with less well-established epidemics were unlikely to be infected with HIV. Only 30 of 509 sentinel surveillance sites—all in the west and southwest—reported HIV rates over 1%, and the aggregate rate of infection in this group was 0.2% nationwide in 2014 (Fig. 1.5; National Health and Family Planning Commission 2015). Some 800,000 FSW in China were also tested for HIV in 2015 in outreach testing programs, and only 2500 new cases were found—a rate of 0.3% (National Center for AIDS/STD

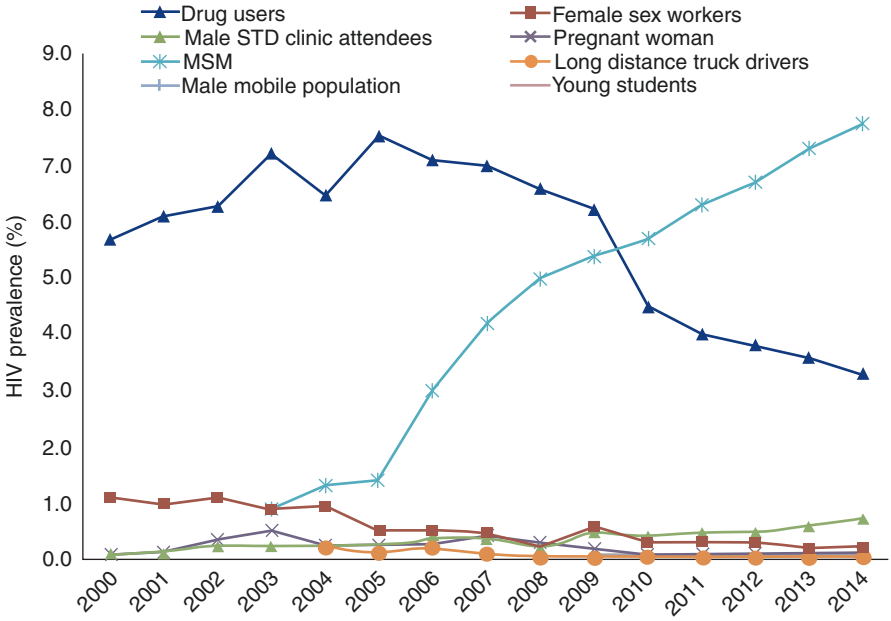

Fig. 1.5 Graph depicting changes in HIV prevalence for different risk groups over time. Figure reproduced with permission from the National Center for AIDS/STD Control and Prevention (2015b)

Control and Prevention 2015b). By comparison, in the most affected areas of Thailand and Cambodia at the height of their epidemics, greater than 30% of FSW tested positive for HIV in sentinel surveillance.

Dire predictions made over a decade ago that HIV would explode through China's sex industry appear not to have been realized. Nevertheless, the extent of the heterosexual HIV epidemic in the country remains a topic of much debate. Other than the commercial sex trade, the most obvious source of heterosexual HIV transmission is sexual contact between individuals with HIV infection (diagnosed or undiagnosed) and individuals without HIV infection (i.e., the spouses or regular partners of PLWH)—in other words, within HIV-discordant couples. Since the mid-2000s, China's public health authorities have worked hard to identify discordant couples. Starting with testing the spouses and partners of FPD and recipients of potentially contaminated blood products who were diagnosed with HIV, public health workers sought to prevent onward transmission of the virus.

Outside of groups known to be at high risk of infection, HIV prevalence among men and women in the general population remains very low in China, even in the worst-affected provinces such as Yunnan. Yet, public health officials remain vigilant. Because China's population is so large, even very low rates of HIV transmission can translate into tens of thousands of men and women becoming infected and in need

of care. However, with the exception of risk reduction in known discordant couples and of course in commercial sex settings, it is rather difficult to effectively target prevention programs to minimize the risk of heterosexual transmission, because sources of potential infection are so diffuse. Thus, the heterosexual contact transmission route has grown year by year, and from 2011 to 2014 it was responsible for two-thirds of new infections diagnosed annually (Fig. 1.6; National Health and Family Planning Commission 2015).

In 2016, 95% of newly diagnosed infections in women and 59% in men were reported to have been acquired through heterosexual contact. Among the women, 25% reported acquiring HIV from their husbands, and surprisingly, 62% reported becoming infected during casual sex (with a non-spouse, non-commercial partner). By contrast, among the men, 53% reported they were infected during commercial sex with a woman while 40% reported they were infected by their girlfriends or casual lovers (Fig. 1.7; National Center for AIDS/STD Control and Prevention 2016). Clearly there is something strange going on as it is difficult to believe that among all men in 2016 who reported heterosexual contact as their route of HIV infection, more than half pointed to FSW as the source of their infection yet the prevalence of HIV among FSW in 2016 was less than 1%. A closer examination of these figures suggests that the proportion of men infected by FSW may be overstated, at least in some areas.

In 2015, between 1.6 and 3.0 million women were estimated to be selling sex in China, and 15,000–27,000 of them were thought to be infected with HIV. Given the lower biological probability of transmission from a woman to a man (compared to from a man to a woman) in a single sexual contact, the likelihood that most FSW known to be infected were on treatment and thus not very infectious, and high background levels of condom use in commercial sex, it is implausible that a high

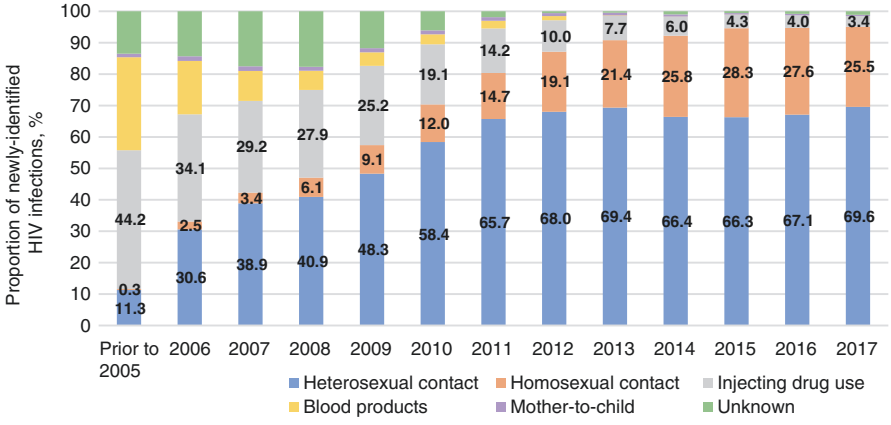

Fig. 1.6 Graph depicting annual changes in the proportion of newly diagnosed HIV cases attributed to different transmission routes. Figure reproduced with permission from the National Health and Family Planning Commission of the People's Republic of China (2015)

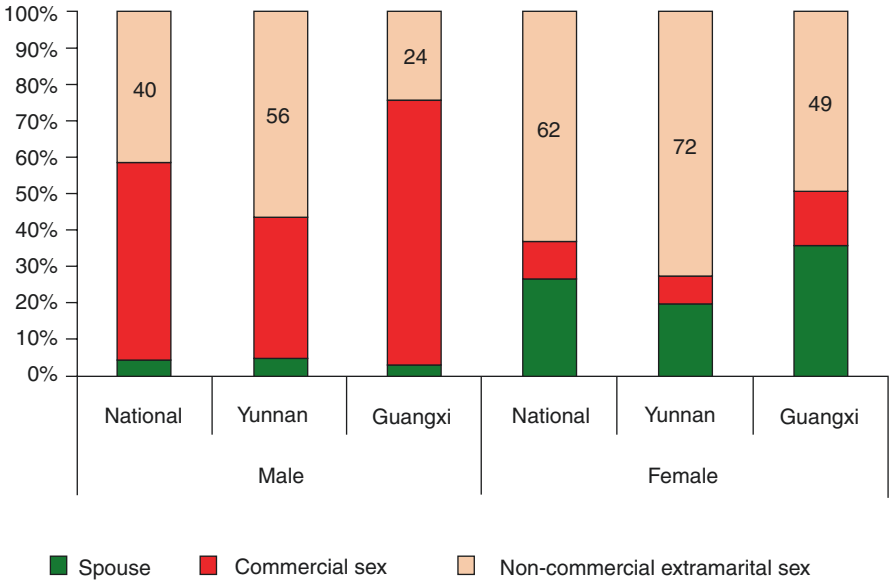

Fig. 1.7 Graph showing the proportion of newly diagnosed male and female PLWH in 2016 who attributed their infection to their spouse, commercial sex partner, or non-commercial extramarital sex partner at the national level, as well as in Yunnan and Guangxi separately (National Center for AIDS/STD Control and Prevention 2016)

transmission rate could occur in contacts between FSW with HIV and their uninfected male clients (even accounting for the fact that many of these infections would have been acquired in years past). Nevertheless, in 2015, 28,000 men newly identified as having HIV said they had been infected by a sex worker. It is actually much more likely that a large proportion of these men were in fact infected as part of the growing homosexually driven epidemic and were deliberately misreporting their transmission route because commercial sex with a woman is less stigmatized than sex in any context between men.

While men who say they acquired HIV from a woman continue to report buying sex as their greatest risk, women now report casual sex as their greatest risk factor for HIV infection, at least at a national level. However, national figures can conceal geographical differences (see, e.g., Fig. 1.7) that underscore the importance of tailoring prevention approaches, aimed at reducing heterosexual transmission rates, to the features of the local community.

The demographics of PLWH who reported heterosexual contact as their route of infection has also been changing over time. For example, a significant rise in new HIV diagnoses among older men has been observed. In 2016, 17% of newly identified HIV cases among men were in the over-60 age group, compared with just 4% in 2005 (National Center for AIDS/STD Control and Prevention 2016). This may be due, at least in part, to increased availability of HIV testing in routine healthcare